Cervical Cancer

A Medical Dictionary, Bibliography,
and Annotated Research Guide to
Internet References

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and Philip M. Parker, Ph.D., Editors

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FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with cervical cancer is indexed in search engines, such as **www.google.com** or others, a non-systematic approach to Internet research can be not only time consuming, but also incomplete. This book was created for medical professionals, students, and members of the general public who want to know as much as possible about cervical cancer, using the most advanced research tools available and spending the least amount of time doing so.

In addition to offering a structured and comprehensive bibliography, the pages that follow will tell you where and how to find reliable information covering virtually all topics related to cervical cancer, from the essentials to the most advanced areas of research. Public, academic, government, and peer-reviewed research studies are emphasized. Various abstracts are reproduced to give you some of the latest official information available to date on cervical cancer. Abundant guidance is given on how to obtain free-of-charge primary research results via the Internet. **While this book focuses on the field of medicine, when some sources provide access to non-medical information relating to cervical cancer, these are noted in the text.**

E-book and electronic versions of this book are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). If you are using the hard copy version of this book, you can access a cited Web site by typing the provided Web address directly into your Internet browser. You may find it useful to refer to synonyms or related terms when accessing these Internet databases. **NOTE:** At the time of publication, the Web addresses were functional. However, some links may fail due to URL address changes, which is a common occurrence on the Internet.

For readers unfamiliar with the Internet, detailed instructions are offered on how to access electronic resources. For readers unfamiliar with medical terminology, a comprehensive glossary is provided. For readers without access to Internet resources, a directory of medical libraries, that have or can locate references cited here, is given. We hope these resources will prove useful to the widest possible audience seeking information on cervical cancer.

The Editors

[1] From the NIH, National Cancer Institute (NCI): **http://www.cancer.gov/cancerinfo/ten-things-to-know**.

CHAPTER 1. STUDIES ON CERVICAL CANCER

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on cervical cancer.

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and cervical cancer, you will need to use the advanced search options. First, go to **http://chid.nih.gov/index.html**. From there, select the "Detailed Search" option (or go directly to that page with the following hyperlink: **http://chid.nih.gov/detail/detail.html**). The trick in extracting studies is found in the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Journal Article." At the top of the search form, select the number of records you would like to see (we recommend 100) and check the box to display "whole records." We recommend that you type "cervical cancer" (or synonyms) into the "For these words:" box. Consider using the option "anywhere in record" to make your search as broad as possible. If you want to limit the search to only a particular field, such as the title of the journal, then select this option in the "Search in these fields" drop box. The following is what you can expect from this type of search:

- **HIV - Positive Women and Their Care**

  Source: Positively Aware; Jan./Feb. 1996.

  Contact: Test Positive Aware Network, 5537 N Broadway, Chicago, IL, 60640, (773) 989-9400, http://www.tpan.com.

  Summary: This article considers the incidence of HIV among women and highlights the importance of regular gynecological examinations to detect HIV and female-specific conditions. The author explains that, following an initial examination, an HIV-positive woman should undergo the same tests as a man to determine where she stands in the course of HIV progression. Complications and treatment are addressed, including vaginal candidiasis, human papilloma virus, **cervical cancer,** and menstrual problems.

All women are advised to have regular Pap smears, pelvic exams, and a general gynecological assessment.

- **Gynecology for the Gastroenterologist: The Woman in Her Forties and Beyond**

  Source: Practical Gastroenterology. 20(5): 29-30, 32, 34-36. May 1996.

  Contact: Available from Shugar Publishing, Inc. 99B Main Street, Westhampton Beach, NY 11978. (631) 288-4404. Fax (631) 288-4435. E-Mail: info@practicalgastro.com.

  Summary: This article, one in a series on gastrointestinal (GI) diseases of the elderly, considers gynecology for the gastroenterologist. The authors review a number of gynecologic conditions that may produce signs or symptoms suggesting GI disease. Indeed, they stress that distinguishing GI disease from gynecologic pathology may be difficult. A thorough understanding of pelvic anatomy, a careful history, and strong clinical suspicion will clarify the nature of the complaints. If doubt persists, expert consultation and a multidisciplinary approach are recommended. Benign conditions discussed include disorders of pelvic support, leiomyomata (uterine fibroids), endometriosis, and infections. Malignant conditions include ovarian cancer and uterine or **cervical cancer.** The article concludes with a discussion of anal incontinence and rectovaginal fistulas. 3 references. (AA-M).

- **Opportunistic Infections**

  Source: The News; Vol. IX, No. 1, Feb.-Mar. 1993.

  Contact: Atlanta Gay and Lesbian Center, 159 Ralph McGill Blvd Ste 600, Atlanta, GA, 30308, (404) 523-7500, http://www.aglc.org.

  Summary: This journal article lists opportunistic infections alphabetically and references them by common names, causes, symptoms, diagnoses, and treatments. It includes candidiasis, **cervical cancer,** cytomegalovirus, herpes simplex, HIV wasting syndrome, Kaposi's sarcoma, lymphoma, pneumonia, salmonella, toxoplasmosis, and tuberculosis. It also indexes coccidiomycosis, cryptococcosis, cryptosporidiosis, HIV dementia, Microsporidosis, Maycobacterium avium complex (MAC), and progressive multifocal leukoencephalopathy.

- **Special Edition Women's Treatment Issues - Special Issue**

  Source: Treatment Issues; Vol. 6, No. 7.

  Contact: Gay Mens Health Crisis, 119 W 24th St Tisch Bldg, New York, NY, 10011-1995, (212) 367-1205, http://www.gmhc.org.

  Summary: This journal special edition describes HIV disease in women and focuses specifically on the different manifestations of HIV and AIDS in the female. It addresses the barriers to care for women; discusses women, sex hormones, and HIV-infection; and includes information on fertility, menstruation, and birth control in HIV-positive women. The edition features articles on sexually transmitted diseases (STDs), with special emphasis on the stages, symptoms, and treatment of syphilis. It explains pelvic inflammatory disease (PID), concentrating on symptoms and treatment, and examines the relationship between human papillomavirus (HPV) and **cervical cancer.**

Federally Funded Research on Cervical Cancer

The U.S. Government supports a variety of research studies relating to cervical cancer. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.[2] CRISP (Computerized Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other institutions.

Search the CRISP Web site at **http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen**. You will have the option to perform targeted searches by various criteria, including geography, date, and topics related to cervical cancer.

For most of the studies, the agencies reporting into CRISP provide summaries or abstracts. As opposed to clinical trial research using patients, many federally funded studies use animals or simulated models to explore cervical cancer. The following is typical of the type of information found when searching the CRISP database for cervical cancer:

- **Project Title: 2ND INTERNATIONAL CERVICAL CANCER CONFERENCE**

  Principal Investigator & Institution: Follen, Michele; Professor; Biomedical Engineering Center; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2003

  Summary: "The 2nd International Conference on Cervical Cancer" is an interdisciplinary conference focused on innovative research in **cervical cancer.** The conference is expected to attract approximately 300 participants from around the world. The 1st International Conference on Cervical Cancer" was held one year ago, organized by the same committee, and was considered immensely successful by the participants. "The 2nd International Conference on Cervical Cancer" will touch upon subjects not addressed in the first conference including: decision science, behavioral science, optical imaging, diagnostic imaging, diagnostic imaging, chemoprevention trials, innovative advances in the biology of **cervical cancer,** the role of nursing in **cervical cancer** prevention and treatment, and grant writing. Progress in this area will rely on the synthesis of knowledge from many fields including clinical medicine, epidemiology, fundamental optical science, biomedical engineering, medical imaging and device technology. This conference is a vehicle to facilitate the interdisciplinary interaction necessary to see ideas brought to fruition as research proposals. The conference is designed to encourage discussion and interaction, not only in the formal scientific sessions, but throughout the day and evening. The conference will be held at the University of Texas M.D. Anderson Cancer Center, Houston, Texas. This venue will provide a rich atmosphere for the conference and makes use of existing resources so that funds for the conference can be used to support travel for participants and publishing results in a special edition of "Cancer." An "all inclusive" fee covers registration, accommodation and meals. Formal sessions will be held from Thursday, April 11, in the afternoon through Sunday April 14, in the morning. There is time at the conclusion of each session to summarize findings and make research recommendations. The research recommendations, published in a special edition of the journal "Cancer", will disseminated the findings of the conference to a broad audience. There will be nine formal sessions. Each of these will be lead by an

[2] Healthcare projects are funded by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDCP), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH).

outstanding scientist, engineer, radiologist, or clinician. These session chairs have already invited speakers and the majority of speakers have confirmed their participation in the meeting. Each invited speaker will provide a review of their topic before presenting the most recent results from their group. Approximately one third of each session will be devoted to discussion. The session leaders have been selected partially on their ability to moderate a productivity interchange that will allow the exploration of topics from the perspective of both the basic scientist and the clinician. Each session chair and speaker has been chosen based on his/her publications, funding and national reputation.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: A NOVEL DIAGNOSTIC FOR ONCOGENIC HPV**

  Principal Investigator & Institution: Lu, Peter S.; Arbor Vita Corporation 772 Lucerne Dr Sunnyvale, Ca 940853844

  Timing: Fiscal Year 2003; Project Start 22-JUL-2003; Project End 31-DEC-2003

  Summary: (provided by applicant): Arbor Vita proposes to detect and quantify oncogenic E6 proteins as a diagnostic test for Human Papilloma Virus (HPV) infection and **cervical cancer.** Oncogenic variants of HPVs have been correlated with **cervical cancer** at a frequency of 99.7%. Accumulated data unequivocally demonstrate that oncogenic E6 proteins are crucial for initiation and maintenance of cervical cell transformation and cancer progression, potentially representing a superior diagnostic marker. E6 proteins have not been successfully analyzed by standard methods. Research by Arbor Vita and others has shown that oncogenic E6 variants specifically bind to cellular PDZ domain proteins. Arbor Vita proposes to exploit this property as the basis of a simple test for the detection of oncogenic E6 variants. Specifically, Arbor Vita proposes to develop a PDZ domain-based oncogenic E6 detector that, as part of an ELISA-based test, selectively detects E6 oncoproteins: first, in vitro; secondly, in transfected cells; and thirdly, in HPV infected cancer cell lines. To accomplish these aims, Arbor Vita will utilize its proprietary in vitro assay. Tasks will include cloning, protein expression and purification, design of a ELISA based test system, and optimization of cell lysis conditions.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: A-007: IMMUNE MODULATION OF HPV - CERVICAL CANCER**

  Principal Investigator & Institution: Morgan, Lee Roy R.; Chief Executive Officer; Dekk-Tec, Inc. 4200 Canal St, Ste a New Orleans, La 70119

  Timing: Fiscal Year 2001; Project Start 01-APR-2001; Project End 31-MAR-2002

  Summary: (Applicant's Description) 4,4'-Dihydroxybenzophenone-2,4-dinitrophenylhydrazone (A-007) has recently completed a Phase I clinical trial in advanced cancer with minimal toxicity and objective responses noted. Preliminary observations suggest that A-007 is able to stimulate lymphocyte mobilization when applied topically to normal skin, as well as, to metastatic cutaneous lesions. The specific objectives of this Phase I study will be to document A-007's ability to stimulate lymphocyte migration/activation in cancers associated with immunodeficiency related infections. A-007's functional groups will be modified to maximize pharmacophore activities. All new hydrazones, as well as, A-007 will be assayed in vitro/in vivo for lymphocyte stimulation properties. These studies will be expanded for use as a stimulant of local cervical immunity in a simian immunodeficiency virus (SIV) monkey model and as local treatment for young females with HPV-associated cervical cancers.

PROPOSED COMMERCIAL APPLICATION: 4,4'-Dihydroxybenzophenone-2, 4-dinitrophenylhydrazone (A-007) is showing lymphocyte stimulation and anticancer activities in clinical trials. A new agent with anticancer/immune modulation activity in HPV associated **cervical cancer** would have wide use as a single agent or in combinations therapy.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: AIDS-ONCOLOGY CLINICAL SCIENTIST DEVELOPMENT PROGRAM**

  Principal Investigator & Institution: Levine, Alexandra M.; Medical Director; Medicine; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

  Timing: Fiscal Year 2001; Project Start 11-AUG-1998; Project End 31-JUL-2004

  Summary: (Applicant's Description) As survival has increased in patients with HIV infection, it is apparent that greater numbers of individuals are living long enough to eventually develop malignant disease. Further, with maturation of the AIDS epidemic, it appears that the spectrum of HIV associated diseases has expanded, with malignant diseases becoming more prominent as the cause of death in infected individuals. Aside from the current AIDS-defining malignancies, including Kaposi's sarcoma, lymphoma, and **cervical cancer,** additional types of cancers are now being reported in HIV infected individuals, with significantly increased standardized incidence ratios (SIRs) of anal cancer, Hodgkin's disease, lung cancer, multiple myeloma and others. In terms of public health policy, it is apparent from these data that the appropriate health care of our nation will require specific training of oncologist in the area of HIV disease. At the present time, there is no formalized mechanism to provide such cross-training, nor is there a mechanism to pay for such training. The goals of this Training Grant will be to train such individuals, who will then be prepared to treat HIV infected patients with malignant disease; to conduct research in this area; and, in time, to teach others these same skills. The specific aims of the proposal are: (1) To provide comprehensive, multidisciplinary clinical training in HIV disease to individuals who have recently completed one or more years of formal fellowship training in Hematology'/Oncology; (2) To provide a didactic core curriculum, which will give a broad understanding of the advances in HIV disease, per se, as well as the opportunistic cancers, infections, and other illnesses which ensue; (3) To provide a didactic core curriculum, as well as practical, day-to-day training in the area of clinical research methods, to allow development of future clinical researchers in the area of AIDS-related malignancy; (4) To provide didactic training in the area of basic scientific research methods, to allow development of future clinical researchers who will understand the principles of translational research in the area of AIDS-malignancy; and (5) To provide close mentoring support from both clinical and basic scientific mentors, in order to assure that the candidates will engage in a specific translational research project related to the field of HIV-malignancies. We will offer a two-year Fellowship program. The first year will be spent in clinical work, with assignment of a specific clinical mentor to each Trainee. The year will consist of attendance at weekly general HIV/AIDS clinic; weekly AIDS/Lymphoma clinic; weekly AIDS/KS clinic; one month on in-patient HIV/AIDS ward; three months on inpatient AIDS malignancy ward; and attendance at didactic lectures and symposia. The second year will emphasize training in clinical and translational research in the area of AIDS-related malignancy, with assignment of specific scientific mentors, and development of research projects, as well as attendance at didactic lectures and symposia in the area of research methods and biologic principles.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ANIMAL MODEL OF PROLIFERATIVE VERRUCOUS LEUKOPLAKIA**

  Principal Investigator & Institution: Murrah, Valerie A.; Diagnostic Scis/Gen Dentistry; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, Nc 27599

  Timing: Fiscal Year 2001; Project Start 01-AUG-2001; Project End 31-JUL-2003

  Summary: (provided by applicant) Oral squamous cell carcinoma is a significant global health problem, comprising one of the ten most common cancers, worldwide. Over the past decade, there has been increased interest in viruses as etiologic agents for cancers of all types. Human papillomavirus (HPV) is the leading candidate for a role as a viral co-factor in oral cancer. In women, estrogen has been linked to multiple malignancies, including breast, cervical and uterine cancers, but, heretofore, estrogen has not been studied as a possible factor in oral cancer, despite the fact that well-recognized hyperplastic lesions of the oral cavity occur as a result of hormonal changes during pregnancy and puberty. We hypothesize that HPV and estrogen interact in the oral cavity to cause proliferative verrucous leukoplakia, an oral condition, seen predominantly in women, which is associated with a high prevalence of HPV infection and which ultimately eventuates in oral cancer. Interactions between HPV and estrogen in the pathogenesis of **cervical cancer** have been studied in a specific transgenic mouse model (K14-HPV16), in which a portion of the HPV16 genome is targeted to the progenitor compartment of the epithelium; by means of the keratin 14 promoter. Preliminary data on the oral cavity in this model strongly support its value for studies of the interactions between these two agents at this site as well. To that end, our specific aims are: 1) to determine whether estrogen can promote transformation of the oral epithelium to a premalignant or malignant phenotype in the K14-HPV16 transgenic mouse model, 2) to perform a prospective analysis of changes in biomarkers associated with proliferation and transformation in the oral epithelium of K14-HPV16 mice that have been exposed to estrogen in a longitudinal manner, and 3) to analyze changes in biomarkers in human specimens of proliferative verrucous leukoplakia to determine correlations with the mouse model. The proposed study is unique in that it addresses the question of estrogen and viral interaction as a possible etiology of oral cancer, an important issue which has not ever been investigated. We feel strongly that this knowledge will ultimately result in appropriate timing of specific interventional therapies and preventive strategies for proliferative verrucous leukoplakia and oral cancer in the future, and will address an oral health problem that is a significant women's health issue.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: BREAST AND CERVICAL CANCER SCREENING IN KOREAN-AMERICANS**

  Principal Investigator & Institution: Choi, Eunice E.; None; University of San Diego 5998 Alcala Pk San Diego, Ca 92110

  Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 31-AUG-2004

  Summary: The long-term objective of this program of research is to develop, implement, and evaluate a culturally tailored intervention to increase the rates of obtaining mammogram, CBE, and Pap smear screens and practicing BSE in Korean American (KA) women. Dr. Choi's goals during this proposed training are to: 1) Gain advanced

skills in developing culturally valid instruments; 2) Enhance her understanding of health promotion and disease prevention issues; 3) Generate knowledge related to KA women's utilization of the cancer screening tests; and 4) Generate knowledge related to health care providers' recommendations of the screening tests for KA women. The theoretical framework of this proposed project is based on Anderson's Behavioral Model supplemented with the Cultural Explanatory Model. The specific aims of this proposed study of KA immigrant women older than 40 years of age and their utilization of these tests are: 1) To develop culturally appropriate instruments and test them; 2) To test the hypothesis that KA women's predisposing variables; enabling variables, and need variables will be related to their utilization of the screening tests; and 3) To identify culturally specific and demographic variables that influence physicians' recommendation or practice of the screening tests. To achieve the specific aims, this proposed project will be conducted in 5 phases: 1) individual interviews with 30 KA women; 2) six focus groups with KA women; 3) modification of existing instruments and/or development of new instruments based on the results of individual interviews and focus groups; 4) individual interviews with 10 KA and 10 Caucasian American physicians; and 5) a survey with a community based random sample of 350 KA women in order to pilot test and to establish psychometric properties of the instruments. This proposed project is innovative since no published project has approached cancer screening services from the perspectives of both recipients as well as their providers to provide a comprehensive understanding of the reasons KA women have lower utilization rates of these tests. This project is significant in generating culturally accurate information and instruments to be used in both epidemiological research and culturally tailored intervention research for cancer screening test utilization in KA women.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CANCER AWARENESS NETWORK FOR IMMIGRANT MINORITY POPULATI**

  Principal Investigator & Institution: Gany, Francesca; Assistant Professor of Clinical Medicine; Medicine; New York University School of Medicine 550 1St Ave New York, Ny 10016

  Timing: Fiscal Year 2001; Project Start 04-APR-2000; Project End 31-MAR-2005

  Summary: We propose the establishment of a Cancer Awareness Network for Immigrant Minority Populations (CANIMP) in the NY metropolitan area to increase cancer control activities and access to clinical trials in NY's foreign-born minority community. This will be achieved through the linkage of two major initiatives at NYU School of Medicine: (a) the New York Task Force on Immigrant Health (NYTFIH), Division of Primary Care, and (b) the NCI- designated Kaplan Comprehensive Cancer Center (KCCC). Community based organizations representing five immigrant groups (Haitian, Latino, ES-Caribbean, Korean, and Chinese) will be partners in this project. This diverse group will allow to conduct unique comparative research and coordinated outreach. Other network partners will include cancer prevention and screening programs such as the Breast Health Partnership and ACS Chinese Unit, NCI- CIS at Memorial Sloan Kettering, DHHS Office of Minority Health and NYC community health clinics. In Phase I interviews, focus groups, and roundtables on lung, prostate, breast, and **cervical cancer** will be conducted in five immigrant groups. In Phase II junior scientists will be partnered with established KCCC researchers to develop pilot cancer research projects. These projects will develop into peer- reviewed competitive proposals in Phase III. Bilingual CANIMP staff will provide cancer community education, ethnic provider education on clinical trials, review written materials, provide interpreter

services, and staff a multilingual information line. The project will be evaluated through an annual patient survey, a provider survey in years 3 and 5, and through diverse process and outcome indicators such as percentage of minorities recruited into clinical trials and number of minority junior scientists developing pilot projects.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CANCER CHEMOPREVENTION--ROLE OF INFECTION/IMMUNITY**

  Principal Investigator & Institution: Loprinzi, Charles L.; Professor; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

  Timing: Fiscal Year 2001; Project Start 01-JUN-1999; Project End 31-MAR-2004

  Summary: Over the past decade, a substantial body of data has accumulated which implicates the human papillomaviruses (HPVs) in epithelial cancers, especially **cervical cancer.** More recently, a new family HPV has been identified in skin cancers that are related to those found originally in patients with heritable skin cancer prone condition, epidermodysplasia verruciformis. With the advent of new chemoprevention strategies directed against each of these cancer types, it appears prudent to develop novel secondary endpoint biomarkers (SEBs). Accordingly, a central Theme of this project is to develop HPV-related SEBs in the context of two novel chemoprevention strategies, one of which is expressly directed against HPV infection. Two Phase II chemoprevention clinical trials are planned at the Mayo Clinic and in the North Central Cancer Treatment Group (NCCTG) member institutions, with support for protocol development, data management, and statistical analysis deriving primarily from NCCTG CCOP grants (i.e. research base and individual institution grants). The first is a randomized pilot evaluation of topical imiquimod, and immunomodulatory agent which has proven to be safe and effective for the treatment of genital warts. This trial will be conducted on patients with recurrent and/or high-grade cervical intraepithelial neoplasia (CIN). For skin cancers. This trial will attempt to reproduce and further substantiate a previous randomized trial in the which a treatment benefit was demonstrated. Broad-range PCR techniques will be used to monitor the type-specific persistence of HPV in cervical specimens after imiquimod therapy. Similar techniques will be used to characterize the potential role of HPV in skin cancers, strategies will also be developed to determine if HPV - specific immune responses can be used as SEBs in CIN related gene expression and AP-1 expression/activity will be developed for the skin cancer chemoprevention project.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CANCER SCREENING, MANAGED CARE, AND THE UNDERSERVED**

  Principal Investigator & Institution: Pasick, Rena J.; Associate Director; Northern California Cancer Center 32960 Alvarado Niles Rd, Ste 600 Union City, Ca 94587

  Timing: Fiscal Year 2002; Project Start 30-SEP-1992; Project End 30-NOV-2003

  Summary: Low-income women are at high risk for developing **cervical cancer** due not only to the higher prevalence of risk factors and lack of access to screening, but also because of barriers to timely follow-up when screened and found to have an abnormality. Lack of follow-up, therefore, contributes to the racial and ethnic health outcome disparities that exist for **cervical cancer.** While other interventions have shown some success at improving Pap smear follow-up rates, there is no existing randomized intervention trial that has demonstrated such high rates of improvement in follow-up as the Pathfinders study that addresses follow-up barriers in a very high-risk population of

ethnically diverse, low-income, inner city women. The intervention consisted of computer-assisted tracking, education, counseling in consumer skills and ways of coping, transportation vouchers, and referrals for suspected mental health, alcohol/drug abuse, and domestic violence. When analyzed by intention to treat, of 348 women who were randomized at the time of the institutional receipt of the abnormal result, twice as many women in the intervention group were confirmed to have a follow-up test within 6 mos. of their abnormal Pap smear than in the control group, 70% versus 36% ($p<0.01$). By using an expanded tracking protocol, we were able to locate and to deliver the intervention to 128/178 women in the intervention group. Of those who received the intervention, 83% had a documented follow-up test with 6 mos. versus 36% in the intervention group who did not receive the intervention ($p<0.01$). Overall, we were unable to contact 18 (10%) women, 16 (9%) moved, and 11 (6%) refused the counseling intervention. The average time-cost of tracking and outreach counseling per woman was 109 min. With this project, we have demonstrated that low follow-up rates can be substantially improved by the implementation of a more personal and culturally tailored approach, coupled with utilization of state-of-the-art computer assistance. This supplement addresses the need for dissemination of cost-effective interventions that improve Pap smear follow-up in high-risk populations. We propose a strategy for dissemination and maintenance of the intervention on a local-scale. If successful, we will adapt the intervention, based on what we have learned, for more widespread dissemination.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CANCER SURVEILLANCE IN HMO ADMINISTRATIVE DATA**

  Principal Investigator & Institution: Wei, Feifei; Health Partners Research Foundation 8100 34Th Ave S Minneapolis, Mn 55425

  Timing: Fiscal Year 2001; Project Start 01-APR-2001; Project End 31-MAR-2004

  Summary: (provided by applicant): The purpose of this study is to identify the existence and extent of biases associated with HMO full electronic and claims-type encounter data when they are used to characterize patterns of care and to analyze the relationship between treatment and outcomes of breast and cervical cancers. Electronic data assessed will include inpatient and outpatient visits, pharmacy, cancer registry, pathology, radiology, laboratory, and electronic physician notes. This project is a joint venture between four not-for-profit HMOs: Fallon/Meyers Primary Care Institute, Kaiser Permanente/Northern California, Health Partners Research Foundation and Henry Ford Health System. A patient who was diagnosed for breast cancer between January 1, 1996 and December 31, 1997 or for **cervical cancer** between January 1, 1996 and December 31, 2000 will be included in the study. A study central database will be established to contain all electronic and claims-type encounter data on medical care of these patients. Medical record information will be abstracted for a random sample of 925 breast cancer and 995 **cervical cancer** patients. The study will compare information in the electronic data sources to information abstracted from medical records, and assess differences in completeness and accuracy of diagnostic, treatment, and outcomes by patient characteristics, among HMOs, and by source of data. Using data abstracted from medical record and electronic data, we will characterize the patterns of care and assess the relationship between treatment and outcomes among women of any age with **cervical cancer** and women age 55 or older with breast cancer. This study will provide important information about the feasibility of using computerized claims data as well as other computerized resources for the study of cancer treatment and outcomes. The primary strength of the study is that it uses routinely and efficiently collected

population based electronic data to identify cancer patients, treatments and outcomes. If these databases are shown to be valid, they provide promising resources for cancer studies, with extensive information on treatment, follow-up and outcome far exceeding those available from traditional cancer registries.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CANCER VACCINES TO HPV-16 ASSOCIATED TUMOR**

  Principal Investigator & Institution: Ertl, Hildegund Cj.; Professor; Wistar Institute Philadelphia, Pa 191044268

  Timing: Fiscal Year 2001; Project Start 01-APR-1998; Project End 31-JAN-2003

  Summary: (Applicant's Abstract) Vaccination is the most effective medical intervention to reduce human morbidity and mortality due to infectious diseases. The development of efficacious vaccines for treatment or prevention of cancer has been less successful, which is in part due to a lack of well-defined tumor-specific antigens. Most cervical cancers, the second most common cause of malignancies in women worldwide, are associated with genital infections by human papilloma viruses (HPV) strains, 16 or 18 that express two oncoproteins, i.e., E6 and E7 which might provide highly suitable target antigens for immunological intervention. The aim of this application is to test three different vaccine prototypes, i.e., DNA vaccines, vaccinia virus recombinants and E1-deleted replication defective adenovirus recombinants expressing the E6 or E7 protein of human papilloma virus (HPV)-16, in a mouse model for their efficacy in limiting the spread of E6 and E7 expressing tumors. The applicant's long-term goal is to develop a vaccine for treatment of women with HPV-16 associated **cervical cancer.** She has developed a mouse tumor model to study vaccines to E6 and E7 of HPV-16. The applicant also generated a number of vaccines, i.e., DNA vaccines, recombinant vaccinia and E1-deleted adenoviral vaccines, expressing the oncoproteins of HPV-16. All of these types of expression systems, that have distinctive advantages and disadvantages as vaccine carriers, were shown to induce partial protection against a low dose tumor challenge. The applicant's hypothesis is that a combination of different types of vaccines given as prime-boost regimens either alone or with a cytokine adjuvant might significantly improve the efficacy of vaccination in providing long-term protective immunity against HPV-16 E6 and E7 transformed tumors. To test this hypothesis she will initially compare the three different types of vaccines given individually analyzing basic parameters such as the kinetics of the response, dose-response curves, different routes of immunization, effect of pre-existing immunity to the vaccine carrier, and induction of different types of immune responses. The applicant will then test the effect of different vaccine combinations including interleukin(IL)-12 as an adjuvant on solid and metastatic tumors both in a prophylactic immunization model as well as in treatment of already established tumors. In case the applicant's hypothesis is correct, data gathered within the realm of this application will serve as the basis for a clinical Phase I trial.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CAP-PAP TEST FOR SPECIMENS COLLECTED IN SOLUTION**

  Principal Investigator & Institution: Markovic, Nenad; Bioscicon, Inc. 259 Congressional Ln, Ste 602 Rockville, Md 20852

  Timing: Fiscal Year 2002; Project Start 15-APR-2002; Project End 31-MAR-2003

  Summary: The CAP-PAP test is a single-slide, double-staining, in vitro method for labeling dysplastic cervical cells on Pap smears (USPTO#6, 143, 512). A recently

completed clinical laboratory trial (1R43CA86767-01) has shown that this test is easily applicable in a routine cytopathology laboratory for **cervical cancer** screening. The safety of the new method was equal, and its efficacy and prognostic value was superior to the control Pap test. We propose to study how the CAP-PAP test could be applied on thin and monolayers of cervical cells collected with any of the new liquid-based cervical specimen collection technologies. It is CAP-PAP test will help users of these technologies to improve the accuracy of cancer detection of the original CAP-PAP test procedure, will e considered for patient application. Recently, the business reports signaled that the FDA approved liquid- based specimen collection technologies have penetrated the Pap test market in the US up to 30%. This means that a modified CAP-PAP test could face a market of 10-30 million test per year. PROPOSED COMMERCIAL APPLICATIONS: If approved as an in vitro diagnostic medical device, this test will face a market of 10-30 million Pap tests per year (specimen collected using any of the liquid-based specimen collection technologies).

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CENTER FOR PSYCHO-ONCOLOGY RESEARCH**

  Principal Investigator & Institution: Antoni, Michael H.; Psychology; University of Miami Coral Gables University Sta Coral Gables, Fl 33124

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2004

  Summary: This application is for a 5-year Center for Psycho-Oncology Research (CPOR) grant to conduct behavioral, psychological, social, and biomedical research on the interrelationships among cognition, emotion, biological processes, and physical health in patients with different forms of cancer including breast cancer, prostate cancer and AIDS-related cervical neoplasia. The Center will systematically evaluate the efficacy group-based Cognitive Behavioral Stress Management (CBSM) intervention in Projects 1, 2 and 3., and a pharmacological hormonal treatment in Project 4, for improving quality of life and physical health in patients with different types of cancer or carcinogenic processes associated with reproductive health or hormonal functioning. These include women with breast cancer, older men with prostate cancer, and women at high risk for **cervical cancer** due to co-infection with Human Immunodeficiency Virus (HIV+) AND Human Papillomavirus (HPV+). Our prior work has shown that CBSM intervention can improve mood, change cognitions and build coping resources; that it modulates the output of sympathetic nervous system (SNS), Hypothalamic Pituitary Adrenal (HPA), and Hypothalamic Pituitary Gonadal (HPG) hormones; and that it helps normalize immunologic status in different populations. The Center will directly address these issues through four (4) randomized clinical trials as follows. Project 1 will (a) evaluate the effects of CBSM intervention on psychological distress, quality of life and biopsy- determined level of cervical cellular atypia; and (b) examine the putative psycho-biological mediators (psychosocial, endocrine, and immunologic changes) on intervention effects observed. Project 2 will (a) investigate the effects of CBSM intervention and quality of life and disease status (change in CA15-3) antigen levels) in women with early-mid stage breast, and (b) examine the putative psycho-biological mediators of intervention effects observed. Project 3 will (a) investigate the effects of CBSM in combination with Viagra (sildenafil citrate) on quality of life and physical health in older men with prostate cancer, and (b) examine the putative psycho-biological mediators of intervention effects observed. Project 4 will (a) evaluate the effects of estrogen therapy (chronic low-dose oral 17- beta estradiotherapy) on mood and quality of life, and physical health in patients with metastatic prostate cancer, and (b) examine the putative psycho-biological mediators of intervention effects observed. The Center

will also support and conduct pilot studies of interventions in men and women with other cancers, and will also develop and test other forms of intervention as well as Spanish translations of CBSM for Spanish- speaking Breast and Prostate cancer patients.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CERVICAL CANCER MULTI-MEDIA TOOLBOX FOR VIETNAMESE WOMEN**

  Principal Investigator & Institution: Thorp, Richard L.; Multi-Media Systems, Inc. Box 99 Church Hill, Md 21623

  Timing: Fiscal Year 2001; Project Start 01-FEB-2001; Project End 31-JUL-2001

  Summary: Multi-Media Systems will develop and evaluate a mediated TOOLBOX of medical intervention/education materials to inform Vietnamese-American women of the importance of regular screening for early detection of **cervical cancer** (CV). This medically underserved minority suffers from an unequal burden of CV, with 5 to 7 times higher incidence than other U.S. populations. Due to resulting late stage detection, morbidity/mortality rates are needlessly high. Inhibiting factors include language, lack of knowledge, cultural beliefs, attitudes, fears and distrust of scientific/medical organizations. Outreach organizations and health departments lack resources to develop comprehensive effective, professionally-produced and tested intervention materials. Phase I formative research, employing structured interviews, questionnaires, and focus-groups will determine the best intervention strategy(ies) and the most effective way(s) to Aframe@ the message. Three Vietnamese language radio spots, three video vignettes, and three newspaper ads, each using different approaches, will be produced and reviewed by separate focus groups of Vietnamese women and outreach professionals. In Phase II, the final TOOL BOX materials will be developed, produced and formally evaluated for effectiveness through a multiple site trial. A Subject-Matter-Expert Board will assure content accuracy. The materials will be available to outreach organizations on a subscription basis, through an innovative website featuring publishing-on-demand, down-loadable-digital-video and outreach planning/tracking/reporting system.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CERVICAL CANCER TREATMENT THROUGH HPV VIRUSLIKE PARTICLE**

  Principal Investigator & Institution: Kast, W Martin.; Professor; University of Chicago 5801 S Ellis Ave Chicago, Il 60637

  Timing: Fiscal Year 2003; Project Start 25-JUN-2003; Project End 31-MAR-2008

  Summary: In **cervical cancer,** the third most common cancer among women worldwide, human papillomaviruses (HPV) play a causative role. Most preventive and therapeutic vaccine developments against HPV are concentrated on HPV16 since it is linked to about 50% of **cervical cancer.** HPV18 is second in rank with respect to frequency worldwide at 14% of cases but predominates in Asian women as well as in cervical adeno and adenosquamous carcinomas which are the most aggressive type of cervical carcinomas and therefore also warrants research efforts. HPV virus like particles (VLP) consisting of the capsid protein L1 have emerged as the leading preventive vaccine strategy for HPV associated lesions. However, they are unlikely to have effects in the millions of women that are already infected or have developed **cervical cancer.** Immunization with chimeric HPV VLP expressing the early HPV gene products E6/E7 has therapeutic potential since these gene products are maintained even at late stages of **cervical cancer** but the induction of neutralizing antibodies against the capsid protein

limits their therapeutic capacity. They are, however, powerful tools for induction of T cell responses against early HPV gene product and antigenic peptide mapping. Based on these characteristics we propose to explore the following aims: 1) The use of HPV VLP for inducing human T cell responses to human endogenously presented antigenic epitopes of HPV18 E6/E7 proteins and for generating HPV18 specific T cell clones. 2) in order to avoid the effects of neutralizing antibodies, transferring HPV16 or 18 E6 or E7 specific T cell reactivity induced by chimeric HPV VLP to alternate human effector cells, and 3) the same as aim 2 but now transferring their reactivity to alternate mouse effector cells, To achieve these aims the following methods will be used: 1) in vitro immunization of human peripheral blood T cells with autologous DC loaded with HPV VLP expressing HPV18 E6/E7 protein. 2) identify and clone the HPV16 or 18 specific TCR genes obtained from the chimeric HPV VLP induced T cells and transferring them to alternate human T cells, and 3) the same as in aim 2 but transferring the TCRs to mouse T cells and testing their antitumor activity in vivo. These combined aims will increase the potential of chimeric HPV VLP for treatment of **cervical cancer** which is our long term objective.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CERVICAL CANCER--PREDICTIVE ASSAY BY MR IMAGING**

  Principal Investigator & Institution: Mayr, Nina A.; Radiological Sciences; University of Oklahoma Hlth Sciences Ctr Health Sciences Center Oklahoma City, Ok 73126

  Timing: Fiscal Year 2001; Project Start 21-SEP-1998; Project End 31-JUL-2003

  Summary: Radiotherapy is the principal treatment modality for advanced **cervical cancer,** but local control is frequently not achieved. The failure rate may be reduced by treating high-risk patients with more intense therapies including higher doses of radiation, chemotherapy, and/or surgery. However, there is no well-established predictor to identify patients whose high risk for failure justified the increased morbidity of more aggressive therapy. The investigators seek to identify those at high risk early, such that more aggressive treatment can be rendered that may improve outcome. Quantitative tumor volume and enhancement pattern analysis based on sequential MRI examination were shown to provide very early signals of failure in plot studies. Tumor size and dynamic enhancement pattern judged by the MRI prior to radiation therapy and temporal changes during the early course of radiation therapy appear to be sensitive predictors of tumor response; consistent with the notion that tumor blood supply and or oxygenation status strongly influence radiation response. The overall goal of this project is to test the hypothesis that MR-based measurements predict the likelihood of tumor control in patients with advanced **cervical cancer** treated by conventional radiation therapy. This will be achieved by three specific aims: (1) further develop, test, and refine predictive metrics of advanced **cervical cancer** radio-responsiveness based on contrast enhanced MRI and MR-based tumor volumetry, (2) apply MRI in a clinical population through their course of therapy and correlate tumor response with image-based metrics, and (3) determine predictive value (positive and negative) of MRI-based metrics. On completion, this project will provide a clinically validated MR protocol for prediction of tumor radio-responsiveness in advanced **cervical carcinoma** treated with radio-therapy. A prognostic index using MRI in a clinical setting to identify the high-risk patients who require more aggressive multi-modality therapy will be developed. The pixel signal distribution within the entire tumor between the radiosensitive and resistant groups will be further defined using multi-spectral and multi- temporal analysis, and characterized to discern subgroups contributing to treatment failure within the heterogeneous tumor.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CYTOTOXIC T LYMPHOCYTE RESPONSE TO HPV 16**

  Principal Investigator & Institution: Nakagawa, Mayumi; Laboratory Medicine; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

  Timing: Fiscal Year 2001; Project Start 01-FEB-1998; Project End 31-JAN-2003

  Summary: (Applicant's Description) As a student in an M.D.-Ph.D. program at Albert Einstein College of Medicine, Dr. Nakagawa studied the structure function relationships of murine Major Histocompatibility Complex in terms of its immunological and physiological properties. After completing a residency program in laboratory medicine at the University of California at San Francisco, where she still is, she began a research project studying cell-mediated immunity to Human Papilloma Virus type 16 (HPV 16) which is a causative agent of cervical dysplasia and cancer. Data collected thus far, using a T cell proliferative assay as well as a cytotoxic lymphocyte assay, support her working hypothesis that cell-mediated immunity to HPV is instrumental in its elimination and thus is protected against the development of associated diseases. The experiments proposed in this application are nested with an ongoing longitudinal study in which HPV 16 infected women who have not developed high grade intraepithelial lesions are tested for cytotoxic T lymphocyte responses to HPV 16 oncogenic proteins, E6 and E7. The specific aims of this project are to characterize the lymphocyte subset(s) responsible for anti-HPV activity, to eliminate background activity, to explore alternative methods of in vitro stimulation, and to develop a protocol to perform cytotoxic T lymphocyte assay using T cell lines instead of bulk cultures. The last aim will give us a tool to identify immunodominant epitopes of HPV 16 in the future. The long-term goal of this project is to develop effective vaccines and immunotherapy for prevention and treatment of **cervical cancer.** Dr. Nakagawa's long-term career goal is to continue research in HPV immunology as an independent investigator. She envisions this will be best accomplished by becoming a faculty member at an academic medical center where she will also have clinical responsibilities as a laboratory medicine physician. The University of California at San Francisco, which is a major academic medical institution with many distinguished scientists, offers an excellent environment to develop skills and further her expertise in the field to accomplish her goals.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DEVELOPING NEW APPROACHES FOR CERVICAL CANCER CONTROL**

  Principal Investigator & Institution: Kiviat, Nancy B.; Director of Pathology; Pathology; University of Washington Seattle, Wa 98195

  Timing: Fiscal Year 2002; Project Start 16-AUG-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): Invasive **cervical cancer** (ICC) is an AIDS defining disease [CDC Update, 1993]. Our studies show that women with HIV-2 or HIV- I infection are at increased risk of ICC and development of cervical intraepithelial neoplasia 3/carcinoma in situ (CIN 3/CIS). Screening programs based upon cytology, detection of human papillomavirus (HPV), and visualization of the cervix have all been proposed for use in resource poor settings, however, none of these methods are practical approaches to **cervical cancer** control in areas of endemic HIV infection. Novel approaches must be developed to identify and treat women at high risk for ICC in HIV endemic areas. We hypothesize that, in contrast to most HIV seronegative women who are infected with oncogenic types of HPV; HIV seropositive women co-infected with

oncogenic types of HPV acquired the molecular changes which permit, and are associated with progression to ICC even before cytologic changes are detected, or when only mild changes such as CIN 1 are present. We further hypothesize that such molecular changes, which are predictive of increased ICC risk can be identified and could serve as the basis for sensitive and specific assays, with high predictive value, for the early identification of HIV, infected women at high risk of ICC. Our approach to developing relevant molecular assays is based on the knowledge that the set of expressed genes, or "expression profile" of normal cells differs from that of cancer and dysplastic cells of the same tissue type [Fields, 1994]. We propose to biopsy HIV seropositive and HIV seronegative women infected with oncogenic HPV types and with varying grades of cervical lesion abnormalities (CIN 1, CIN 2/3, CIS, ICC) and examine the expression profiles of these different lesions to identify changes in gene expression that are characteristic of malignancy but occur prior to ICC (i.e., in CIS). Once such profiles are identified, we will determine and compare the frequency with which abnormally expressed genes are present in earlier precursor lesions among HIV seropositive and HIV seronegative women. Validation on additional samples, and proof of principle testing on stored longitudinal samples from women who did and did not subsequently develop CIN 3/CIS, will be performed. This will provide the rationale for future development of "low tech" ELISA assays for detection of the protein products of the over-expressed genes of interest and for longitudinal studies demonstrating the utility of this approach.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DEVELOPMENT OF A NOVEL HPV IDENTIFICATION SYSTEM**

  Principal Investigator & Institution: Hepburn, Angus G.; Profile Diagnostic Sciences, Inc. 510 E 73Rd St, 2Nd Fl New York, Ny 10021

  Timing: Fiscal Year 2001; Project Start 01-APR-1998; Project End 31-MAR-2003

  Summary: Invasive carcinoma of the cervix is-one of the most common cancers in the world. Human papillomavirus (HPV), progressing through cervical intraepithelial neoplasia (CIN), is the primary causal agent for the development of invasive **cervical cancer.** However, of the 70 or more HPV subtypes, few progress to cancer. Although early detection coupled with eradication of **cervical cancer** precursors has been shown to lead to a decreased incidence of invasive **cervical cancer,** the present state of the art employs diagnostic techniques that are too costly or too time consuming to screen large populations efficiently. Accurate strain identification is presently only possible through cumbersome DNA hybridization analyses utilizing either Southern blot technology or in situ hybridization technology. In the following proposal, an enzyme-assisted, sequence-specific identification system will be developed. The simple, rapid, sensitive, accurate, and low-cost DNA diagnostic system described herein will detect HPV at very early stages of infection and will distinguish between low-oncogenic-risk strains and high-oncogenic-risk strains. This will enable large scale screening by establishing a diagnostic protocol that is sensitive, rapid, simple, and relatively inexpensive. The diagnostic tool described by this proposal is applicable in detection of other infectious diseases and genetic diseases with only simple modifications. PROPOSED COMMERCIAL APPLICATION: The proposal describes a rapid and inexpensive DNA diagnostic tool suitable for routine used which matches the specificity, accuracy and sensitivity of hybridization or PCR-based assays. In addition to the screening of HPV, the diagnostic tool described by this proposal is applicable in the detection of other infectious diseases and genetic diseases with only simple modification.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DEVELOPMENT OF A URINE PCR ASSAY FOR HPV DNA DETECTION**

  Principal Investigator & Institution: Hagensee, Michael E.; Associate Professor of Clinical Medicine; Medicine; Louisiana State Univ Hsc New Orleans New Orleans, La 70112

  Timing: Fiscal Year 2001; Project Start 05-APR-2000; Project End 31-MAR-2002

  Summary: Human papillomavirus (HPV) is the most common virally sexually transmitted disease, and high-risk types of HPV have been implicated in over 90% of cervical cancers worldwide. Current preventative me measures of **cervical cancer** include routine Pap smear evaluation, which appears to be effective. Current preventative measures for **cervical cancer** include routine Pap smear evaluation, which appear to be effective. However, a small but significant proportion (>10%) of females in the United States have either never had a Pap smear or (>30%) do not have them on a routine basis. This may be due, in part, to the invasiveness and discomfort of the requirement pelvic examination. Although HPV cannot be routinely grown in the laboratory, its DNA can be deleted by amplification techniques such as PCR. Detection of HPV DNA from cervical swab or cervical lavage specimens has been used as an epidemiological tool to determine the prevalence rates of HPV infection. These procedures also require a pelvic examination that limits its widespread applicability. A method that is equally sensitive and efficient but does not require a pelvic examination to detect HPV infection will be able to identify more women at risk for **cervical cancer** and greatly aid in epidemiologic surveys. The recent advances in the diagnosis of gonorrhea and chlamydia infection by screening urine using amplification techniques demonstrate the feasibility of diagnosis a cervical infection by a urine test. Preliminary date have demonstrated the ability to detect HPV DNA in urine specimens from women at high risk for HPV infection. For these reasons, we hypothesize that a urine PCR test for the detection of HPV DNA will reflect the state of infection for the cervic. The goal of this proposal is to fully develop and validate a urine PCR test for HPV DNA detection that can be utilized for epidemiologic screening purposes. We propose to initially develop the urine PCR assay for HPV DNA detection by studying 20 women with no detectable HPV DNA in their urine. The ability to detect beta-globin DNA (internal control for the presence of cells) and known amounts of clon4ed HPV DNA spiked into these urine specimens will be measured and optimized. Next, urine will be obtained from 50 women previously tested to have HPV DNA detected in cervical/vaginal swabs. The extraction method by the initial experiments will be verified by testing these known HPV positive "field" specimens. Finally, utilizing the conditions optimized in specific aims #1 and verified in specific aim #2, a cohort of 250 women at high-risk and 250 women at low-risk for HPV infection will be enrolled. Paired urine and cervico-vaginal swabs will be obtained and the ability to detect any HPV DNA, any high-risk HPV DNA and type-specific HPV DNA will be compared. A validated urine test for HPV DNA detection could be used to better define the epidemiology of HPV, to explore the natural history of HPV infection, and to identify women at higher risk for **cervical cancer.**

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DISCRETE ASSAY FOR INTEGRATED HPV DNA IN CERVICAL CELLS**

  Principal Investigator & Institution: Moen, Phillip T.; Senior Scientist; One Cell Systems, Inc. 100 Inman St, Ste 200 Cambridge, Ma 02139

  Timing: Fiscal Year 2001; Project Start 01-SEP-2000; Project End 31-MAR-2001

Summary: Current studies indicate that development of **cervical cancer** is strongly linked to the DNA integration of several subtypes of the human papillomavirus (HPV). The Pap test has helped in the early detection of precursor lesions; however, results are inconclusive when low grade lesions are detected. In these cases, a solution based hybridization method can be used to screen for the presence and viral burden of common HPV subtypes associated with **cervical cancer.** The presence of HPV, however, is not a useful indicator of subsequent development of **cervical cancer.** A test which can determine the occurrence of viral integration is a better indicator of disease. Current in situ hybridization methods have limited success in distinguishing integrated virus from episomal virus. Analysis is difficult because both episomal and integrated virus often coexist, and the "diffuse" pattern indicating episomal virus often masks the "dot" pattern indicating integrated virus. By combining single cell gel microdrop (GMD) encapsulation technology, in situ hybridization and nuclear fractionation techniques, this Phase I proposal aims to develop an assay which will unambiguously distinguish integrated virus from episomal virus. Use of GMD technology will also reduce cell loss, facilitating rare cell detection. PROPOSED COMMERCIAL APPLICATIONS: The assay will permit early detection of **cervical cancer** and highly specific assessment of viral pathogenic mechanisms directly linked to **cervical cancer,** facilitating early treatment and reducing mortality rates.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DNA DAMAGE RESPONSE AND DNA REPLICATION**

  Principal Investigator & Institution: Gautier, Jean; Genetics and Development; Columbia University Health Sciences New York, Ny 10032

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2007

  Summary: Following DNA damage cells activate a multi-faceted response including cell cycle arrest and the coordinated activation of DNA repair. Failure to activate or to coordinate the DNA-damage induced signal transduction pathways can lead to chromosome breakage and loss, and to the propagation of mutations. Indeed, several cancer-prone syndromes reflect defects in the DNA damage response. These include, but are not limited to, Ataxia-Telangiectasia, Nijmegen Breakage Syndrome, Ataxia-Telangiectasia Like Disorder, Li-Fraumeni Syndrome and familial forms of breast and cervical cancers. Our long-term objective is to understand the mechanisms by which the different facets of the DNA damage response are integrated within cell cycle progression at the time of DNA replication. The ability to undergo DNA replication in the presence of DNA damage, called Radio-Resistant DNA Synthesis (RDS), is a hallmark of the cellular phenotypes of cancer-prone disorder as well as of tumor cells. We have established a cell-free system derived from Xenopus eggs that recapitulates different aspects of the DNA damage response. In particular, we have been able to identify a novel ATM- dependent cell cycle checkpoint that prevents initiation of DNA replication. We will determine whether the Xenopus homologues of Chk1 and/or Chk2/Cds1 are components of this pathway. We will also determine whether Wee1, Myt1 and/or Cdc25 are components of the pathway. We will take advantage of this cell-free system to identify which type of damages can elicit a checkpoint in vitro and whether such responses are ATM or ATR-dependent. Finally, we will examine how ATM and Mre11 complex participate in the coordinated and harmonious response to DNA damage and how cell cycle arrest is integrated with DNA repair. We anticipate that these studies will help understand some of the biochemical pathways activated by DNA damage and that, in turn; it will provide valuable information on how the DNA damage response can be impaired or lost in the case of cancer.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EARLY DETECTION OF COMMON CANCERS IN WOMEN IN INDIA**

  Principal Investigator & Institution: Dinshaw, Ketayun; Director; Tata Memorial Hospital Tata Memorial Ctr Bombay,

  Timing: Fiscal Year 2002; Project Start 30-SEP-1997; Project End 31-AUG-2003

  Summary: (Adapted from applicant's abstract): The study is a continuation of a randomized trial initiated under the NIH Project NO.ROI CA74801-01. Cancer of the breast and cervix account for almost 4O percent of cancer deaths in Indian women. The objective is to investigate whether low-cost technology approaches-- i.e. physical examination of the breast plus teaching of BSE and visual inspection of the cervix painted with 2 percent acetic acid, to be done by trained female health workers--will be effective in down-staging the disease and eventually lead to reduction in mortality. The initial grant of 3 years ends in October 2000. A fresh application is now made for the next 3 years of the study. 100,000 socioeconomically disadvantaged women between the ages of 35-64 years are being randomized to 2 arms--one to receive intervention every 18 months for 6 years and the other to act as control. The first of 4 cycles of 18 months began in May 1998 after 5-months training of the field staff and will end in November 1999, to recruit half the cohort; the other half will be recruited in the second cycle. Baseline survey of 177,449 women registered on the election rolls of 10 localities was undertaken to match names/addresses with those in the rolls. Each locality is subdivided into 2 sections. All women of one section, which were selected randomly, are eligible to receive intervention, and none from the other. Up to October 31, 1999, 21,542 women have been recruited in the intervention arm and 19,228 in the control arm, from 5 localities. The target of 25,000 women per arm is expected to be reached in the remaining month. Overall 68 percent of the women in the intervention area and 79 percent of the women from the control area responded to the invitation to participate in the study. To date 73 percent of the women referred for further investigations have complied and this proportion is likely to improve since sufficient time has not elapsed for those referred recently. After the completion of 4 rounds of screening, the women will be followed-up for 5 more years, with skeleton staff, to assess mortality due to breast and **cervical cancer.** The findings of this trial--one of the first of its kind in a developing country--may be relevant for other countries with limited financial resources.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EARLY DIAGNOSIS OF CERVICAL CANCER**

  Principal Investigator & Institution: Mathur, Subbi P.; Professor; Obstetrics and Gynecology; Medical University of South Carolina 171 Ashley Ave Charleston, Sc 29425

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2004

  Summary: {NCI pa: Exploratory Studies in Cancer Detection, Prognosis and Prediction (similarity to NCI-PA98-022); revised R21 application. **Cervical cancer** is a leading gynecologic malignancy with 14,500 new cases and 400 deaths yearly. Eighty to 90% of women with **cervical cancer** are infected with human papillomavirus (HPV). Cervical intra- epithelial neoplasia (CIN) markers the pre-cancerous stage. Ten to 20% of women develop **cervical cancer.** Paper smears and HPV testing have limitations in identifying women progressing to cancer, not helpful in the patients with ASCUS/AGUS (atypical squamous/glandular cells of undetermined significance) and for monitoring therapy efficacy (paucity of tissue after therapy) in recurrence. Our data-supported hypothesis is

that progression of squamous cell **cervical cancer** from CIN is related to up-regulation of EGF-R and insulin-like growth factor-II (IGF-II) proteins in cervical epithelium, followed by significant increases in serum IGF-II levels (specific to **cervical cancer;** levels decrease after therapy. Our latter finding provides us with an excellent opportunity to develop a non-invasive screening test that gives an added value to pap smear and HPV testing. We propose that: Serum IGF-II levels can be used to identify patients who are at risk of developing **cervical cancer** and, more importantly, to monitor therapy efficacy in the patients with **cervical cancer.** We shall obtain serum levels of IGF-II (ELISA) in women with: 1. Normal Pap smear; 2. Abnormal Pap smear with no CIN; 3. Endometrial or ovarian cancer; 4. CIN-I, II or III pre-treatment; 5. CIN-I, II or III, post-treatment; 6. Invasive **cervical cancer** pre- treatment or at a time of hysterectomy; and, 7. Invasive **cervical cancer** (6 months and a year) post-treatment. We shall correlate the levels of IGF-II with clinical diagnosis of CIN or **cervical cancer,** size of neoplasm and resolution or recurrence of the disease and the smoking history. We believe that serum IGF-II test could compliment the Pap test to reduce deaths by **cervical cancer.**

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EFFECTS OF BENZO[A]PYRENE IN TRANSGENIC MODEL OF CERVICA**

  Principal Investigator & Institution: Rorke, Ellen A.; Associate Professor; Environmental Health Sciences; Case Western Reserve University 10900 Euclid Ave Cleveland, Oh 44106

  Timing: Fiscal Year 2001; Project Start 01-FEB-2000; Project End 31-JAN-2003

  Summary: Human **cervical cancer** development begins with infection by the DNA tumor virus, human papillomavirus (HPV). The HPV genome encodes two oncoproteins, E6 and E7, that are required for cell immortalization, E6 causes degradation of the cell cycle checkpoint/tumor suppressor protein, p53. However, development of invasive diseases requires additional events including the activation of secondary oncogenes. In this regard, environmental carcinogens play a major role. Cigarette smoking is correlated with an enhanced risk for **cervical cancer** development. An active agent in cigarette smoke is the ubiquitous environmental carcinogen, benzo[a]pyrene. Metabolites of B[a]P are potent DNA mutagens. B[a]P is mutagenic in cervical cells in vitro, accumulates in cervical mucus in vivo, and ras oncogene, a known target of B[a]P, is mutated at a high frequency in cervical tumors. p53 is an important cell cycle control protein. Following DNA damage, p53 pauses cell cycle progression until DNA repair is complete. Our previous in vitro studies show that treatment with B[a]P strongly inhibits the proliferation of cultured normal cervical epithelial cells This inhibition is correlated with a large increase in p53 level. In contrast, in HPV-immortalized cells, which have low p53-immortalized cells do not significantly pause in the cell cycle. Based on these studies, we hypothesize that B[a]P should be a more potent mutagen in HPV-immortalized cells, because these cells do not pause in proliferation long enough to adequately repair DNA following B[a]P exposure. Although our in vitro results are consistent with this hypothesis, our goal is to test this hypothesis in vivo. However, work in this field has been stymied by the lack of a suitable animal model of HPV-dependent neoplasia. During the past two years, we have developed an innovative transgenic mouse model of **cervical cancer,** in which the mice express the HPV16 E6 and E7 oncoproteins in the cervical epithelial, and we are now ready to test our hypotheses in vivo. In Specific Aim 1 we test the hypothesis that B[a]P treatment should increase tumor formation in HPV-immortalized cervix compared to normal cervix, and examine the tumorigenic phenotype of the cells in nude mice, in soft agar, and in microinvasion

assays. In Specific Aim 2 we hypothesize that B[a]P treatment should increase tumor formation in HPV-immortalized cervix compared to normal cervix, and examine the tumorigenic phenotype of the cells in nude mice, in soft agar, and in microinvasion assays. In Specific Aim 3 we examine the hypothesis that in vivo B[a]P treatment should differentially increase DNA mutations in HPV-immortalized cells, and that the increased mutation rate should be correlated with reduced p53 levels. We examine the effects of B[a]P treatment on p53 level, DNA adduct formation, and mutation at the H-ras and K-ras loci. The ultimate aim of these studies is use our HPV16 E6/7 cervical neoplasia mice to provide new understanding regarding the role of environmental carcinogens (polycyclic aromatic hydrocarbons) in the genesis of **cervical cancer.** Use of our novel transgenic model provides an innovative approach for addressing these questions.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EPITOPE DRIVEN HPV VACCINE TARGETING DENTRITIC CELLS**

  Principal Investigator & Institution: Martin, William D.; Chief Information Officer; Epivax, Inc. 365 Hope St Providence, Ri 02906

  Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 31-AUG-2003

  Summary: Human Papilloma Virus (HPV) types 16 and 18 are detected in roughly 70% of all invasive cervical tumors. Among cytologically normal women, detection of HPV infection by PCR has been shown to increase the subsequent risk of cervical cytologic abnormalities by 12 fold, suggesting that effective vaccines (preventive/therapeutic) for HPV infection would be a useful medical advance in the battle against this cancer. EpiVax is developing a dendritic cell-directed DNA vaccine against HPV 16, 18, and other cervical cancer-associated HPV types. For this project, we have selected 100 novel HPV peptides that represent putative MHC class I and class II restricted T cell epitopes, primarily derived from the E1, E2, E6, E7 and L1 proteins of selected HPV types. Binding studies and CTL studies will be performed to select the best candidates for vaccine development Selected epitopes will be inserted in a DNA vector. Additional DNA vaccine development, safety, toxicity, and protection studies will be carried out in Phase II. The specific aims of this project are to: * Screen putative HPV epitopes for MHC binding and HPV-specific T cell recognition * Construct DNA vaccine vectors containing candidate HPV epitopes * Evaluate DNA vector expression in human dendritic cells in vitro. PROPOSED COMMERCIAL APPLICATIONS: A therapeutic anti-HPV vaccine would have a tremendous market impact since existing cervical screening programs cost nearly $6 billion annually in the United States. Also, most sexually active women have been exposed to HPV, so it is unlikely that a prophylactic HPV vaccine will confer protection. A novel immunologic therapy to treat existing HPV infection as well as HPV-associated **cervical cancer,** such as the one we propose, may represent an attractive and cost effective treatment alternative.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ESTROGEN, HPV, AND CERVIX CANCER IN TRANSGENIC MICE**

  Principal Investigator & Institution: Arbeit, Jeffrey M.; Associate Professor of Surgery; Surgery; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

  Timing: Fiscal Year 2001; Project Start 01-JUN-1997; Project End 31-MAR-2003

  Summary: (adapted from the investigator's abstract) "High risk" human papillomaviruses (HPV's). such as HPV type 16, are associated with over 80% of cervical

cancers. HPV16 expression alone is insufficient to induce carcinogenesis, which requires specific co-factors. We have developed an animal model in which one co-factor associated with HPV neoplasia, chronic estrogen treatment, induces multi-step cervical and vaginal carcinogenesis in transgenic mice expressing the entire early region of HPV16 under control of the human keratin-14 promoter (K14-HPV16 transgenic mice). We will investigate the hypothesis that the cooperation between estrogens and the oncogenes of HPV is a major determinant of cervical carcinogenesis. The specific aims are: 1. Examine whether cervical neoplasia is decreased by decreasing doses of estrogen or by the addition of progesterone, and determine whether carcinogenesis persist after the cessation of estrogen treatment. 1.1. Determine a threshold dose of estrogen for cervical carcinogenesis. 1.2. Investigate growth of cervical neoplastic lesions or carcinoma independent of exogenous estrogen. 1.3. Investigate alteration of estrogen induced cervical carcinogenesis by progesterone. 2. Investigate the functional role of estrogen receptor in estrogen induced cervical carcinogenesis in K14-HPV16 transgenic mice. 2.1. Examine the level of expression of the estrogen receptor, and an estrogen inducible gene containing an estrogen response element, during cervical carcinogenesis. 2.2.1 Test the contribution of estrogen receptor signaling to cervical carcinogenesis by creating and treating composite 14K-HPV16/estrogen receptor knockout (ERKO) with estrogen. 2.2.2. Investigate the effect of pharmacological inhibition of estrogen receptor on estrogen induced cervical carcinogenesis. 2.3. Manipulate expression of the estrogen receptor in different target cells of the reproductive tract to examine contributions of both epithelium and stroma to cervical carcinogenesis. 2.3.1. Determine the role of the epithelium and stroma in estrogen induced cervical carcinogenesis by expressing both the estrogen receptor and the HPV oncogenes in squamous epithelium in ERKO mice lacking receptor function in the stroma. 3. Examine the mechanisms of cooperation between HPV oncogenes and estrogen during cervical carcinogenesis. 3.1. Create transgenic mice with 14K-HPV16 constructs containing mutations in the HPV16 E6, E7, or E5 oncogenes, and investigate of each of the HPV oncoproteins to estrogen induced cervical carcinogenesis. Elucidation of synergism between estrogen and HPV may lead to new insights into the role of sex hormones in the genesis and progression of **cervical cancer.**

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- **Project Title: FOGARTY AIDS INTERNATIONAL TRAINING AND RESEARCH PROGRAM**

  Principal Investigator & Institution: Beyrer, Chris R.; Associate Research Professor; Epidemiology; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 30-SEP-1998; Project End 31-MAY-2003

  Summary: Despite the availability of a screening test and a range of treatment options. **Cervical cancer** remains the single most important cause of malignancy- associated death for Thai women. Thailand also has one of the highest population prevalences of HIV in Asia, with disproportionately high rates among women and men in northern Thailand. As many as 1 in 50 women of child-bearing age in northern Thailand are HIV epidemic and a long- standing chronic endemic of HPV infection and **cervical carcinoma.** Evidence demonstrating that women with HIV infection are at an increased risk of **cervical carcinoma,** highlights the critical challenge facing northern Thailand with the intersection of these two diseases. Prevention, detection And early treatment of **cervical carcinoma** in Thailand are already public health priorities, although pap smears remain under-utilized, are far from routine. Thus, there is an urgent need for the latest technology and information for diagnosis, treatment and prevention of **cervical**

carcinoma in the setting of the heterosexual epidemic of HIV and HPV in the northern Thailand. This Fogarty Training Supplement has four specific aims: To train Thai scientists in the etiology, epidemiology, natural history, surveillance, screening, diagnosis, and secondary prevention and treatment of **cervical carcinoma.** To train investigators from Thailand to evaluate the effects of HIV on HPV acquisition, persistence and risk for **cervical carcinoma** in Thai women. To upgrade programmatic approaches in Thailand for prevention of **cervical cancer,** including the sensitivity, specificity and predictive value of screening methods and options for treatment of early lesions. To investigate the use of visual inspection with acetic acid combined with cryotherapy for early detection and treatment of cervical lesions at district level health facilities. This administrative supplement to our existing Forgarty AITRP award seeks to continue and expand the training and in-country research efforts of this collaboration. Specifically, we propose the following training activities: Year I - One in-country workshop plus 4 short course trainees (Epidemiology, HPV laboratory diagnosis, Cytopathological diagnosis of cervical neoplasia and clinical diagnosis and management of cervical carcinoma) Year II One in- country workshop plus 4 short course trainees (Epidemiology, HPV laboratory diagnosis, Cytopathological diagnosis of cervical neoplasia and clinical diagnosis and management of cervical carcinoma) Year III One in-country workshop plus 3 Advanced Research Training Awards.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: FUSOGENIC MEMBRANE PROTEINS AS THERAPEUTIC TRANSGENES**

  Principal Investigator & Institution: Galanis, Evanthia; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

  Timing: Fiscal Year 2001; Project Start 01-MAY-2000; Project End 31-MAR-2005

  Summary: Measles virus exerts its cytopathic effect by cell-cell fusion which eventually leads to cell death. We have cloned the cDNA for the measles F and H fusogenic membrane glycoproteins into eukaryotic expression vectors and have shown significant cytotoxicity through induction of cell-cell fusion in different human tumor cell lines including A431 (epithelial carcinoma), C170 (colon cancer), HeLa (cervical cancer), TE671 (rhabdomyosarcoma), and the glioma cell lines U87 and U118. In addition, we have shown significantly higher bystander effects as compared to the herpes simplex thymidine kinase (HSV-tk) system. This proposal utilizes the fusogenic membrane proteins F and H of the measles virus to develop a clinician investigator's career in gene transfer/gene therapy. The applicant proposes to: 1) Investigate the use of fusogenic measles virus proteins F and H as novel therapeutic transgenes using the U87 and U118 glioma models. Gliomas were selected because they are highly lethal tumors despite the therapeutic use of surgery, radiation therapy, and chemotherapy. They also offer the further advantage of their limited metastatic potential that makes them appropriate targets for intratumoral gene transfer/gene therapy. We plan to a) construct retroviral vectors encoding the F and H transgenes, b) compare the developed vectors with the gold standard of cytotoxicity which is HSV-tk producing retroviral vectors in both glioma cell lines and tumor xenografts, and c) target vectors to the tumor environment by exploiting the over-expression of matrix metalloproteinases in gliomas. The long-term goal is to introduce this novel transgene system into clinical trials as a new therapeutic alternative. 2) Develop expertise to pursue an independent clinician scientist career within the area of gene transfer/gene therapy. In addition to the interaction with the mentor and co-mentors, this will be achieved through attending Mayo Graduate

School courses and major scientific meetings, such as the American Association for Cancer Research and the American Society of Gene Therapy meetings.

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- **Project Title: GENETIC RESISTANCE TO ONCOGENIC HUMAN PAPILLOMAVIRUSES**

  Principal Investigator & Institution: Tyring, Stephen K.; Professor; Microbiology and Immunology; University of Texas Medical Br Galveston 301 University Blvd Galveston, Tx 77555

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2005

  Summary: (provided by applicant): Infection with certain human papillomaviruses (HPV-16 and -18) has been associated with the development of invasive **cervical cancer** in women. To develop a vaccine to prevent HPV-16 and -18, the human immune response to HPV and its underlying genetic bases must be profiled. Important to the development of a vaccine is the documentation that some women have the capability to "clear" or eradicate HPV virus. Human leukocyte antigens (HLAs) may play a role in identifying biomarkers for the immune response to HPV infection. No one has ever reported typing of HLA in women who are seropositive for HPV-16 and/or-18, but who have negative Pap smears and no HPV DNA. There is also some indication that immune response to HPV-16 and -18 infections may vary by ethnic group. Hispanic women were selected for this study because they have one of the highest rates of **cervical cancer.** In Houston, Texas, the third largest city in the U.S., the rate for **cervical cancer** is one of the highest in the country. Our aim is to determine the HLA profile of women who have successfully cleared HPV infection. We will obtain HPV-infection rate and genetic profiles of 1250 Hispanic women undergoing their annual well-woman examination. By taking one additional cervical smear and drawing one additional vial of blood during the routine physical, additional risk to the patient is small. If a woman has a negative Pap smear, the additional cervical smear will be used to detect any presence of HPV-16 or 18. For those women with antibodies to HPV-16 and/or -18, but who have no HPV DNA and a negative Pap smear, HLA serotyping will be done using the lymphocytes from the vial of blood. This study will provide the preliminary data necessary to complete larger studies to compare ethnic diversity in the immune response to HPV infection and the genetics determining those immune responses. Standard statistical analyses will be used to estimate the association between HLA polymorphism and genetic resistance to monogenic HPV infection. Thus, this study is an important step in the development of an HPV vaccine to prevent infection.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GENETIC SUSCEPTIBILITY TO CERVICAL CANCER**

  Principal Investigator & Institution: Rader, Janet S.; Obstetrics and Gynecology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 31-JUL-2008

  Summary: (provided by applicant): **Cervical cancer** kills more than 200,000 people each year worldwide, disproportionately affecting women of low socioeconomic status. Infection with high-risk human papillomavirus (HPV) is the main causal factor, but additional factors must be involved because only a small proportion of HPV-infected women develop cancer. Epidemiologic studies suggest that some predisposing factors are genetic heritability accounts for about 27 percent of the total variation in liability to cervical tumor development. Because the responsible genes (or gene variants) have not

been uncovered, it is not yet possible to develop methods for identifying the small proportion of women with preinvasive cervical intraepithelial neoplasia (CIN) who will need treatment. To address this deficit, we plan to identify markers that associate with **cervical cancer.** Such markers might also be useful for screening women in the general population. To elucidate the role of genetic factors in the development of **cervical cancer,** we will study DNA from women who have invasive **cervical cancer** (ICC) or CIN III and are also infected with high risk HPV subtypes. We will select candidate genes that appear critical for the development of the cancer, including the HLA DQB1/DRB1 locus and other immune markers, genes that are cellular targets of HPV E6, E7, and E5 oncoproteins, and genes implicated in the progression of cervical neoplasia. Within each gene, we will focus on small variations, such as differences in single bases. Such single nucleotide polymorphisms (SNPs) are the most common genetic variations among individuals, accounting for a substantial proportion of phenotypic variability. We will evaluate their influence on interactions between HPV and cervical cells by using the transmission/disequilibrium test (TDT). Unlike the case-control method, the TDT assesses associations between specific alleles and disease endpoints without being vulnerable to errors caused by stratification of genetically disparate populations or undiagnosed preclinical disease in "controls.'" We will test each variation for association with ICC or CIN Ill by comparing frequency distributions of patient alleles (cases) with those of nontransmitted parental 'alleles, which provide a perfect ethnically matched control sample. If a polymorphism is inherited with higher-than-Mendelian frequency by the women with ICC or CIN III, we will suspect that variant of predisposing HPV-infected women to **cervical cancer.** Subsequent case control and cohort studies could then confirm the association. This investigative sequence is much more cost-effective than population studies that begin without first identifying potentially culpable genes. Determining how small variations in host DNA influence vulnerability to **cervical cancer** is critical to understanding the pathogenesis of the disease and therefore to the development of superior screening and diagnostic tests. As the field of pharmacogenetics expands, this information might enable vaccine and drug developers to tailor their products to "cervical cancer genotypes."

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- **Project Title: GREATER DENVER LATINO CANCER PREVENTION/CONTROL NETWORK**

  Principal Investigator & Institution: Flores, Estevan T.; None; University of Colorado at Denver Campus Box 129 Denver, Co 802173364

  Timing: Fiscal Year 2001; Project Start 04-APR-2000; Project End 31-MAR-2005

  Summary: (Applicant's Description) A cancer awareness and training collaboration coordinated by the Latino/a Research & Policy Center (LRPC: Drs. Flores and Espinoza) at the University of Colorado at Denver, will build a network infrastructure among 20-25 Latino community based organizations, health clinics, social service agencies, school-based clinics, faith-based groups, and employee-based organizations serving Latinos in the greater Denver metro area. The partners include file University of Colorado Health Sciences Center, Cancer Center and the Chancellor's Office of Diversity, the Colorado Department of Health and Environment, Division of Prevention, Colorado ACCESS, the Medicaid HMO with 43,000 clients, the Rocky Mountain Cancer Information Service and the American Cancer Society. During Phase I, the major partners will build the infrastructure for cancer awareness and education projects in the Latino community based on already extant associations and past intervention and education activities. This would include efforts in breast and **cervical cancer** awareness and prevention, smoking

cessation and prostate, colorectal and lung cancer. The project will also target 3 nearby migrant health clinics. The Steering Committee formed will review pilot project proposals for submission to the NCI. During Phase II of the project we will begin the pilot projects with the community groups. The CUHSC and the CDPHE will participate in developing the community education, health promotion and prevention pilot projects. During Phase III of the project the pilot projects will evolve into long-term funded projects benefitting the constituencies of the various members of the Network. Recruitment of Latino/a students to the cancer research and health professions areas will expand. Recruitment of patients to cancer clinical trials will benefit from the professional and lay education programs facilitated by the Network infrastructure.

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- **Project Title: GROWTH CONTROL OF NORMAL AND MALIGNANT KERATINOCYTES**

  Principal Investigator & Institution: Reiss, Michael; Professor; Medicine; Univ of Med/Dent Nj-R W Johnson Med Sch Robert Wood Johnson Medical Sch Piscataway, Nj 08854

  Timing: Fiscal Year 2001; Project Start 01-JUL-1986; Project End 31-DEC-2003

  Summary: For the past 15 years, the principal goal of my research program has been to elucidate the biological differences between tobacco-induced squamous cell carcinomas (SCC) of the upper aero-digestive tract (ADT) or cervix uteri and normal keratinocytes. Since our discovery in 1989 that most if not all SCC cell lines are refractory to Transforming Growth Factor-beta (TGFbeta)-mediated cell cycle arrest, we have focused specifically on elucidating the molecular mechanism underlying this phenotype. My long term goal is to use this information to develop novel approaches to the prevention and treatment of ADT cancers which still account for as many cancer deaths as 30 years ago. During the past 3 years, we have made significant progress. We were the first to identify missense mutations in the TGFbeta type II receptor (TbetaR-II) gene in head-&-neck SCC cells that nearly complete abrogate TbetaR-II kinase activity and signaling, and a novel nonsense mutation that encodes a truncated soluble TbetaR-II receptor in a **cervical carcinoma.** In addition, loss of mRNA expression of TbetaR-II accounts for TGFbeta resistance in approximately 25% of esophageal carcinomas and in nearly all small cell lung carcinoma (SCLC) cell lines. In this study, we have identified an in-frame deletion of 3 repeating GGC trinucleotides in exon 1 in 6 of 16 cases that probably affects the receptor processing and appear to confer an increased risk for the development of **cervical cancer.** Our specific goals for the coming five years are: 1. To develop and refine the reagents and assays necessary to evaluate the molecular and functional status of the TGFbeta signaling pathway in carcinoma tissue specimens in a comprehensive fashion. 2. To determine at which stage of tumor development and progression the TGFbeta signaling pathway becomes inactivated, and whether or not the emergence of TGFbeta-resistant clones is tied to the presence of a biologically active TGFbeta in the tumor microenvironment. 3. To determine how cancer-associated mutations in TGFbeta receptor genes alter the biochemical and biological properties of the receptors. 4. To develop novel therapeutic strategies designed to activate the TGFbeta signaling pathway downstream of functionally deficient TbetaR receptors.

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- **Project Title: GUIDELINES--MANAGE CERVICAL CYTOLOGICAL ABNORMALITIES**

  Principal Investigator & Institution: Wright, Thomas C.; Associate Professor; Amer Soc of Colposcopy & Cervical Pathol and Cervical Pathology (Asccp) Hagerstown, Md 21740

  Timing: Fiscal Year 2001; Project Start 26-SEP-2001; Project End 31-AUG-2002

  Summary: (Provided by Applicant): Each year approximately 50 million Papanicolaou smears are taken in the United States and of these, approximately 7% are classified as abnormal. Currently there are no nationally accepted guidelines for management of women with abnormal Papanicolaou smears and **cervical cancer** precursors. Moreover, most guidelines that have been published by individual societies/organizations are out of date since the do not incorporate recent changes in our understanding of the pathogenesis and natural history of **cervical cancer** and its precursors, or address recent technological innovations such as liquid-based cytology and HIV DNA testing. The lack of up-to-date national guidelines is causing widespread confusion among both health care providers and patients as to how best to manage abnormal Papanicolaou smears and **cervical cancer** precursors, and appears to be producing widely varying approaches to clinical care. The American Society of Colposcopy and Cervical Pathology (ASCAP) will hold a workshop on September 6-9, 2001 in Bethesda, MD at the NIH to develop Consensus Guidelines for the Management of Cytological Abnormalities and **Cervical Cancer** Precursors. The objective of the workshop is to develop comprehensive, evidence-based guidelines to guide clinicians of all subspecialties of medicine and nursing. Representatives from the American Academy of Family Physicians, American Cancer Society , American College Health Association, American College of Obstetricians and Gynecologists, American Society for Clinical Pathologists, American Society for Cytopathology, Am. Social Health Association, Centers for Disease Control and Prevention, Eurogin, International Academy of Cytology, International Federation of Cervical Pathology and Colposcopy, International Society of Gynecologic Pathologists, National Cancer Institutes, Nurse Practitioners in Women's Health, Pan American Health Organization, Planned Parenthood Federation of America, Society of Canadian Colposcopists, and Society of Gynecologic Oncologists will participate in the workshop. The participation of these diverse and prestigious societies/organizations in the development of the management guidelines should insure their widespread acceptance.

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- **Project Title: GYNECOLOGIC ONCOLOGY GROUP**

  Principal Investigator & Institution: Disaia, Philip J.; Professor and Chairman; American College of Ob and Gyn 409 12Th Street Sw Washington, Dc 20024

  Timing: Fiscal Year 2002; Project Start 01-MAY-1980; Project End 31-MAR-2003

  Summary: The Gynecologic Oncology Group (GOG) is the foremost multi-disciplinary cooperative clinical trial research group devoted to the study of gynecologic malignancies. Since its inception in 1970, the GOG has been a recognized leader in the development of new forms of treatment and has relied on the phase III trial as the design to identify new information. Supporting that major activity are the concerted efforts of modality committees providing recent approaches and procedures in each of the relevant diagnostic and therapeutic disciplines. The GOG has an active, effective program in the study of new chemotherapeutic agents in gynecologic cancers and this program has introduced important findings for study in the Phase III setting. In patients

with advanced cervical, endometrial and ovarian cancers, the GOG has defined significant improvement associated with the use of cisplatin. The GOG has performed a series of trials to examine the role of paclitaxel either as a single agent or in combination with other agents. Isofamide was found to be one of the most active single agents in squamous carcinoma of the cervix. The results of Phase III studies by the GOG have provided a new standard of treatment in suboptimal ovarian cancer using platin and taxol. Two recently completed trials of post-operative patients with intermediate risk endometrial and **cervical cancer** showed a significant improvement with adjuvant radiotherapy. The benefit of post-operative adjuvant chemotherapy has been confirmed for patients with totally resected, early stage ovarian cancer. In addition, the GOG has been active in developing new mechanisms to enhance translational research, cancer prevention and control and medical informatics. The Group has collaborative actively with the NCI in evaluating new data management collection and reporting systems. After more than 25 years, the GOG continues to be foremost in developing new strategies in the management of these cancers.

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- **Project Title: HEALING TOUCH AND IMMUNITY IN ADVANCED CERVICAL CANCER**

  Principal Investigator & Institution: Lutgendorf, Susan K.; Associate Professor; Psychology; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 01-FEB-2002; Project End 30-NOV-2002

  Summary: (provided by applicant): Although a large percent of the US population reports use of alternative therapies, there is little substantive empirical research examining effectiveness of many alternative modalities, nor is there a clear understanding of putative mechanisms whereby such treatments may have their effects. Healing touch is a therapy classified by NIH as a "biofield" therapy as its effects are proposed to be secondary to manipulation of hypothesized "energy fields" around the body of a patient. Although HT is frequently used as a complementary treatment by cancer patients undergoing chemotherapy and radiation to reduce toxic side effects of the treatments and to maintain immune competency, effects of this treatment during cancer treatment have not been investigated. Additionally, little is known about physiological mechanisms by which HT may work. This study is designed to examine effects of HT versus standard care on cellular immune function and short-term side effects of treatment among 44 women with advanced **cervical cancer** receiving a standard protocol of chemotherapy and radiation. Although combined chemotherapy and radiation treatment is potentially curative in 70 percent of cases, many patients experience acute side effects and late radiation effects have also been reported as much as 4 years following treatment. Severe immune compromise has also been reported following intensive radiation. Identification of interventions that could reduce side effects and help maintain resistance in advanced **cervical cancer** patients undergoing treatment is an important health problem. There are no data on the effects of healing touch on immune function or treatment side effects among **cervical cancer** patients, or among cancer patients receiving chemotherapy and radiation. Therefore this study is designed as an exploratory study to determine whether such immune effects exist, and if so, whether specific immune parameters associated with **cervical cancer** are affected. Effects of healing touch on mood and treatment-specific side effects will also be examined. The significance of this study is that it will provide preliminary data on the impact, if any, of HT on various parameters of cellular immune function and whether

the magnitude of that impact is large enough to be of sufficient clinical significance to be examined in future trials.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HPV & CERVIX NEOPLASIA IN A LARGE, LONG TERM HIV+ COHORT**

  Principal Investigator & Institution: Strickler, Howard D.; Associate Professor; Epidemiology & Population Health; Yeshiva University 500 W 185Th St New York, Ny 10033

  Timing: Fiscal Year 2001; Project Start 15-JAN-2000; Project End 31-DEC-2004

  Summary: Human papillomavirus (HPV) is the central etiologic agent in the development of most cervical neoplasms, including invasive **cervical cancer.** HIV-positive women are at substantially elevated risk for HPV infection as well as cervical disease, and this risk increases with diminished CD4+ T-cell and/or higher HIV RNA levels. Surprisingly few studies, however, have assessed the natural history of HPV infection in HIV-positive women. Gaps in our knowledge include the persistence of HPV DNA in HIV-positive women and its relation with risk of cervical neoplasms. Reactivation of latent HPV infections has been suggested to be important in immune compromised individuals, but clear evidence that this occurs is lacking. The effects of highly active anti- retroviral therapy (HAART) on HPV natural history are unknown. The purpose of this application is to study the long term effects of HIV on the natural history of HPV infection and the development of cervical neoplasms, using specimens obtained from the Women's Interagency HIV Study (WIHS). The WIHS cohort is a large, geographically and ethnically diverse population of HIV- positive (n=2056), and risk-matched HIV-negative women (n=569). Since enrollment (October, 1994 - November 1995) WIHS subjects have been followed at 6 month intervals, and follow-up is funded through 2002. We have analyzed HPV and cytologic results at enrollment, but HPV DNA testing for most planned visits (years 2- 7 of follow-up) has not been arranged. Under this application we will test all untested cervical specimens for HPV DNA, and specimens positive for HPV 16, 18 and/or 31 will be further tested to identify the type-specific variant. Serum antibodies to papillomavirus antigens, including a panel of virus-like particles, will be measured. Our specific aims include: (1) To study the relation of HIV serostatus, CD4+ T-cell, HIV RNA levels, and use of HAART with risk of 3 outcomes, namely, incident type-specific HPV DNA detection, persistence of HPV DNA, and incident cervical neoplasms; (2) To determine whether HPV can become latent and then be reactivated; and (3) To study humoral immune responses to HPV and their relation with HPV natural history in HIV-positive and -negative women.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HPV AND CELL CYCLE DYSREGULATION IN ORAL CANCER**

  Principal Investigator & Institution: Munger, Karl; Associate Professor of Pathology; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2001; Project Start 01-APR-1998; Project End 31-MAR-2003

  Summary: Proper regulation of the cell cycle transition from the resting phase G1, to the DNA synthetic phase, S, is often lost in cancer cells. This can result from the expression of viral oncoproteins, such as the E6 and E7 proteins encoded by the high risk human papillomaviruses (HPVs), which abrogate the functions of the tumor suppressor proteins p53 and pRB and, thus, mechanistically contribute to human carcinogenesis. Indeed, the importance of this function of E6 and E7 is underscored by the observation

that **cervical cancer** cells that do not express these viral oncoproteins have suffered inactivating mutations in p53 and pRB. It is now clear that several different genetic events can lead to inactivation of these tumor suppressors in different tumor types. For example, cyclin D1 or cdk4 over expression is an alternative to pRB inactivation in some cancers, and deletion of p16/INK/4A, a negative suppressor of cyclin D/cdk4 function, is also a common alternative to pRB loss. This work has defined a pathway of alternative biochemical targets in cancer cells, alteration of any one of which may suffice to significantly dysregulate the G1-to-S phase transition. Our preliminary results suggest that cdk6 is also a potential oncogene acting in the pRB pathway, since it is preferentially activated in oral cancers. Furthermore, we have shown that over expression of cdk6 can render cells insensitive to p53-mediated G1 arrest, in part by interfering with the function of the cdk inhibitor p21 cip1/WAF1. The work described in this proposal is designed to identify and test the role of novel human papilloma viruses unique to oral squamous carcinomas and to identify alterations in the G1 cell cycle control machinery that contribute to tumor progression. In particular, the oncogenic role of cdk 6 will be investigated in oral cancer cell lines. These goals will be achieved by 1) identifying the biological and biochemical activities of HPVs associated with oral carcinomas; 2) determining the status of the p53 and pRB pathways in normal and neoplastic cultures of oral epithelial cells; and 3) testing the role of cdk6 in oral epithelial neoplasia through the construction of viral vectors encoding activated or dominant-negative cdk6.

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- **Project Title: HPV DIFFERENTIATION DEPENDENT REPLICATION**

  Principal Investigator & Institution: Meyers, Craig M.; Professor of Microbiology; Microbiology and Immunology; Pennsylvania State Univ Hershey Med Ctr 500 University Dr Hershey, Pa 17033

  Timing: Fiscal Year 2001; Project Start 07-JAN-2000; Project End 31-DEC-2003

  Summary: Worldwide, **cervical cancer** is the second leading cause of death due to cancer in females. Human papillomaviruses (HPV) have been associated with over 90 percent of all cervical cancers examined. The working hypothesis is that all aspects of HPV's differentiation-dependent replication cycle are controlled by the temporal and spatial growth mechanisms of its natural host tissue, squamous epithelium. Therefore, temporal and spatial controls on gene expression, viral DNA replication, and virion morphogenesis are stipulated by the differentiation state of the host cell. Two areas of the HPV differentiation-dependent life that are the focus of this application include: first, describing the cis elements important for viral transcriptional control during different stages of the viral life cycle and second, defining viral protein expression in terminally differentiating host tissue. In the first specific aim, HPV mutants will be utilized to investigate transcriptional control using in vitro model systems for (i) the initial stage of the viral life cycle; (ii) the differentiation of the host epithelial tissue; (iii) the contribution of the viral transactivating protein, E2; and (iv) the complete HPV life cycle. The ability to study mutations incorporated into the HPV genome on viral transcription, viral DNA replication, and late gene expression represents a breakthrough advance for investigating the biology of these human oncogenic viruses. These studies represent the first proposed mutational analysis of a HPV using a permissive in vitro system that is capable of propagating infectious HPV particles. In the second specific aim, we will define the temporal and spatial expression of HPV proteins in differentiating epithelium during the complete viral life cycle. The use of the organotypic (raft) culture system permissive for the complete HPV life cycle, including

the synthesis of infectious viral particles, will be an integral part of these studies. The ability of the raft culture system to reproduce the complete HPV life cycle is a technical advance capable of providing important and novel insights concerning the regulation of viral transcription and protein expression during the complete HPV life cycle. When the proposed studies are completed we expect to have defined the role of cis regulatory elements located upstream of the major HPV31b promoter in viral transcriptional control, viral DNA replication, and virion synthesis. Additionally, we expect to have defined the temporal and spatial expression patterns of HPV31b proteins and to correlate viral protein expression with transcript expression, promoter usage, expression of epithelial differentiation-specific proteins, and virion morphogenesis.

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- **Project Title: HPV ONCOPROTEIN EXPRESSION IN CERVICAL CANCER**

  Principal Investigator & Institution: Johanning, Gary L.; Nutrition Sciences; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2001; Project Start 12-JAN-2000; Project End 31-DEC-2002

  Summary: (Applicant's Abstract) The overall objective of this project is to develop diagnostic assays that are capable of identifying a subset of patients with cervical dysplasia who are at increased risk of developing **cervical cancer.** Human papillomavirus (HPV) type 16 E6 or E7 oncoproteins are major causative agents in **cervical cancer,** and are expressed in high grade dysplastic lesions of the cervix and in cervical tumor tissue. The applicant's goal is to develop and evaluate assays of E6 and E7 expression that can be used to examine tissues from patients at risk for developing **cervical cancer.** He will use this information to determine whether E6 and E7 oncogene expression is associated with the grade of cervical dysplasia. At present the DNA that codes for HPV oncoproteins can be detected for diagnosis of high-risk HPV infection, but the presence of HPV type-specific DNA does not provide information about whether the oncoproteins are actually being expressed. Data from the applicant's preliminary studies using RT-PCR and RNA in situ hybridization demonstrated that E6 and E7 expression can be detected in the tissue of individuals with cervical dysplasia and **cervical cancer.** He hypothesizes that HPV 16 E6 and E7 oncoprotein expression, assessed using diagnostic assays of HPV oncogenes, oncoproteins or their antibodies in blood and tissues of patients with cervical dysplasia or **cervical cancer** will correlate with the grade of cervical dysplasia or **cervical cancer.** To test this hypothesis, he proposes to produce and E6 fusion protein, to develop new diagnostic assays for detecting E6 and E7 RNA and oncogene expression in cervical tissue, and to use the E6 fusion protein to develop assays for detecting antibodies specific against E6 and E7 oncoproteins in sera from patients at risk for developing **cervical cancer.** The assays of expression of these oncogenes and their antibodies can be used to monitor for the effectiveness of **cervical cancer** treatment modalities, and would allow investigators to make interventions in patients with intraepithelial neoplasia to decrease the risk of future development of invasive cancer.

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- **Project Title: HPV SPECIFIC CELLULAR IMMUNITY IN CERVICAL INTRAEPITHELI**

  Principal Investigator & Institution: Sastry, Jagannadha K.; Associate Professor; Veterinary Science; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-MAY-2004

Summary: (Adapted from the Investigator's Abstract) Epidemiological studies have clearly established that human papillomas (HPV) infection is a major risk factor for **cervical cancer.** A number of individuals undergo remission either spontaneously or after clinical intervention, while others, particularly those exhibiting immudeficiency, seem to proceed to develop invasive cancer. It is important to understand the immunological basis for the clinical remission of HPV-associated cervical neoplasia for designing proper intervention strategies. We have determined cell-mediated immunity (CMI) responses specific to synthetic peptides from E6 and E7, the two major oncoproteins of high risk type HPV (HPV-16), in a subset of patients attending the colposcopic clinic. These patients underwent excisional or ablative treatment for cervical intra epithelial neoplasia (CIN) at least six months prior to enrolling in the study. Significant differences were observed in proliferative responses directed against peptides from both the E6 ($p=0.002$) and E7 ($p<0.001$) between women without cytological or histological evidence of CIN (disease-free group) and those with a histological diagnosis of recurrence for CIN. Additional pilot studies on in vitro cytokine production mediated by the E6 and E7 peptides, showed a predominant TH1-cytokine profile in women from the disease-free group, while women with disease recurrence exhibited TH2-cytokine responses. On the other hand, none of the women in any of the study groups exhibited circulating antibodies reactive with the E6 and E7 peptides used in the study. Based on our results showing significantly high levels of HPV-peptide-specific TH1 responses in disease-free patients only, we hypothesize that HPV-specific CMI directed against the E6 and E7 oncoproteins is important for protection/recovery from HPV-associated CIN. To test this hypothesis, we propose to conduct a prospective cohort study of women positive for high-risk HPV types and treated for CIN by loop electrosurgical procedure. Our goals are to identify HPV peptides that can potentially serve as markers of protective immunity and for inclusion in immunotherapeutic and/or immunoprophylactic vaccine formulations against HPV-associated CIN. We will assess the pattern of the HPV-specific immunological responses over time, in particular CMI against E6 and E7 peptides corresponding to high-risk HPV types. We will also determine as to whether an association exists between the immune responses and additional HPV-related factors (persistence of infection and HPV type), and other risk factors associated with CIN such as smoking, sexual behavior, intrinsic and extrinsic hormonal factors.

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- **Project Title: HPV: BIOLOGY, CLINICAL SIGNIFICANCE AND EPIDEMIOLOGY**

  Principal Investigator & Institution: Galloway, Denise A.; Member and Program Head; Fred Hutchinson Cancer Research Center Box 19024, 1100 Fairview Ave N Seattle, Wa 98109

  Timing: Fiscal Year 2003; Project Start 10-APR-1987; Project End 31-MAR-2006

  Summary: We propose to continue multi-disciplinary studies of the role of human papillomaviruses (HPV) in the etiology of anogenital cancers. The program incorporates epidemiologic and molecular biology approaches in the three projects, with support form four core functions including virology, pathology, biostatistics and administrative support. The nucleus of this effort is a series of case-control studies investigating the risk factor involved in squamous cell **cervical cancer,** anal cancer, vulvar cancer, vaginal cancer, adenocarcinoma of the cervix and penile cancers. The results from these studiers will increase the data base developed over the past thirteen years of this Program Project. Established polymerase chain reaction procedures for identification of HPV

DNA together with the serologic tests developed in this program will continue to be used to establish virus infection and evidence of immune responses. A new focus on the occurrence of multiple cancers of the genital area is introduced, with the goal of establishing the primary and/or secondary state of tumors subsequent to an initial diagnosis. A group of women who have developed at least one additional primary anogenital cancer will be re- interviewed, together with appropriate controls, about exposures that may have contributed to the risk of a second primary tumor. Tissue and blood samples will be acquired for virus sequence, serologic and genetic testing. Determinations will be made of the uniqueness of the viral integration sites and the contribution of virus variants to the disease process. Studies of the roles of HLA genotypes in susceptibility to HPV- initiated cancer will be expanded. Comparative genome hybridization will continue to be used to id4entify loss or gain of chromosome regions and microarray methods used to investigate abnormal genes expression, with a particular focus of genes mapping on chromosomes 3, 5, and 20.

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- **Project Title: HUMAN PAPILLOVIRUS TESTING IN ADOLESCENTS**

  Principal Investigator & Institution: Kahn, Jessica A.; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, Oh 45229

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2007

  Summary: (provided by applicant): Jessica Kahn, M.D., M.P.H., completed clinical training in Adolescent Medicine and Gynecology at Children's Hospital, Boston and an MPH degree at the Harvard School of Public Health in 1999. She then joined the faculty at Children's Hospital Medical Center to pursue a career in patent-oriented research. David Bernstein, MD, the project Sponsor, brings expertise in clinical research regarding viraI STI, has extensive NIH funding, and has experience mentoring new investigators. The Sponsor, Advisory Board Members and Collaborators form a multidisciplinary research team with diverse expertise. The research environment will support a didactic program that includes relevant courses in advanced qualitative and quantitative methods, training in research ethics, and interaction with other clinical investigators. Dr. Kahn's overall career goal is to become an independent clinical investigator whose work will focus on the prevention of HPV infection and **cervical cancer.** She plans to achieve this goal through the translation of data regarding 1) the biomedical aspects of HPV infection and 2) the psychological and behavioral impact of testing for HPV into adolescent- specific, effective clinical strategies for **cervical cancer** prevention at the individual and population levels. The objective of this research plan is to explore the potential role of HPV testing in **cervical cancer** prevention programs targeting adolescents. The specific aims and methods for achieving each aim follow. Aim 1 To determine predictors of Pap smear foIlow-up in adolescents. Aim 1 will be examined using existing prospective data from a sample of 490 urban, racially diverse adolescents. Aim 2 To examine the psychological and behavioral effects of positive HPV testing in female college students. Aim 2 will be examined using existing longitudinaI data from a sample of 608 racially diverse college women. Aim 3 To explore the psychological, behavioral, and relationship-related effects of positive HPV and Pap smear testing in adolescents. Aims 3, 4, and 5 will be examined using prospectively collected, qualitative and quantitative data in a sample of 250 urban adolescent girls at high risk for HPV infection. Aim 4 To determine the accuracy and acceptability of self-testing for HPV DNA in the above sample of urban adolescent girls. Aim 5 To determine the cumulative prevalence and rates of persistence and regression of HPV infection, and correlation of HPV test results with cervicaI cytology, in the above sample of urban adolescent girls.

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- **Project Title: IMMUNE MECHANISMS OF HUMAN PAPILLOMAVIRUS**

  Principal Investigator & Institution: Mosmann, Tim R.; Professor and Director; Microbiology and Immunology; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2001; Project Start 01-AUG-2000; Project End 31-JUL-2004

  Summary: Human Papillomavirus is a widespread pathogen that causes different types of warts, and is also the main cause of **cervical cancer.** In many patients, the immune system limits the spread of infection, but does not destroy the wart. Patients with deficient immune systems, or those taking immunosuppressants, have increased susceptibility to the spread of warts. Regression of warts can occur spontaneously or in response to some treatments, suggesting that under some circumstances, the immune system can cure the infection. We believe that the immune response is capable of presenting or eliminating HPV lesions. An understanding of the immune response against HPV that results in rejection or prevention of lesions is necessary to design vaccines that will prevent infection or induce the immune system to attack and destroy warts. In both cases, the prevention of long- term epithelial lesions should also prevent the higher rates of cancer that are associated with lesions induced by some strains of HPV. In this project, we will mount a comprehensive effort to understand the ways in which HPV interferes with the immune response in the skin (Project 1), the antigen specificity of the immune response against HPV (Project 2) and the type of immune mechanisms that are effective against HPV lesions (Project 3). This will lead to a more complete picture of the interplay between HPV and the immune system, allowing the rational design of two types of vaccine: protective vaccines that will prevent infection from becoming established or causing a skin lesion; and therapeutic vaccines that will be given to individuals who already have warts or cervical lesions, to cause regression of the lesions and reduce the risk of cancer.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: INFRARED MICROSPECTROSCOPY FOR CERVICAL CANCER SCREENING**

  Principal Investigator & Institution: Diem, Max; Professor; Chemistry; Hunter College 695 Park Ave New York, Ny 10021

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2007

  Summary: (provided by applicant): This proposal is aimed at establishing Infrared Microspectroscopy (IR-MSP) as a faster, less expensive, more objective and more accurate technology for the detection of cervical dvsplasia than presently used methods. Screening for cervical disease is presently carried out via a cytological procedure (the Papanicolaou, or "Pap" test), that was first proposed in the late 1940's [Papanicolaou, 1948]. Although regularly scheduled gynecological screening using the Pap test has reduced the incidence of, and mortality from, **cervical cancer** enormously, there remains a relatively high rate of inaccurate or inconclusive diagnoses [US Department of Health and Human Services, 1989]. Classical cytology is a visual inspection method based on locating and recognizing cells with altered morphology as an indicator of disease. The morphological changes are a consequence of cellular mutations. Although well established, this approach suffers from the fact that the interpretation of morphological change is human-based and therefore, subjective in nature. Furthermore, operator fatigue, training and experience influence the quality, reliability and reproducibility of

cytological diagnoses. To alleviate the inherent limitation of visual inspection, computer based inspection by imaging technology has been developed and utilized over the past ten years. However, computer based image analysis has not significantly improved the reliability of the diagnoses, and has not proved cost effective [Hutchinson, 1996]. IR-MSP is a novel technique that recognizes abnormality by detecting cellular composition and variations therein, rather than by changes in morphological features. In fact, IR-MSP detects the precursor of the morphological change. The actual measurement carded out in IR-MSP is objective and quantifiable; consequently, the diagnostic method is more sensitive, specific, reproducible and reliable than existing methods. In this proposal, the methodology for IR-MSP testing of cervical smears will be developed, including the purification of the exfoliated cells, preparation of a cell monolayer on a suitable substrate, spectral imaging of about 104 individual cells via an infrared microspectrometer equipped with a focal plane array detector, and analysis of the collected data via multivariate statistical methods to arrive at a diagnosis. This work has the potential to improve **cervical cancer** screening by further reducing false positive and false negative diagnoses, and introducing fast and point-of-care routine screening tests.

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- **Project Title: LATINA CERVICAL CANCER SURVIVORSHIP**

  Principal Investigator & Institution: Wenzel, Lari B.; Associate Adjunct Professor; Anesthesiology; University of California Irvine Campus Dr Irvine, Ca 92697

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2004

  Summary: (provided by applicant): The incidence and mortality rates for invasive **cervical cancer** in minority, low-income, and poorly educated women exceeds that for white, higher income, and better educated women. In southern California the incidence and morality rates for **cervical cancer** are nearly twice that of non-Latina white women. Despite the disproportional disease burden in the Latina community, the Latina **cervical cancer** survivorship experience has not been addressed. Our preliminary data indicates that non-Latina white **cervical cancer** survivors report significant long-term QoL disruptions and late-effects of treatment. However, we cannot assume that non-Latina data are generalizable to other cultures. Representation from the Latina survivor cohort is essential if we hope to advance cancer prevention and cancer control for this growing population. Therefore, we propose to conduct an exploratory study utilizing an ethnographic research methodology to identify QoL, survivorship and gynecologic health variables within the Latina community. This approach is ideal for exploratory studies which are designed to better understand culturally based beliefs and generate hypotheses for future research. Specifically, we will (1) identify QoL and survivor-specific variables through ethnographic interviews in a Latina **cervical cancer** survivor sample, and identify QoL and gynecologic health variables in age-matched Latina controls; (2) explore QoL differences among Latina **cervical cancer** survivors and age-matched Latina controls; and (3) examine the feasibility of longitudinal QoL data collection in this population. To achieve these aims, we will enroll 30 survivors from the estimated 425+ Latina cases identified through the Cancer Surveillance Program of Orange, San Diego and Imperial Counties (CSPOC/SanDIOC) tumor registry who completed cancer treatment 1-5 years earlier. Age-matched Latina controls will be identified through the Single Visit **Cervical Cancer** Prevention Program (SVCCP), which has accrued 2,000 Latina participants in Orange County from 1999-2001. As the population of Hispanics grows in the United States, it will become critical to proactively address **cervical cancer** prevention, treatment and survivorship within the Latina

community. An exploratory study to identify issues and examine follow-up feasibility is an essential step toward this effort.

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- **Project Title: LIGHT SCATTERING AND NORMAL TISSUE MODELS**

  Principal Investigator & Institution: Mourant, Judith R.; Professor; None; University of Calif-Los Alamos Nat Lab Ms G758 Los Alamos, Nm 87545

  Timing: Fiscal Year 2001; Project Start 15-MAY-1997; Project End 31-JUL-2006

  Summary: Optical techniques for tissue diagnosis without the removal of tissue are now being developed which offer significant advantages over standard techniques, such as tissue biopsy, both in terms of patient care and medical costs. For example, optical techniques are faster, sedatives are not needed, and complications associated with tissue removal such as infection are eliminated. The aim of this proposal is to develop and test polarized elastic scattering spectroscopy. Elastic scattering spectroscopy (ESS) measures the wavelength dependence of light that has entered the tissue, been scattered within the tissue and re-emitted. In polarized ESS the delivered light is polarized and the detected light is measured through polarizers. The detected light can provide information about both the morphological properties and the hemoglobin concentration. For example, a sensitivity to the rate at which cells are replicating has been demonstrated and measurements of model systems have shown that scatterer size and concentration can be determined. In order for this technique to reach its full potential an understanding of the fundamental interactions of light with tissue is needed. The first specific aim of this proposal is to determine how specific structural features of cells contribute to light scattering. The next aim will be to examine light scattering differences between tumorigenic and non-tumorigenic epithelial cells. Epithelial cells are particularly interesting, because most cancers originate from epithelial cells. Previous work demonstrated that the environment induced by cells in 3-D culture can cause a difference in light scattering from tumorigenic and non-tumorigenic cells. In parallel with the study of scattering properties improved measurement techniques will be developed and implemented for in vivo use. Finally, clinical trials will be performed to determine the utility of polarized elastic scattering spectroscopy to detect/diagnose squamous epithelium, reactive/repairing tissue, low grade dysplasia, high grade dysplasia and invasive carcinoma. Screening and diagnosis of **cervical cancer** is an ideal arena for the entry of optical techniques for cancer detection. The tissue is easily accessible and the low-accuracy Pap smear test has already demonstrated the utility of screening methods. ESS has the potentially to rapidly sample tissue and pinpoint locations of specific pathologies. Potentially ESS could replace Pap smears as a less frequent test or serve as an adjunct. If polarized ESS could be used to determine the significance of an ASCUS (atypical squamous cells of uncertain significance) Pap smear result, it could result in significant cost savings. ASCUS is the most common anomaly detected by Pan smears and annual follow up is estimated to cost 4.5 billion dollars per year.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MALIGNANT PROGRESSION IN PAPILLOMAVIRUS TRANSGENIC MICE**

  Principal Investigator & Institution: Hanahan, Douglas A.; Professor; Hormone Research Institute; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

Timing: Fiscal Year 2001; Project Start 01-SEP-1988; Project End 31-DEC-2001

Summary: (adapted from the investigator's abstract) Transgenic mouse models of human cancers present the opportunity to elucidate pathways of cancer development, through which a normal cell in its natural microenvironment is progressively converted into an aberrant cancer, acquiring characteristics that contribute to the resultant cancer phenotype. This laboratory has developed transgenic mice that express the human papillomavirus type 16 (HPV-16) oncogenes in basal keratinocytes; these 'K14-HPV16' mice develop squamous cell carcinomas of the epidermis, and, in concert with chronic estrogen treatment, cervical and vaginal squamous cancers. Both epidermal and cervical pathways to carcinoma are characterized by progression through histologically distinct stages. In humans, the oncogenes of HPV16 and related HPV subtypes are found in a majority of cervical carcinomas, and in premalignant lesions thought to precede those cancers. The overall goal of this proposal is to characterize and assess the function contributions of cellular parameters that appear during tumor progression in this mouse model of squamous carcinoma, parameters hypothesized to be influencing the developing cancers in distinct and complementary ways to those directly effected by the human viral oncogenes; these parameters are: 1. Selective upregulation of a fibroblast growth factor receptor in aggressive, metastatic cancers. 2. The acquired resistance to induction of apoptosis, the process of programmed cell suicide, which is implicated as a growth-limiting mechanism that must be controlled by successful cancers. 3. The upregulation of telomerase, an enzyme that protects the ends of chromosomes during cell proliferation and thereby sustains tumor growth potential, in aggressive epidermal carcinomas. 4. The apparent capability of CD8+ T cells to restrict the appearance of invasive squamous cancers. 5. Dermal infiltration by mast cells in epidermal dysplasias, and their role in malignant progression. The long term goal is to define the pathways to epidermal and **cervical cancer** in mice expressing oncogenes implicated in a relevant human cancer, identifying the critical cellular and molecular parameters governing progression, and eventually utilizing the knowledge of mechanism to design therapeutic and preventative interventions that can be evaluated in this preclinical model of human carcinogenesis.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MDA-7: NOVEL CANCER THERAPEUTIC GENE**

  Principal Investigator & Institution: Fisher, Paul B.; Professor/ Chernow Research Scientist; Pathology; Columbia University Health Sciences New York, Ny 10032

  Timing: Fiscal Year 2002; Project Start 10-SEP-2002; Project End 31-AUG-2007

  Summary: (provided by applicant): Abnormalities in differentiation are common occurrences in human cancers. Treatment of human melanoma cells with combination of recombinant human fibroblast interferon and the protein kinase C activating compound mezerein results in a loss of tumorigenic potential that correlates with an irreversible suppression in proliferative ability and induction of terminal differentiation. It is hypothesized that this process involves the differential expression of genes, which regulate cancer cell growth and differentiation. Through the use of subtraction hybridization, we have identified a gene associated with induction of irreversible growth arrest, cancer reversion and terminal differentiation in human melanoma cells, melanoma differentiation associated gene-7 (mda-7). Mda-7 is a novel gene that displays reduced expression in metastatic human melanoma versus normal human melanocytes. Remarkably, when metastatic human melanomas are induced to irreversibly growth arrest, terminally differentiate and lose cancerous properties, mda-7 expression increases dramatically. Ectopic expression of mda-7 using a recombinant adenovirus,

Ad.mda-7, results in growth suppression and apoptosis in diverse cancer cell types, including tumor cells with wild-type p53 or mutant for p53, Rb, or p53 + Rb. Moreover, growth and progression of human breast and **cervical cancer** cells in vivo in nude mice is inhibited by Ad.mda-7. In contrast, no deleterious effect is apparent after infection of normal human epithelial or fibroblast cells with Ad.mda-7. Based on these pre-clinical findings, Phase I Clinical Trials are now being performed to evaluate mda-7 for cancer therapeutic applications. In these contexts, an in-depth mechanistic analysis of this fascinating and potentially significant tumor suppressor molecule is warranted. Selective induction of apoptosis in human breast cancer cells correlates with an elevation in the level of the pro-apoptotic protein BAX and an increase in the ratio of BAX to BCL-2, an inhibitor of apoptosis. The mechanism by which mda-7 modifies cancer progression an suppresses human cancer cell growth will be evaluated with a particular emphasis on its functional relationship to apoptosis. Recent information indicates that mda-7 is a novel member of the IL-10 cytokine gene family. Experiments will focus on defining the functional domains of mda-7 that determine biological activity and identifying biochemical pathways, interacting partners and potential targets or mediators of activity. Studies will also examine the mechanism underlying mda-7's "bystander effect." These investigations will provide important insights into a novel cancer growth-suppressing gene with potential relevance to a broad spectrum of human cancers. As such, this gene may serve as a target for selectively intervening in the neoplastic process, thereby attenuating or eliminating cancer aggressiveness and metastasis. Understanding the mode of action of mda-7 will promote translational applications for cancer therapy.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MOLECULAR APPROACHES TO CERVICAL CANCER SCREENING**

  Principal Investigator & Institution: Smith-Mccune, Karen K.; Assistant Professor; Ob, Gyn and Reproductive Scis; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 94122

  Timing: Fiscal Year 2001; Project Start 15-SEP-2000; Project End 31-AUG-2003

  Summary: (Adapted from the investigator's abstract) **Cervical cancer** is the leading cause of cancer morbidity and mortality in women worldwide. (1) In United States, precancerous changes, known as cervical dysplasia, are detected on Pap tests in approximately 2 million women annually. Serious limitations of the Pap test are: (1) It is too expensive and labor-intensive for use in developing nations. (2) Although it is successfully at detecting invasive cancer and cancer precursors, it also detects 2.5 million minor abnormalities annually in the USA that are for the most part clinically insignificant. The availability of prognostic markers to distinguish patients with clinically benign atypical changes from those with cancer and high grade dysplasia would be extremely useful. The goal of this proposal is to characterize novel molecular markers of dysplasia that can be identified in cells scraped from the cervix. Work performed in her laboratory and others has established that molecular markers of angiogenesis are upregulated progressively in the different grades of cervical dysplasia, and between neoplastic cervical disease and normal cervix (4-12). The research outlined in this grant proposal is based upon the following hypothesis: Factors mediating angiogenesis in cervical dysplasia can be detected in exfoliated cervical cells and can be exploited to assist in more effective **cervical cancer** screening. Specific Aim 1. Determine the association between the relative mRNA levels of angiogenic factors with the clinical cytological diagnosis in cells scraped from the cervix. 1A: Determine relative mRNA levels of vascular endothelial growth factor/vascular permeability factor (VEGF/VPF),

angiopoitin-1 (ang-1) and angiopoitin-2 (ang-2) in a cohort of 60 cytologically verified cervical samples representing 20 with normal cytology, 20 with low grad squamous intrepithalial lesions (SIL), and 20 with high grade SIL. 1B: Determine the sensitivity, specificity, and positive and negative predictive values of BEGF/VPF, ang-1 and ang-2 mRNA levels as markers for low grade and high grade SIL. Specific Aim 2. Determine the association between VEGF/VPF protein levels with the clinical cytological diagnoses in cells scraped from the cervix. 2A: Determine relative protein levels of VEGF/VPF in a cohort of 60 cytologically verified cervical samples representing 20 with normal cytology, 20 with low grade SIL, and 20 with high grade SIL. 2B: Determine the sensitivity, specificity, and positive and negative predictive values of VEGF/VPF protein expression as a marker for low grade and high grade SIL.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MOLECULAR EPIDEMIOLOGY OF PERSISTENT HPV INFECTION**

  Principal Investigator & Institution: Franco, Eduardo Lf.; Professor and Director; Mc Gill University James Admin. Bldg., Room 429 Montreal, Pq H3a 2T5

  Timing: Fiscal Year 2003; Project Start 11-SEP-1996; Project End 31-JUL-2004

  Summary: (provided by applicant): This competing continuation grant is the second and last request for renewal of CA70269, the original funding for an epidemiologic study of the natural history of human papillomavirus (HPV) infection and cervical neoplasia in a low-income female population in Sao Paulo, Brazil. In collaboration with Brazilian colleagues, three of the authors began the study in 1993 in an attempt to understand attributes of the natural history of HPV that could be instrumental in designing strategies for preventing **cervical cancer.** Considering the public health and economic importance of **cervical cancer** and the widespread interest in HPV vaccines and in using HPV in cancer screening there is a need for long-ranging multidisciplinary studies of the natural history of HPV. The study accrued 2529 female subjects through March 1997. Subjects have been followed up in scheduled returns every 4 months in the first year, and twice yearly thereafter for a total of 5 years. Participants undergo a questionnaire-based interview have a cervical specimen taken for Pap cytology and HPV testing, and a blood sample drawn for HPV antibody serology. Follow-up will have been completed at the time current funding for the cohort study finishes in August 2002. The study's original objectives (1996-99 funding period) were: (1) to study the prevalence and incidence of persistent HPV infection in asymptomatic women; (2) to verify the hypothesis that persistent HPV infection increases risk of cervical lesions; (3) to search for determinants of persistent cervical HPV infection; (4) to search for molecular variants of HPV that may lead to an increased risk of cervical lesions; (5) to verify the hypothesis that viral burden in the cervix may be correlated with persistent infections and with lesion risk; and (6) to study the antibody response to HPV as a predictor of persistent HPV infection and of lesion risk. In the last successful continuation (1999-02 funding period) these objectives were expanded to include: (7) the search for specific HLA haplotypes associated with HPV persistence and lesion severity, and (8) to test the hypothesis that p53 gene polymorphism may influence resistance against viral persistence and to lesion development. This competing continuation is to conduct in-depth statistical analyses of the database accrued during the study and to add a new objective: (9) to study the role of insulin growth factors in mediating risk of persistent HPV infection and cervical lesions.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MOLECULAR GENETICS OF CERVICAL CANCER PROGRESSION**

  Principal Investigator & Institution: Vundavalli, Murty V.; Pathology; Columbia University Health Sciences New York, Ny 10032

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): **Cervical Carcinoma** (CC) is preceded by distinct preneoplastic changes called"cervical intraepithelial neoplasia" (CIN). CC provides a prototype system for studying evolution of genetic mutations in progression because of its characteristic preinvasive stages. The biological behavior of CINs varies in their progression to invasive cancer and the genetic basis of it is poorly understood. Molecular genetic studies to date in CC have identified amplification of oncogenes such as ERBB2, c-myc genes and frequent allelic imbalances affecting multiple chromosomal arms such as 2q, 3p, 4q, 5p, 6p, and 11q. Reports indicate the occurrence of similar genetic alterations in precancerous lesions, suggesting that these changes play crucial role in the progression of CC. However, the sequence of genetic alterations and their role in predisposition of CINs to invasive cancer is unclear. To address these questions, we propose to undertake a systematic study of genetic alterations through the spectrum of tumor progression with the following specific aims: Characterization of genetic changes in invasive and preinvasive cervical cancerous lesions. We propose a detailed study of the genetic alterations of gene amplification and deletion mapping utilizing the techniques such as laser microdissection, comparative genomic hybridization, microarray cDNA chips, and loss of heterozygosity. The study is expected to generate gene amplification profiles, and allelic deletions through the spectrum of CC development. This will enable us to define the temporal relationship of genetic alterations with various stages of progression that might provide insights into the genetic mechanisms of CC. 2. Development of a genetic prognostic model for identifying high-risk dysplastic lesions. The data generated from these studies will be used to determine the clinical significance and to develop a genetic prognostic model for identifying high-risk CINs that progress into invasive cancer.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MULTIMODAL SPECTROSCOPIC EVALUATION OF CERVICAL CANCER**

  Principal Investigator & Institution: Bambot, Shabbir B.; Spectrx, Inc. 6025-A Unity Dr Norcross, Ga 30071

  Timing: Fiscal Year 2001; Project Start 01-AUG-2001; Project End 31-JUL-2002

  Summary: (Verbatim from the Applicant's Abstract): **Cervical cancer** is the second most common cause of cancer in women worldwide and the leading cause of cancer related mortality in women in developing countries. We have developed real time non-invasive point-of-care devices to detect early cancerous conditions of cervix. Our preliminary analyses on data collected from a total of 133 patients and have shown promising results. We are continuing to collect data and will include the entire data set into the analysis as part of our phase I objective. Given our limited data set, however, it is not possible to project any definite performance benchmark. We will propose this task to the training and validation phase in a Phase 2 proposal. For the present we want to analyze the data for the purpose of determining the optimum clinical device for the validation phase. To support data accrual in the validation phase we will make multiple clones of this device for deployment in a multicenter clinical trial. The objective of the data analysis is to arrive at this validation device by simplifying and consolidating the complexity and the many features built into each prototype. This will also reduce the

possibility of overtraining by reducing the number of parameters we build into our algorithm. PROPOSED COMMERCIAL APPLICATION: The product of this research will be a prototype device capable to spectroscopically detecting and/or diagnosing **cervical cancer.** Our device has, upon commercialization, the potential to replace or aid the current Pap test as well as to replace the current methods of colposcopy, biopsy and histology. The target physician group for the cervical application is the Ob-Gyn segment. It is estimated that there are at least 30,000 physicians in this segment and upwards of $6 billion spent each year in the US on cervical disease.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NOTCH-1 IN REGULATION OF APOPTOSIS IN TUMOR CELLS**

  Principal Investigator & Institution: Miele, Lucio; Associate Professor; Ob, Gyn, and Reproductive Med; Loyola University Medical Center Lewis Towers, 13Th Fl Chicago, Il 60611

  Timing: Fiscal Year 2001; Project Start 13-JAN-2000; Project End 31-AUG-2001

  Summary: Notch genes encode transmembrane receptors that control cell differentiation in numerous cell types during development. Humans and mice have 4 homologous notch genes. Mutations causing constitutive activation of notch-1,-2 and 4 are oncogenic in vivo and in vitro. Clinically, constitutive activation of notch-1 is associated with T-cell acute lymphoblastic leukemia (T-ALL), and strikingly increased expression with altered intracellular distribution of notch-1 have been demonstrated in various human malignancies and pre-neoplastic lesions (uterine cervix, colon and lung). We and others have recently discovered that notch-1 has anti-apoptotic activity in vitro in transformed cells in various experimental models. Additionally, we found that downregulating the expression of notch-1 in murine erythroleukemia (MEL) cells in the presence of differentiation- inducing hybrid polar drugs leads to massive apoptosis. Whether notch-1 affects apoptosis in non-transformed cells which do not overexress it remains unknown. Our hypothesis is that notch-1 plays an important role in regulating apoptosis susceptibility in notch-1 expressing tumor cells. This implies that interfering with notch-1 expression or signaling may be used to enhance the efficacy of chemotherapy or radiotherapy in human malignancies expressing notch-1. Our long term objective is the development of therapeutic regimens targeting notch-1 using gene therapy, recombinant notch-1 antagonists or notch-1 monoclonal antibodies for clinical testing in human malignancies expressing notch-1. We have generated experimental agents in each of these catagories. Our Aims our as follows: 1. To determine if notch-1 participates in apoptosis regulation in normal cells, by studying its role in thymocyte apoptosis using notch-1 antagonists and novel transgenic mice we have developed. 2. To elucidate the mechanism(s) through which notch-1 protects MEL cells from apoptosis, by investigating signaling pathways known to be linked to notch-1 which participate in regulating apoptosis. 3. To conduct pre-clinical studies of notch-1 inducible antisense retrovirus vectors, a recombinant notch-1 antagonists and a notch-1 blocking monoclonal antibody in mouse tumor models. The experimental agents will be studied alone and in combination with antineoplastic drugs. Studies will be conducted in both immunodeficient animals with human **cervical cancer** cells and immunocompetent animals with syngeneic murine tumor cells transformed by human papillomavirus 16 (HPV16). These experiments will elucidate the possible uses of notch-1 as a target for cancer treatment and the mechanisms of notch-1 targeting agents. Additionally, they will provide information on the safety profile of these agents and initial proof of concept for clinical trials of notch-1 targeting agents in notch-1 expressing malignancies.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NOVEL APPROACH TO CERVICAL CANCER PREVENTION**

  Principal Investigator & Institution: Chen, Jason J.; New England Medical Center Hospitals 750 Washington St Boston, Ma 021111533

  Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 30-SEP-2001

  Summary: Cervical cancer is one of the most frequent causes of cancer and death in women worldwide. Each year in the United States, 15,000 women develop **cervical cancer** and approximately 4,500 die from the disease. Cervical infection with human papillomaviruses (HPV) is the primary risk factor for **cervical cancer. Cervical cancer** has a long preclinical phase between HPV infection and invasive carcinoma that makes its prevention possible. My long-term goal is to understand the mechanisms by which HPV induces tumors and to develop preventive strategies for elimination of **cervical cancer.** HPV encodes a protein E6 that is essential for viral replication and HPV-induced cellular transformation. E6 is a multi-functional protein that performs its functions through interaction with cellular proteins. We have recently identified an alpha helical E6 binding domain that is conserved among E6-binding proteins. Our mutational analysis has identified amino acids within the consensus motif that are important for E6 binding. These amino acids and the three- dimensional structure of the E6-binding domain defined a first generation pharmacophore-the spatial distribution of the atoms needed to bind E6. We hypothesize that small molecules mimicking the pharmacophore will bind E6 and block the interaction of E6 with its cellular binding proteins and thus inhibit E6 biological activities that lead to the transformation of HPV-infected cells. We have used this structure-based drug design to select small molecules that could inhibit the interaction of E6 with its cellular partners. Our preliminary in vitro studies have identified multiple potential E6 inhibitors. In this proposal, we will describe experiments to further characterize these compounds. Our specific aims are 1) In vitro specificity test for the potential E6 inhibitors; 2) To examine the ability of potential E6 inhibitors to disrupt biological activities of E6 in tissue culture assays. These studies may lead to the development of drugs to treat HPV infection and to prevent **cervical cancer.**

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NOVEL OPTICAL SYSTEM FOR EARLY CERVICAL CANCER DETECTION**

  Principal Investigator & Institution: Mcnichols, Roger J.; Chief Scientist and Vice President; Biotex, Inc. 8018 El Rio Houston, Tx 770544104

  Timing: Fiscal Year 2003; Project Start 09-SEP-2003; Project End 31-AUG-2004

  Summary: (provided by applicant): Approximately 13,000 cases of invasive **cervical cancer** will be diagnosed in the United States, in 2002, and approximately 4,100 women will die from the disease. The 5-year relative survival rate for the earliest stage of invasive **cervical cancer** is 91%. The overall (all stages combined) 5-year survival rate for **cervical cancer** is about 70%. For cervical precancer the 5-year survival rate is nearly 100%. Thus, early detection of cervical precancerous lesions can have a dramatic impact on **cervical cancer** mortality rates, increasing five-year survival rates from 70% to about 100%. Routine Papanicolaou (Pap) smear is the current standard for **cervical cancer** and pre-cancer screening, however, a number of studies have indicated that this method may miss as many as 20-30% of cervical cancers. For this reason, tissue autofluorescence examination of cervical tissue has been examined as a means for increasing sensitivity to early neoplastic changes in the cervix. While sensitivity of this technique can be as high as 85-90%, its specificity is low resulting in significant numbers of false positives.

Optical coherence tomography (OCT) is a new non-invasive imaging technique which can image morphological details of soft tissues with resolution close to that of conventional light microscopy. However, the time and small imaging field associated with OCT make it impractical for routine screening by itself. Previously, in an animal model of epithelial cancer, we have demonstrated that the use of tissue autofluorescence imaging used to guide selective application of OCT imaging results in a technique with superior sensitivity and specificity over fluorescence imaging alone. We hypothesize that fluorescence image guided OCT (FIGOCT) may become a useful clinical tool for the evaluation and screening of cervical tissues. In this proposal we design, build, and test a new optical probe suitable for exploring the feasibility of FIG-OCT in the human cervix. Such a probe would be useful in detecting epithelial cancers in other easily accessible sites in the body including the urinary tract, bladder, gastro-intestinal tract, colon, and oral cavity.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ONCOLYTIC ADENOVIRUSES--CERVICAL CANCER GENE THERAPY**

  Principal Investigator & Institution: Lieber, Andre M.; Medicine; University of Washington Seattle, Wa 98195

  Timing: Fiscal Year 2001; Project Start 18-MAR-1999; Project End 31-DEC-2003

  Summary: (from the abstract) The investigator writes that the majority of malignant tumors are resistant to radio- or chemotherapy in advanced stages mainly due to loss of p53 function. New tumor gene therapy approaches must consider targeting every cell in the primary tumor and all metastases with a maximal cytotoxic index for cancer cells. First generation adenovirus (Ad) vectors are attractive for cancer therapy because of their potential to transduce all tumor sites after systemic application. These vectors are deleted in the E1 region, rendering them highly replication-defective. This proposal is based on the observation that E1-deleted Ad vectors replicate selectively in HPV associated **cervical carcinoma** cells because the HPV E6/E7 proteins which are responsible for the maintenance of the malignant phenotype effectively complement the deleted Ad E1 proteins. The goal is to develop oncolytic Ad vectors for **cervical cancer** that replicate in tumor-specifically and disseminate throughout the tumor, selectively killing all tumor cells by viral cytolysis or p53-independent apoptosis. The studies will be performed in immunodeficient mice with hepatic tumors derived from **cervical carcinoma** cell lines or in immunocompetent mice with HPV induced tumors. The specific aims are: 1. To develop an expression system based on a unique Ad-AAV hybrid vector, which activates a tumor-specific promoter only upon viral DNA replication. 2. To test whether virus dissemination throughout the tumor can be obtained if virus release from infected tumor cells is supported by cytolysis or apoptosis induced after viral replication is completed. For this purpose the investigators will use the AD-AAV system and investigate virus spread and anti-tumor efficacy after a) E3-11.6K expression, and b) expression of a transdominant i-kB mutant to sensitize tumor cells to apoptosis induced by TNF treatment or TRAIL expression. 3. To investigate the effect of antiviral immune responses on oncolytic vector spread and, if required, to suppress these responses by expression of Ad E3 proteins and/or transient immuno-modulation. These studies will give valuable information about the influence of apoptosis and host immune responses on replication-competent Ad vectors developed for tumor gene therapy. This proposal may provide a means for treatments of **cervical carcinoma** and has potential application for other malignancies with deregulated pRb/p16 functions that allow for replication of E1-deleted Ad vectors.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ORAL IMMUNIZATION AGAINST ANOGENITAL HPV DISEASE**

  Principal Investigator & Institution: Rose, Robert C.; Assistant Professor; Medicine; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2001; Project Start 02-APR-2000; Project End 31-MAR-2004

  Summary: It is now accepted that invasive **cervical cancer** is caused by infection with human papillomaviruses (HPVs), and that the development of an effective vaccine would reduce the incidence of this disease. HPV virus- like particles (VLPs) and vasomeres are promising vaccine candidates, A major advantage of these immunogens is the ability to induce serum neutralizing antibodies. Results from studies performed in animals have shown that parenterally administered VLPs induce serum antibodies that provide protection against disease. We have found recently that comparable responses are induced in mice after VLP oral immunization which suggests that oral vaccination against anogenital HPV disease may be feasible. The long-term goal of this proposal is to reduce the incidence of anogenital HPV disease through the development of cost-effective and easily administered oral vaccines. Specific aims include: 1) Characterization of systemic/mucosal responses in animals following VLP/capsomere mucosal immunization. Relative immunogenicities of VLPs/capsomere of multiple HPV types will be evaluated in mice, with and without adjuvant, and using alternative mucosal routes for immunization Oral immunogenicity will also be tested in non-human primates (i.e., baboon), and efficacy will be tested in a mucosal papillomavirus challenge model (i.e., COPV). 2) Elucidation of mechanisms of VLP enteral uptake and presentation to the immune system. We will determine anatomic localization and patho of uptake of VLPs introduced into the gastrointestinal tract. 3) Development of recombinant plants for HPV vaccine delivery. HPV-11 and -16 L1 and L2 sequences will be expressed in potato; oral immunogenicity of these materials will be tested in mice. 4) Development of novel vaccine formulations. HPV VLPs containing factors that may elicit and/or enhance cellular immune responses (i.e., HPV early region gene products or genetic sequences encoding immunomodulatory factors), will be developed and tested in vitro and in vivo. Results will yield information germane to the development of cost-effective easily administered oral vaccines against invasive **cervical cancer** and other HPV associated diseases.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PHYTOCHEMICALS AND ESTROGEN-ENHANCED CANCERS**

  Principal Investigator & Institution: Auborn, Karen J.; Associate Professor, Head Phytochemical; Long Island Jewish Medical Center 270-05 76Th Ave New Hyde Park, Ny 11040

  Timing: Fiscal Year 2002; Project Start 30-SEP-1996; Project End 31-JAN-2007

  Summary: Many cancers could be prevented by diet. The connection between plant-derived dietary ingredients and the prevention of major cancers, especially the hormone-dependent cancers, is just beginning to be appreciated. Ongoing research concerns the phytochemical indole-3- carbinol (I3C), from cruciferous vegetables. I3C uniquely causes detoxification of marry carcinogens and "favorable" metabolism of estrogen. I3C and its acid condensation products are proving useful in preventing many cancers including those initiated by papillomavirus, viruses which increase susceptibility of cells to malignant transformation, as in the case of **cervical cancer.** 13C is anti-estrogenic and prevents estradiol-promoted **cervical cancer** in the HPV-

transgenic mouse. Current studies show that I3C induces apoptosis and decreases proliferation of cervical cells, both processess incompatible with cancer. We find I3C decreases Bcl-2 and increases BRCA-1, PTEN and TNFalpha; others show I3C affects CDK6. This proposal is to understand the mechanisms underlying the anti-cancer activities of I3C. It is probable that regulation of tumor formation and growth by I3C has estrogen-dependent and estrogen-independent components. Two different but related approaches include: in vivo experiments using normal mice and mice expressing BPV16 transgenes, and in vitro experiments to test specific mechanistic hypothesis. In vivo, the specific aims are to determine whether BC and its acid condensation product diindolymethane (DIM) both prevent and are useful in the treatment of **cervical cancer** , and whether DC/DIM decreases cell proliferation and increases apoptosis in developing tumors. In vitro, effects of I3C/D1M on cervical cells will be evaluated in relation to regulation of Bcl-2, BRCA-1, TNFalpha, P'TEN, CDK2 and CDK6, either by direct action at their promoters through the Ah receptor, or indirectly, by post-translational modification induced by estrogen metabolites such as 2-methoxy-estradiol. We will use gene chip technology to look for induction or repression of other genes involved in apoptosis and cell cycle progression.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: POR LA VIDA INTERVENTION MODEL IN CANCER EDUCATION**

  Principal Investigator & Institution: Navarro, Ana M.; Associate Professor; Family and Preventive Medicine; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, Ca 92093

  Timing: Fiscal Year 2001; Project Start 01-SEP-1994; Project End 31-AUG-2003

  Summary: The potential for reducing cancer incidence and mortality through prevention and early detection appears to be large.Research is showing the important role of nutrition in preventing cancer. Because many members of the Hispanic community have limited access to health care services and are in need of health promotion services, the Hispanic community is an appropriate target for specialized cancer prevention efforts. In particular, Hispanics of low level of acculturation and low level of formal education are a most important target for education about nutrition cancer control. The Por La Vida intervention model establishes community-based health promotion interventions, utilizing existing social networks and building on contemporary theories of social learning and social support Interventions based on the Por La Vida model have been successful in modifying behaviors relevant to cardiovascular risk and, most recently, breast and **cervical cancer** prevention. This study is a competing renewal of a project that examines the effectiveness of the Por La Vida intervention in the area of breast cancer education. This proposal will expand the scope of the intervention to nutrition cancer education. An additional goal of this proposal is to familiarize UCSD medical students and residents in the Family Medicine program with the Por La Vida intervention model in cancer education, and to encourage students to develop and complete related research projects. Approximately 36 consejeras will be recruited from the Hispanic community in San Diego and trained to conduct-the educational sessions. Each consejera will then recruit between 10 to 15 peers from the community to participate in the educational program. In addition, each of the program participants will identify two adults in their existing social networks with whom they will share information about cancer prevention. A randomized experimental control study with pretest, posttest, and follow-up has been designed to assess the impact of the educational interventions. Half of the consejeras will be trained and will conduct educational sessions in the Por La Vida nutrition cancer control curriculum. The other

half of the consejeras will be trained in the Por La Vi ia breast and **cervical cancer** early detection curriculum. We will examine the extent to which the interventions are implemented as planned. Furthermore we will investigate (l) the impact of the intervention on knowledge of nutrition cancer prevention and breast cancer screening on program participants, and (2) the impact of the diffusion of cancer prevention information mediated through program participants to friends and family. Outcome measures will be collected through telephone interviews and review of medical records. In addition, face-to-face interviews will be conducted to collect three-day food records from 15% of the program participants.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: POSITION EMISSION TOMOGRAPHY IN CERVICAL CANCER**

  Principal Investigator & Institution: Miller, Tom R.; Professor; Radiology; Washington University Lindell and Skinker Blvd St. Louis, Mo 63130

  Timing: Fiscal Year 2001; Project Start 03-APR-2001; Project End 31-MAR-2005

  Summary: (Verbatim from the Applicant's Abstract): The overall goal of this project is improved radiotherapy treatment of patients with **cervical cancer** with use of positron emission tomography (PET). PET with F-18 fluorodeoxyglucose (FDG) will be used to provide three-dimensional definition of the primary tumor volume and regional spread of disease to more accurately administer brachytherapy. PET-based prognostic indicators will be developed. The first step will be verification of the ability of PET to accurately define tumor volume and to differentiate recurrent tumor from radiation-induced inflammation. Tumor size and extent of disease will be correlated with the results of magnetic resonance imaging in patients receiving radiotherapy with evaluation of FDG uptake before, during and after radiotherapy. Techniques will be developed to accurately determine the position of the brachytherapy applicator in relation to the tumor volume. FDG-PET images showing the primary tumor and regional spread of disease will-be spatially registered with the position of the brachytherapy applicator after placement of the applicator in the patient, thus permitting modification of the source loading in the future to optimize the dose to the tumor while minimizing radiation of the adjacent normal structures. The dose to the tumor and normal structures will be evaluated and follow-up will be performed to assess the rate of recurrence and complications in relation to the calculated doses the patients actually received. The potential impact of PET-guided alterations in source loading and treatment duration will be evaluated. To determine the prognostic value of PET, the volume of the primary tumor and the tracer uptake and heterogeneity of uptake within the tumor, obtained from FDG-PET images, will be correlated with the rate of tumor recurrence to determine PET markers that will identify patients at high risk for early recurrence who may need more aggressive initial treatment.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PREDICTING ADHERENCE TO FOLLOW UP OF ABNORMAL PAP SMEARS**

  Principal Investigator & Institution: Radecki Breitkopf, Carmen; Assistant Professor; Obstetrics and Gynecology; University of Texas Medical Br Galveston 301 University Blvd Galveston, Tx 77555

  Timing: Fiscal Year 2001; Project Start 01-APR-2001; Project End 31-MAR-2003

  Summary: ABSTRACT=Regular screening for **cervical cancer** via the Papanicolaou (Pap) smear and appropriate treatment when indicated can prevent over 90% of **cervical**

cancer mortality. However, many women do not obtain regular Pap smears, and among those who do, a large percentage fail to return for follow-up when notified of abnormality. Consequently, **cervical cancer** remains one of the most common malignancies in the US today accounts for over 4,000 deaths per year. Among African-American and Hispanic women rate of morbidity and mortality due to **cervical cancer** are 2 to 7 times that observed among Caucasian women. To decrease mortality due to this disease, clinicians must be able to identify women who are at risk of nonadherence and influence patient behavior. Few data are available to direct clinicians on how to assess patient reliability and little understood about factors that determine women's motivation to adhere to follow-up. The proposed research designed to identify psychological and behavioral determinants of women's motivation to adhere to follow-up recommendations for an abnormal Pap smear. We apply the unified theory of behavior to identify cognitive, normative, affective, environmental and social mechanisms underlying adherence to follow-up. Furthermore, this research is designed to understand sociocultural-based differences in motivation through the use of qualitative and quantitative methods of assessment. We propose to study 585 African-American, Hispanic and white women between 25-50 yeas of age over the course of three phases of research. Using interview survey methodology, the proposed research will yield a rich corpus of qualitative information about the social psychological dynamics of Pap smear follow-up. Phase one is an elicitation study in which we empirically derive the nature and structure of the theory constructs. In phase two, we will develop psychometrically-sound survey instruments for use in a prospective examination of adherence to follow-up. In phase three, we will conduct a prospective pilot investigation of adherence to follow-up to collect preliminary data for a large-scale study in which we use the methodology and measures developed during phases one and two. This research will improve clinical outcomes by identifying women at risk of nonadherence so that clinicians can plan management of the abnormal Pap smear accordingly. Additionally, it will assist in the design of tailored interventions to improve adherence. By informing both clinicians and researchers who are involved with **cervical cancer** prevention, this research will ultimately reduce the morbidity and mortality due to this disease.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PROSPECTIVE STUDY ON VIRAL LOAD OF CERVICAL CANCER**

  Principal Investigator & Institution: Adami, Hans-Olov H.; Karolinska Institute Tomtebodavagen 11F Stockholm,

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-AUG-2006

  Summary: (provided by applicant): Our long-term objective is to bring about prevention of cervix cancer through improved biologic understanding and more cost-effective screening strategies. Although human papilloma virus (HPV) infection is an established cause of **cervical cancer,** it is incompletely known if viral load of HPV influences progression from cancer in situ (CIS) to invasive cancer and/or interacts with genetic factors. Since clinical intervention precludes direct observation of this progression. unconventional approaches are needed. Our main specific aims are to; 1) quantify the absolute and relative risks for CIS and invasive cancer as a function of time since detected HPV and HPV 16 high viral load, 2) assess whether persistent HPV 16 high viral load is a determinant for development of CIS and invasive cancer, 3) assess whether the specific HLA DQ6/DR15 haplotype is associated with risks for CIS and invasive cancer, and if the association is mediated via a higher viral load and/or persistence of HP V. and 4) assess whether Chlamydia infection is associated with risks

for CIS and invasive cancer. Building on experience from an earlier study of CIS (funded by NCI). we will take advantage of unique prerequisites in Sweden created by extensive population-based PAP smear screening documented in computerised registers. ascertainment of all incident cases of CIS and invasive cancer. and access to archival smears and tissue specimens. Using a nested design in this large study base with up to 25 years of complete follow-up, we will identify 600 women with invasive cancer, 600 women with CIS and 600 individually matched control women to each case-group. Using validated and sensitive PCR assays, the presence of viral DNA - and for HPV 16, also the viral load -will be analyzed in all available smears from each participant (on average four per individual, giving a total of about 9600 smears). HLA and C trachomatis will be analyzed in the first smear from all included women. Relative risks and interactions will be estimated by conditional logistic regression and absolute risk functions by non-parametric methods.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: REDUCING CERVICAL CANCER IN APPALACHIA**

  Principal Investigator & Institution: Paskett, Electra D.; Marion N. Rowley Professor of Cancer Res; Comprehensive Cancer Center; Ohio State University 1800 Cannon Dr, Rm 1210 Columbus, Oh 43210

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-AUG-2008

  Summary: (provided by applicant): The overall goal of the proposed project is to increase early detection of **cervical cancer** by increasing the proportion of Appalachian women, age 18 and older, who receive Pap smears at appropriate intervals, and return for follow-up care when necessary. The proposed project will be implemented in Appalachian Ohio, a mainly rural and underserved area with a population comprised of 1.5 million adults, aged 18 and older and will utilize a CBPR approach and community relationships already established in the area by Center investigators. **C**ervical cancer prevention is a concern for this community, thus a CAB and a consortium of local community agencies are partnering with the Center in this effort. The first phase of the project will involve surveying 1,600 randomly selected women aged 18 and older who are patients of 16 primary care practices in Appalachian Ohio. The investigators will survey these women to identify social, environmental and behavioral barriers to obtaining risk-appropriate Pap smears within guidelines. Approximately half of these women will be in need of a Pap smear and will be entered into Phase 2 of the project. In this phase, an individualized health education program will be compared to a brochure and letter in a quasi-experimental trial design among 614 women. The education program will use two innovative strategies to address barriers to **cervical cancer** screening in these women: 1) educational sessions will be at the individual level in the woman's home; and 2) lay health educators supervised by local agricultural extension agents will deliver the education program. Specific Aims of the proposed project are to: 1) identify social-, environmental- and individual-level barriers to obtaining Pap smears; 2) develop and evaluate a health education program to improve knowledge, to address the identified barriers to behavior change, and to motivate women in the target populations to obtain Pap smears and understand the risky behaviors associated with developing **cervical cancer** (interaction with Projects 2 and 3); and 3) evaluate, through use of a quasi-experimental trial design the impact of the health education program compared to a brochure and physician letter on the proportion of women obtaining Pap smears. Approximately 30% of the 1,600 women will be current smokers and will be eligible to participate in Project 2, thus allowing the investigators to explore the differential effect of the health education intervention to enhance smoking cessation

(interaction with Project 2, aim 4). Secondary aims will relate to assuring adequate follow-up among women with abnormal test results (interaction with Project 3). If this program is successful in improving **cervical cancer** screening practices among this population of women, lay health educators from a variety of community organizations can be trained and supervised by community organizations to deliver similar programs to underserved women in other areas where health disparities exist.

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- **Project Title: ROLLING CIRCLE AMPLIFICATION ANALYSIS OF CERVICAL CELLS**

  Principal Investigator & Institution: Piccoli, Steven P.; Molecular Staging, Inc. 300 George St, 7Th Fl New Haven, Ct 06511

  Timing: Fiscal Year 2001; Project Start 10-SEP-2001; Project End 31-AUG-2002

  Summary: A subset of human papillomavirus (HPV) types have been implicated in **cervical cancer.** The determination of the presence of the HPV types associated with **cervical cancer** may serve as adjunct to Pap smear screening of cervical samples. This analysis could reduce the incidence of invasive **cervical cancer,** while decreasing the human and economic costs associated with Pap smear screening and reflex histological analysis. HPV analysis could distinguish between transient infections that resolve without the development of high-grade cervical lesions, and the presence of rare cells that have been biologically altered by HPV, and are progressing from a localized intraepithelial lesion to invasive cancer. This project will develop a method using Rolling Circle Amplification to analyze individual cells within a cervical sample and establish the presence of HPV DNA and RNA sequences, and in Phase II, establish the relationship of other markers to the early stages of HPV-related **cervical cancer.** The majors goals of this project are to develop a means to detect rare HPV-transformed cells that are missed by conventional cytology and validate RCA protocols for molecular analyses of cells with respect to features of HPV gene expression that present a risk of neoplastic progression rather than a transient infection. PROPOSED COMMERCIAL APPLICATIONS: The successful completion of this project will provide two types of products. The first could serve as an adjunct Pap smears by providing an indication when a "second look" might reveal rare aberrant cervical cells missed by cytology. The ultimate product would enhance or replace the annual Pap smear by providing molecular information, predicting early **cervical cancer** lesions, that is not visible to a trained cytotechnologist or pathologist.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SELECTION OF CHEMICAL INHIBITORS OF ONCOPROTEINS**

  Principal Investigator & Institution: Bocchetta, Maurizio; Ob, Gyn, and Reproductive Med; Loyola University Medical Center Lewis Towers, 13Th Fl Chicago, Il 60611

  Timing: Fiscal Year 2001; Project Start 25-MAY-2001; Project End 31-MAR-2003

  Summary: (provided by applicant) Human Papilloma Viruses (HPVs) have been conclusively proven as causative agents of ano-genital tumors, and some tumors of the head and neck. A growing body of evidence relates Simian Virus 40 (SV40) with tumors of the mesothelium, brain, and bone. Both HPV and SV40 deregulate the p53 and pRb tumor suppressors pathways through binding of virus-encoded oncoproteins to the cellular p53 and pRb. Antisense technology targeting the HPV and SV40 oncoproteins leads to growth inhibition and apoptosis in cell lines derived from HPV-positive cervical cancers, and from SV40-positive malignant mesotheliomas, respectively. This evidence

suggest that the HPV and SV40 oncoproteins represent valuable targets for the treatment of specific types of human cancer. Accordingly, both immuno-therapy and gene-therapy approaches to target HPV E6 and E7 are subjects of pre-clinical or clinical trials for the treatment of **cervical cancer,** and similar strategies have been proposed for the treatment of SV40-positive mesotheliomas. So far, immuno-therapy approaches have failed to provide a sufficient response in vivo, and genetic approaches are hampered by the lack of an efficient delivery system. We propose an alternative approach: the screening of chemical libraries to identify molecules capable of interfering with the binding of SV 40 and HPV oncoproteins to cellular p53 and pRb in vitro. These strategies require the analysis of a large panel of chemicals, a task feasible only if high-throughput assays to study the interactions of the viral oncoproteins with their cellular targets are available. These assays would require relatively high amounts of viral oncoproteins and tumor suppressors with proper post-translational modifications to ensure biological activity. Such requirement can be fulfilled if the protein substrates are expressed in human cells. However, human cell systems for protein over-expression are presently unavailable. We discovered that SV40-transformed human mesothelial cells (HM) can be used to obtain mg amounts of the SV40 large tumor antigen (Tag) in complex with cellular p53 and pRb. We propose to take advantage of this cell system to identify chemical inhibitors of the SV40 Tag-cellular tumor suppressors interactions. Moreover SV40-transformed mesothelial clones can be used as a basis to propagate "high copy number", episomal expression vectors in actively replicating human mesothelial ce!ls. Such vectors may allow over-expression of proteins requiring post-translational modifications for proper biological activity in human cells. We propose to use this experimental system to overproduce and purify carrier-conjugable HPVl6 E6 and E7. Recombinant E6 and E7 will be subsequently used to develop ELISA-based in vitro assays to study the HPVl6 E6 and E7 binding to p53 and pRb, respectively. Finally, we propose to employ the latter assays for the screening of chemical libraries in order to find inhibitors of the HPV E6 and E7. The identification of putative inhibitors of the SV 40 and HPV oncoproteins may lead to the development of novel anticancer drugs. Furthermore, the experiments proposed may contribute novel technology for the over-expression and purification of potentially any protein in actively replicating human mesothelial cells.

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- **Project Title: SEXUAL FUNCTIONING AND QOL IN WOMEN WITH CERVICAL CANCER**

  Principal Investigator & Institution: Bodurka, Diane C.; Gynecologic Oncology; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

  Timing: Fiscal Year 2002; Project Start 16-SEP-2002; Project End 31-AUG-2004

  Summary: (provided by applicant): Sex and sexuality are issues central to women's health. Despite the important nature of this topic, sexual concerns have often been overlooked by health care providers during the treatment and post-treatment surveillance of women with gynecologic cancer. Although it has been demonstrated at least since the early 1980s that sexual dysfunction is perhaps the most significant morbidity of treatment for **cervical cancer,** little progress has been made in specifying the impact of surgery vs. radiotherapy, or in studying the broader impact of sexual dysfunction on the quality of life (QOL) of **cervical cancer** survivors. Virtually all studies have excluded non-English speaking patients. This study will evaluate the sexual outcomes of therapy for **cervical cancer** and the relationship of these issues to QOL. We will prospectively study 144 women receiving treatment and follow-up

surveillance for **cervical cancer.** The aims of the study are: 1.) To assess the entire range of sexual functioning (desire, arousal, orgasmic capacity, dyspareunia, and sexual satisfaction) over the course of treatment and early follow-up in patients with local and locally advanced **cervical cancer;** 2.) To assess general cancer-related QOL over the course of treatment and early follow-up in patients with local and locally advanced **cervical cancer;** 3.) To characterize the relationship between sexual dysfunction and overall cancer-related QOL over time; and 4.) To identify factors that may predict better sexual function outcomes in patients treated for **cervical cancer.** At baseline, and at 1, 2, and 4 months post-treatment, women will fill out standardized questionnaires measuring sexual function and satisfaction, relationship happiness, health-related QOL, and cancer-related QOL. At each assessment, a clinician will use a vaginal probe to assess length and caliber of the vaginal canal. Through completion of questionnaires and measurement of vaginal length and compliance, we plan to develop culturally sensitive, short-term interventions to improve sexual functioning and QOL of cervix cancer survivors. Our long-term goal is to evaluate the effectiveness of such interventions in randomized trials. Ultimately, we hope to integrate our findings into daily clinical practice.

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- **Project Title: SMOKING CESSATION FOR WOMEN AT RISK FOR CERVICAL CANCER**

  Principal Investigator & Institution: Miller, Suzanne M.; Professor of Psychology & Medicine; Fox Chase Cancer Center Philadelphia, Pa 19111

  Timing: Fiscal Year 2001; Project Start 01-APR-1999; Project End 31-JAN-2003

  Summary: This abstract is not available.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SMOKING CESSATION FOR WOMEN AT RISK OF CERVICAL CANCER**

  Principal Investigator & Institution: Whiteley, Jessica A.; Miriam Hospital Providence, Ri 02906

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): Cigarette smoking has been found to be associated with a two-fold increased risk of developing cervical neoplasia or squamous cell cancer. The constituents of smoke, in concert with human papillomavirus (HPV), may promote the development or progression of cervical neoplasia. Thus, women who are positive for HPV and who smoke are at increased risk for developing **cervical cancer.** Counseling regarding smoking cessation may be of particular benefit for women undergoing screening at a colposcopy clinic for the evaluation of an abnormal Papanicolaou (Pap) smear. This is considered to be a "teachable moment" for smoking cessation, in that the perceived risk of progression to **cervical cancer** is heightened. Smoking cessation can reduce this risk as well as other health risks. Additionally, women at the colposcopy clinic represent underserved female smokers in that they are young, of low socioeconomic status, and are more likely to be ethnic or racial minorities. In Phase I, three focus groups of 8 -10 women each will be conducted to adapt an efficacious group-based cognitive-behavioral smoking cessation intervention that is tailored to the needs of women. The adaptations will include modifying the intervention from a group to phone-based delivery format and addressing the unique smoking cessation barriers of the women at our study site colposcopy clinic. In Phase II, the refined materials will be

used in a randomized pilot study. Thirty women will be randomized either to an AHRQ + Enhanced Smoking Cessation group (n = 15) or to an AHRQ + Contact Control group (n = 15). Both groups will receive the AHRQ guidelines for smoking cessation (self help materials, brief counseling, recommendation for nicotine replacement therapy) plus phone delivery of either the adapted smoking cessation intervention (AHRQ + Enhanced Cessation) or a health education intervention (AHRQ + Contact Control). Our primary hypothesis is that the women randomized to the AHRQ + Enhanced Cessation group will have higher quit rates then women in the AHRQ + Contact Control group. Thus, we seek to: 1) conduct the formative work to adapt the cessation materials from a group to phone-based format and to address the needs of this population, 2) pilot the recruitment strategy, and 3) conduct a small randomized pilot trial to determine the preliminary efficacy of the materials for smoking cessation. This study, therefore, will serve as a pilot for a larger clinical trial.

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- **Project Title: SPORE IN CERVICAL CANCER**

  Principal Investigator & Institution: Wu, Tzyy-Choou C.; Professor; Pathology; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 31-AUG-2008

  Summary: (provided by applicant): This application for a Specialized Program of Research Excellence (SPORE) in **Cervical Cancer** at The Johns Hopkins University School of Medicine brings together a highly interactive, multidisciplinary, and interinstitutional program of translational research in **cervical cancer.** The SPORE includes six integrated projects spanning the fields of screening, diagnosis, prevention and treatment. Project 1: Markers of progression to **cervical cancer** in rural India (Keerti Shah, M.D., DR.PH. and Kathleen Cho, M.D). Project 2, Identification of molecular markers for **cervical cancer** progression (Kathleen Cho, M.D. and Carolyn Johnston, M.D.). Project 3, Development of a pan-oncogenic HPV preventive vaccine (Richard Roden, Ph.D. and Raphael Viscidi, M.D). Project 4, Human immunological responses to chimeric Ll/L2-E2- E7 VLP (Clayton Harro, M.D., Sc.M., Drew Pardoll, M.D., Ph.D., and Richard Roden, Ph.D.). Project 5, Vaccination with SigIE7(detox)/HSP70 DNA to treat patients with HPV-associated high grade squamous intraepithelial lesions with or without HIV (Drew Pardoll, M.D., Ph.D., Cornelia Trimble, M.D., and T.-C. Wu, M.D., Ph.D.). Project 6, Combination of antigen-specific cancer immunotherapy and anti-angiogenesis to treat patients with advanced **cervical cancer** (T.-C. Wu, M.D., Ph.D. and Debbie Armstrong, M.D.) These six research projects are supported by three cores. Core 1, Tissue/Pathology (Robert J. Kurman, M. D. and Fredrick Montz, M.D.). Core 2, Biostatistics and Bioinformatics (Mei-Cheng Wang, Ph.D.) The SPORE also includes a major Developmental Research Program (Drew Pardoll, M.D., Ph.D. and T.-C. Wu) for rapid funding of novel ideas and a Career Development Program (T.-C. Wu, M.D., Ph.D. and Fredrick Montz, M.D.) to facilitate career development of individuals with an interest in translational **cervical cancer** research.

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- **Project Title: STATISTICAL ANALYSIS OF CANCER INCIDENCE**

  Principal Investigator & Institution: Fu, Wenjiang J.; Assistant Professor; Epidemiology; Michigan State University 301 Administration Bldg East Lansing, Mi 48824

  Timing: Fiscal Year 2001; Project Start 01-SEP-1999; Project End 31-AUG-2003

Summary: The scope of the proposed study is to develop and test new statistical procedures for age-period-cohort (APC) analysis of cancer incidence and mortality rates. Guided by an expanding literature on statistical methods and experience in statistical modeling and analyses for APC studies, this research plan addresses the development of models that aim to resolve the identifiability problem. A new statistical methodology is developed through eigen-analysis, principal component analysis, shrinkage models and reduce models with bias correction methods. These models address the problem of estimation and bias in log-linear regression models with exact collinearity between the effects of age, period and cohort in APC analysis. A unique estimator is identified, which generates accurate trend estimation with minimal bias or no bias. These new statistical models provide estimates of the age, period and cohort effects of cancer incidence and mortality, which exploit fully cancer summary rate data arising from the Surveillance, Epidemiology, and End Results (SEER) and other cancer registries. These APC models also permit estimation of future cancer rates. The methodology allows for trend estimation, construction of confidence intervals, bias correction and forecasting. The performance of the proposed methods will be evaluated with simulated and real cancer incidence and mortality rate data. The methodology will be applied to several studies on cancer incidence and mortality rates, including one study on mortality rate of **cervical cancer** in Ontario, six studies on incidence rates of breast cancer, prostate cancer, male and female colon cancer, male and female lung cancer in Connecticut. The methodology will also be applied to studies on national mortality rates of various types of cancer in different ethnic groups, such as White, Black, Asian/Pacific islanders and Hispanics, to investigate the differences between these groups as outlined in the Healthy People 2000. The ultimate goal of the investigation is to assess trend estimation and forecasting in APC analyses. The methods proposed in this investigation have immediate application to these studies, and offer an array of promising techniques for use in APC analysis of cancer incidence and mortality.

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- **Project Title: STRESS/IMMUNE RESPONSE EFFECTS ON HPV-LINKED ORAL CANCER**

  Principal Investigator & Institution: Sherman, Eric J.; Fox Chase Cancer Center Philadelphia, Pa 19111

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 31-MAY-2005

  Summary: (provided by applicant): Although the role of certain types of human papillomavirus (HPV) in the etiology of **cervical cancer** is well-established, the involvement of HPV infection in squamous cell carcinoma of extragenital sites, such as the head and neck, is presently under extensive investigation. Prior research indicates that immunosuppression may contribute to the severity and progression of HPV-related lesions. Accumulating data also indicate that psychosocial (e.g., stress) and behavioral (e.g., smoking, alcohol use) factors are associated with immunosuppression and may adversely affect the immune system's ability to control and resolve HPV infection. Thus, the objective of the proposed project is to evaluate cellular immune response and potential moderators of host immunity among two groups: 1) 50 patients with premalignant lesions of the head and neck; and 2) 50 patients referred for definitive management of head and neck squamous cell carcinoma (HNSCC) who have not yet started treatment. Specific aims of the proposed project are: 1) to assess the prevalence of HPV in premalignant lesions of the head and neck in comparsion to the prevalence of HPV in head and neck tumors; 2) to evaluate specific cellular immunity to HPV in this population using an innovative assay that has demonstrated clinical relevance to disease

progression in other cancer contexts (e.g., cervical); and, 3) to examine potential moderators of cellular immune response, such as behavioral (e.g., tobacco and alcohol use) and psychological (e.g., stress) risk factors. The proposed project will utilize a longitudinal, prospective design. Participants will complete a brief psychosocial and behavioral assessment and provide a blood sample for immunologic assays. A sample of cells will be obtained from the lesion or tumor site using a small cytobrush for HPV typing. Self-reported data to be collected include demographic variables, behavioral risk factors (e.g., tobacco and alcohol use), and psychosocial measures (e.g., distress, depression). Immune status will be assessed using functional (e.g.,T-cell proliferative response to HPV16, a specific marker of immunocompetence shown to be associated with viral clearance and disease regression) and quantitative (e.g., enumeration of lymphocyte subsets) assays. Follow-up assessments of HPV status, immunologic measures, and psychosocial and behavioral risk factors will be obtained 1-year post-baseline in order to examine potential associations with clinical outcomes.

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- **Project Title: STRUCTURE/FUNCTION OF HUMAN PAPILLOMAVIRUS ONCOPROTEINS**

  Principal Investigator & Institution: Marmorstein, Ronen; Professor; Wistar Institute Philadelphia, Pa 191044268

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2007

  Summary: (provided by applicant): Viruses are often potent oncogenes and are causally linked to approximately 20 percent of human malignancies. Human papillomavirus (HPV), in particular, is considered to be the etiological agent of human **cervical cancer.** HPV infections are also implicated in other malignancies including cancer of the vulva, vagina, penis, anus, skin, esophagus, and oropharyngeal region. Transformation by HPV is mediated by two relatively small viral oncoproteins, E6 and E7 that mediate their activities through their interaction with host proteins, which are normally involved in controlling cell growth and division. HPV-E6 abrogates the function of the p53 tumor suppressor gene by cooperating with E6AP to target p53 for ubiquitin-mediated degradation, and also inhibits the transactivation properties of the global transcriptional coactivators, CBP and p300. E7 binds to the Retinoblastoma (pRb) tumor suppressor and liberates E2F transcription factors causing premature activation of genes involved in DNA synthesis during the G1 to S cell cycle transition. E7 also interacts with the AP1 family of transcription factors for transactivation of AP1-mediated transcription, with Mi2 and histone deacetylases to perturb pRb-mediated transcriptional repression, and with the p21(WAF1/CIP1) family of cyclin-dependent kinase inhibitors to perturb cell cycle regulation. The functional homologue of HPV-E7, Adenovirus E1A (Ad-ElA), also inhibits the activity of pRb as well as other transcriptional cofactors such as the P/CAF and CBP/p300 histone acetyltransferases. In order to obtain mechanistic insights into the mode of cell transformation by HPV we propose to determine the X-ray crystal structures of HPV-E6 and E7 bound to relevant cellular protein targets and to biochemically characterize their respective protein-protein interactions. Specifically, we will (1) Determine the X-ray crystal structure of HPV-E7 alone and in complex with pRb, (2) Determine the X-ray crystal structure of Ad-E1A in complex with pRb, (3) Determine the structure of a pRb/E2F complex, characterize the binding properties of pRb to E2F in the presence or absence of HPV-E7 or Ad5-E1a, and use mutational analysis to probe the interactions of pRb with E2F, HPV-E7 and Ad-E1A, and (4) Determine the X-ray crystal structure of HPV-E6 alone and in complex with p53 and characterize the binding properties of the complex using mutational analysis. These studies will provide detailed

mechanistic insights into the mode by which HPV-E6 and -E7 disrupt normal cellular processes for cell transformation and will lead to the structure-based design of small molecule E6- and E7- inhibitors to combat HPV-mediated cancers such as **cervical cancer.**

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- **Project Title: T CELL SIGNAL TRANSDUCTION TO MONITOR HPV VACCINES**

  Principal Investigator & Institution: Ochoa, Augusto C.; Associate Professor; Pediatrics; Louisiana State Univ Hsc New Orleans New Orleans, La 70112

  Timing: Fiscal Year 2001; Project Start 01-APR-2000; Project End 30-SEP-2002

  Summary: (Applicant's Abstract) Cancer vaccines and new combinations of chemotherapy and immunotherapy are actively being tested in numerous clinical trials based on the exciting results of the pre-clinical animal studies. However, previous results of immunotherapy trials and the recent findings on the immune response in cancer, suggest that these trials will encounter a major barrier, namely the immune dysfunction present in cancer patients. This immune dysfunction is manifested in vivo by the loss of a delayed type hypersensitivity (DTH), and in vitro by a decreased cytotoxicity, a diminished production of cytokines and the inability to respond to antigenic stimuli. The basis of these changes is unclear, although alterations in T cell function and signal transduction as well as changes in dendritic cell maturation have been demonstrated recently. It is however logical to think that a successful immunotherapy must correct these immunological alterations. The alterations in T cell function appear to be related to changes in the expression of T cell signal transduction molecules. These include a decreased expression of T cell receptor chain (TCR), a diminished level of p56lck and Jak-3 kinases and an inability to translocate NFkB p65 to the nucleus. These changes are not only seen in cancer patients, but also in patients with other diseases characterized by immune dysfunction such as leprosy. Preliminary results from clinical trials suggest that patients responding to the treatment, or developing an immune response to tumor antigens, recover the normal expression of T cell signal transduction molecules. In contrast patients with progressive tumor growth show persistent alterations in signal transduction proteins. Therefore this application proposes to 1) determine the signal transduction alterations present in T cells of patients with **cervical cancer** prior to and after vaccination with human papilloma virus (HPV) peptide vaccine 2) test whether these alterations are paralleled by changes in in vivo and in vitro T cell functions, and 3) determine whether the re-expression of T cell signal transduction proteins correlates with a successful vaccination or the induction of a clinical anti-tumor response.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: TECHNOLOGY FOR DNA DAMAGE MARKERS IN CERVICAL CANCER**

  Principal Investigator & Institution: Matson, Wayne R.; Esa, Inc. 22 Alpha Rd Chelmsford, Ma 01824

  Timing: Fiscal Year 2001; Project Start 12-APR-2001; Project End 31-MAR-2002

  Summary: Prototype carbon column switching (CCS) systems (1) have been applied to measuring free levels of DNA adducts in PAP smear and cervico vaginal lavage sample indicating a possible correlation with various risk factors and cancer. Preliminary work has defined some of the possible role of utility of such measurements in early diagnosis or therapy monitoring. The proposed work is directed at refining, extending and

integrating the technology for the identification and routine measurement of relevant markers. The proposed approach is an iterative study between technology/methodology enchancements and marker significance identification from a cohort of ca. 400 cases spanning a wide range of sampling modalities, risk factors and diagnoses. PROPOSED COMMERCIAL APPLICATION: The proposed work is directed at developing research and clinical instrumentation for relating DNA damage to cercical cancer risk. The commercial markets are in biomedical research, therapy monitoring, and clinical screening.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THE EFFECT OF SMOKING CESSATION ON PLASMA MICRONUTRIENTS**

  Principal Investigator & Institution: Shikany, James M.; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2001; Project Start 22-SEP-1999; Project End 31-AUG-2003

  Summary: High dietary intakes and blood concentrations of the micronutrients vitamin C, 13-carotene, folate, and vitamin B have been associated with a decreased risk of cardiovascular disease and/or cancer in epidemiologic studies. Identifying modifiable risk factors which influence plasma concentrations of these micronutrients could provide a means of decreasing disease risk. Cigarette smoking has been shown in numerous cross-sectional studies to be associated with lower plasma concentrations and dietary intake of these micronutrients, potentially placing smokers at increased risk for disease. However, very few studies have examined the effect of smoking cessation on intake or plasma concentrations of these micronutrients. In the proposed study, subjects in a recently-funded study of smoking cessation and cervical dysplasia progression will be utilized to study the effects of smoking cessation on these plasma micronutrients in a cost-effective manner. Subjects in the Smoking Cessation to Reduce **Cervical Cancer** Risk (WISH) study will be randomized to either usual care or an intensive theory-based smoking cessation intervention and followed for 18 months to assess the effect of smoking cessation on the progression of existing cervical dysplasia. In the proposed study, concentrations of vitamin C, beta-carotene, folate, and alpha-tocopherols will be measured in all 220 randomized WISH subjects at baseline, prior to the intervention, and at the first 6-month follow-up visit, following completion of the intensive portion of the smoking cessation intervention. Dietary assessment will also be conducted at the same two visits, using a food frequency questionnaire. Multiple linear regressions will be used to determine the effect of smoking cessation on plasma concentrations of these micronutrients, controlling for dietary intake and other factors. Regression analysis will also be used to determine the effect of smoking cessation on the dietary intake of these micronutrients. If smoking cessation is associated with increased plasma micronutrients as hypothesized, this would provide further justification for encouraging smokers to quit.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THERAPEUTIC VACCINES FOR HPV DISEASES**

  Principal Investigator & Institution: Trimble, Cornelia L.; Assistant Professor; Gynecology and Obstetrics; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2001; Project Start 14-FEB-2001; Project End 31-JAN-2006

Summary: (Applicant's Description) The overall goal of this project is to evaluate new, therapeutic, antigen-specific vaccine strategies targeted at the E7 antigen of human papillomavirus (HPV) type 16, the most prevalent HPV type found in both **cervical cancer** and its immediate precursor lesions, squamous intraepithelial lesions (SILs). Molecular, biochemical, and cellular studies have unequivocally demonstrated that two HPV gene products, E6 and E7, are consistently expressed in SILs and cervical cancers, and furthermore, lead to malignant transformation of epithelial cells. E6 binds, inactivates, and promotes the degradation of p53 while E7 binds and inactivates pRb. Because HPV 16 is the most commonly found HPV type in **cervical cancer** and its precursor lesions, and because E7 is consistently expressed in transformed epithelial cells, we have focused our efforts inducing an immune response directed at this particular antigen. The correlation between classic measures of immune response and clinical regression of disease is not well characterized. As such, the identification of clinically relevant immunologic assays to monitor vaccine trials is one of the most important scientific endeavors in modern cancer vaccine development. This project will provide not only new insight into this correlation, but also serve as a potential model for the development of other therapeutic cancer vaccines. Our hypotheses are: 1) vaccination will enhance cell-mediated immunity against epithelial cells expressing E7, and 2) this response will be reflected by quantitative changes in lesion size, histopathology, viral activity, and in local tissue and peripheral measures of immune response. Our specific aims are: 1) to evaluate the safety and toxicity of endosomal/lysosomal targeted E7 vaccines in pilot translational trials in women with HPV16+ high grade, preinvasive cervical lesions, 2) to evaluate pathologic, virologic, and clinical measures to determine efficacy of these vaccines against HPV16+ high grade cervical lesions. To this end, we will correlate colposcopic characteristics of HPV lesions, histopathologic findings, and viral load, with serologic assays of HPV16 E7-specific humoral and cellular immune response. This proposal coordinates extensive resources available at the Johns Hopkins Medical Institutions. These facilities will be used to develop Dr. Trimble's ability to design and execute clinical trials evaluating preneoplastic HPV-associated lesions of the female lower genital tract.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: VIRUS-HOST INTERACTIONS IN CANCER**

  Principal Investigator & Institution: Kieff, Elliott D.; Professor; Microbiol & Molecular Genetics; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2001; Project Start 01-JUL-1986; Project End 31-MAY-2004

  Summary: Viruses are significant cause of cancer in normal humans and are an even more common cause of cancer in immune deficient humans such as organ transplant recipients or HIV infected people. Furthermore, analyses of the way viruses alter cell growth has frequently led to the delineation of novel pathways of cell growth control and oncogenicity. This Program enables the training of 2 to 3 pre- and 5 post-doctoral trainees each year in the laboratories of the 20 faculty members working in Viral Oncology at Harvard University. The research objectives of these laboratories include (1) mechanisms by which RNA tumor viruses get into cells (2) mechanisms by which small DNA tumor viruses including human papillomaviruses alter cell growth and cause **cervical cancer** (4) mechanisms by which viruses alter cell signal transduction, transcription, cell cycle regulation, and cell survival and the role of these processes in normal and tumor cell growth. Trainees are recruited by the Virology and Biological and Biomedical Science Programs and enter the program because of their interest in viral

oncology. Pre-doctoral students pursue 3 semesters of course work in molecular biology, genetics, cell biology, virology, and immunology while engaged in laboratory research training in viral oncology. Thereafter, they are fully engaged in mentored thesis research. Post-doctoral fellows engage full time in mentored research training research training. Pre- and post-doctoral students also participate in seminars, journal clubs, and research conferences including viral oncology and oncology research conferences. Trainees are jointly mentored by their principal research trainer and by other program faculty. On completion of their thesis research pre-doctoral students will be prepared for post-doctoral training and post-doctoral students will be prepared for independent research in viral oncology and related disciplines.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: VSV-BASED THERAPEUTIC PAPILLOMA VACCINE**

  Principal Investigator & Institution: Brandsma, Janet L.; Associate Professor; Comparative Medicine; Yale University 47 College Street, Suite 203 New Haven, Ct 065208047

  Timing: Fiscal Year 2003; Project Start 17-JUN-2003; Project End 31-MAY-2008

  Summary: (provided by applicant): Human papillomavirus (HPV) infection of the cervix initiates the development of **cervical cancer.** Vaccination has the potential to prevent **cervical cancer** by preventing primary HPV infection and by eliminating persistent lesions. The ideal vaccine would induce therapeutic as well as protective immunity. The best animal model for therapeutic vaccine development is the cottontail rabbit papillomavirus (CRPV)-rabbit model. Live recombinant vesicular stomatitis viruses (rVSV) expressing foreign viral proteins have successfully protected animals against challenges with several human viruses. We recently generated an rVSV vector expressing the CRPV E6 tumor antigen and used it to vaccinate rabbits with well-established tumors (papillomas) in a preliminary experiment. The treatment induced dramatic therapeutic outcomes including the complete and permanent regression of all disease in some rabbits with a total papilloma burden of 4 cm3, as compared to no regression in the controls. The hypothesis of this application is that the rVSV-E6 vaccine can be improved to induce more rapid and more universal regression. It is based on the observation that the original vaccine expressed a relatively low level of E6 protein and that revaccination with the same rVSV-E6 was probably not effective, due to VSV-specific neutralizing antibodies induced by primary vaccination. The efficacy of the rVSV-E6 could also be improved by modifying the E6 gene to encode a ubiquitin-E6 fusion protein (UbE6), based on our findings, using CRPV DNA vaccines, that a UbE6 fused gene was markedly more effective than the unfused E6 gene. The specific aims are to repeat the preliminary experiment with larger group size and all appropriate controls; to determine if more rapid and more universal tumor clearance can be obtained using VSV vectors giving higher-level expression of E6 or expressing UbE6, using an efficient VSV-E6 boosting vector with the VSV envelope gene from a heterologous serotype, or using a completely heterologous viral vector (adenovirus). We will determine if the most effective therapeutic vaccine also induces protective immunity. The data provided by this investigation are likely to aid in the development a highly effective HPV vaccine to protect women against **cervical cancer.**

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: WELLNESS CIRCLES--AN AMERICAN INDIAN APPROACH**

  Principal Investigator & Institution: Hodge, Felicia S.; Professor-Carra Member; None; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

Timing: Fiscal Year 2001; Project Start 30-SEP-1997; Project End 31-AUG-2002

Summary: (Adapted from the Investigator's Abstract): The health status of American Indians in California is well below national averages and has been for many years. Identified health problems include a pattern of social problems, poverty, and chronic diseases that is unparalleled among ethnic and racial minorities in the U.S. Such long term chronic diseases as diabetes, and tuberculosis are significant threats. Obesity is a serious problem and at 40% cigarette smoking is double the California average. Alcoholism accidence and violence are recorded as the leading causes of inpatient and outpatient care. American Indians have one of the highest mortality and lowest 5 year survival rates for **cervical cancer** compared to other ethnic groups. This population also utilizes less cancer screening, and even when screening is obtained, those Indian patients with abnormal findings are frequently lost to follow-up. California has the second largest number of Indians in the U.S. The majority of Indians who reside in rural communities live on or near the 85 reservations/rancherias and obtain their medical care at one of the 23 rural Indian health clinics. The urban Indian population consists largely of Indians from other states who were relocated under Federal programs to California in the 1950s. The goal of this project is to design, implement and evaluate, a community-based health care model for American Indian families which incorporates culturally appropriate approaches to primary and secondary disease prevention. Our target population is American Indians residing in rural counties throughout the State of California. In Phase I of this three phase study, a needs assessment will be conducted in order to identify the health needs of and health services used by the target population. Data will be collected from adult Indians age 18 and over. The sampling frame will be constructed from lists of patients attending rural Indian clinics. In Phase II, a randomized clinical trial will be implemented. Clinic sites will be matched in pairs according to site, geographic location, and size. They will be randomized into intervention sites, participating in a series of Wellness Talking Circles and control sites receiving usual care. Phase III will consist of data analysis and evaluation. The leadership of this team includes American Indian investigators experienced in cancer control research and knowledgeable in the provision of culturally sensitive care.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

E-Journals: PubMed Central[3]

PubMed Central (PMC) is a digital archive of life sciences journal literature developed and managed by the National Center for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM).[4] Access to this growing archive of e-journals is free and unrestricted.[5] To search, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Pmc**, and type "cervical cancer" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for cervical cancer in the PubMed Central database:

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[3] Adapted from the National Library of Medicine: **http://www.pubmedcentral.nih.gov/about/intro.html**.

[4] With PubMed Central, NCBI is taking the lead in preservation and maintenance of open access to electronic literature, just as NLM has done for decades with printed biomedical literature. PubMed Central aims to become a world-class library of the digital age.

[5] The value of PubMed Central, in addition to its role as an archive, lies in the availability of data from diverse sources stored in a common format in a single repository. Many journals already have online publishing operations, and there is a growing tendency to publish material online only, to the exclusion of print.

- **A "Public" T-Helper Epitope of the E7 Transforming Protein of Human Papillomavirus 16 Provides Cognate Help for Several E7 B-Cell Epitops from Cervical Cancer-Associated Human Papillomavirus Genotypes.** by Tindle RW, Fernando GJ, Sterling JC, Frazer IH.; 1991 Jul 1;
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- **Activation of p53 in cervical carcinoma cells by small molecules.** by Hietanen S, Lain S, Krausz E, Blattner C, Lane DP.; 2000 Jul 18;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=26977
- **Adenovirus-Mediated p21(WAF1/SDII/CIP1) Gene Transfer Induces Apoptosis of Human Cervical Cancer Cell Lines.** by Tsao YP, Huang SJ, Chang JL, Hsieh JT, Pong RC, Chen SL.; 1999 Jun;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=112542
- **An evaluation of the integration of non-traditional learning tools into a community based breast and cervical cancer education program: The witness project of Buffalo.** by Hurd TC, Muti P, Erwin DO, Womack S.; 2003;
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- **Analysis by Multiplex PCR of the Physical Status of Human Papillomavirus Type 16 DNA in Cervical Cancers.** by Yoshinouchi M, Hongo A, Nakamura K, Kodama J, Itoh S, Sakai H, Kudo T.; 1999 Nov;
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- **Antigen-Driven T-Cell Selection in Patients with Cervical Cancer as Evidenced by T-Cell Receptor Analysis and Recognition of Autologous Tumor.** by Pilch H, Hohn H, Neukirch C, Freitag K, Knapstein PG, Tanner B, Maeurer MJ.; 2002 Mar;
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- **Cervical cancer: epidemiology, prevention and the role of human papillomavirus infection.** by Franco EL, Duarte-Franco E, Ferenczy A.; 2001 Apr 3;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=80931
- **Cervical cancer: is herpes simplex virus type II a cofactor?** by Jones C.; 1995 Oct;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=172875
- **Cervical cancer: the increasing incidence of adenocarcinoma and adenosquamous carcinoma in younger women.** by Liu S, Semenciw R, Mao Y.; 2001 Apr 17;
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- **Comparative Evaluation of First- and Second-Generation Digene Hybrid Capture Assays for Detection of Human Papillomaviruses Associated with High or Intermediate Risk for Cervical Cancer.** by Poljak M, Brencic A, Seme K, Vince A, Marin IJ.; 1999 Mar;
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- **Comparison of ViraPap, southern hybridization, and polymerase chain reaction methods for human papillomavirus identification in an epidemiological investigation of cervical cancer.** by Gibbs AC.; 1995 Aug; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=228377
- **Complete switch from Mdm2 to human papillomavirus E6-mediated degradation of p53 in cervical cancer cells.** by Hengstermann A, Linares LK, Ciechanover A, Whitaker NJ, Scheffner M.; 2001 Jan 30; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=14735
- **Comprehensive study of several general and type-specific primer pairs for detection of human papillomavirus DNA by PCR in paraffin-embedded cervical carcinomas.** by Baay MF, Quint WG, Koudstaal J, Hollema H, Duk JM, Burger MP, Stolz E, Herbrink P.; 1996 Mar; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=228883
- **Cross sectional study of conventional cervical smear, monolayer cytology, and human papillomavirus DNA testing for cervical cancer screening.** by Coste J, Cochand-Priollet B, de Cremoux P, Le Gales C, Cartier I, Molinie V, Labbe S, Vacher-Lavenu MC, Vielh P.; 2003 Apr 5; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=152633
- **Cross sectional survey of cervical cancer screening in women with learning disability.** by Stein K, Allen N.; 1999 Mar 6; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=27770
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- **Human Papillomavirus Type 16 E7 Peptide-Directed CD8 + T Cells from Patients with Cervical Cancer Are Cross-Reactive with the Coronavirus NS2 Protein.** by Nilges K, Hohn H, Pilch H, Neukirch C, Freitag K, Talbot PJ, Maeurer MJ.; 2003 May;
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- **Mapping common deleted regions on 5p15 in cervical carcinoma and their occurrence in precancerous lesions.** by Arias-Pulido H, Narayan G, Vargas H, Mansukhani M, Murty VV.; 2002; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=140145
- **Mechanisms of Human Papillomavirus E2-Mediated Repression of Viral Oncogene Expression and Cervical Cancer Cell Growth Inhibition.** by Nishimura A, Ono T, Ishimoto A, Dowhanick JJ, Frizzell MA, Howley PM, Sakai H.; 2000 Apr 15; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=111884
- **Methylation and silencing of the retinoic acid receptor-[beta]2 gene in cervical cancer.** by Ivanova T, Petrenko A, Gritsko T, Vinokourova S, Eshilev E, Kobzeva V, Kisseljov F, Kisseljova N.; 2002; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=101392
- **Rapid induction of senescence in human cervical carcinoma cells.** by Goodwin EC, Yang E, Lee CJ, Lee HW, DiMaio D, Hwang ES.; 2000 Sep 26; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=27134
- **Recombinant Adeno-Associated Virus Expressing Human Papillomavirus Type 16 E7 Peptide DNA Fused with Heat Shock Protein DNA as a Potential Vaccine for Cervical Cancer.** by Liu DW, Tsao YP, Kung JT, Ding YA, Sytwu HK, Xiao X, Chen SL.; 2000 Mar 15; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=111780
- **Repression of human papillomavirus oncogenes in HeLa cervical carcinoma cells causes the orderly reactivation of dormant tumor suppressor pathways.** by Goodwin EC, DiMaio D.; 2000 Nov 7; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=18795
- **Repression of the Integrated Papillomavirus E6/E7 Promoter Is Required for Growth Suppression of Cervical Cancer Cells.** by Francis DA, Schmid SI, Howley PM.; 2000 Mar 15; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=111757
- **Restoration of fragile histidine triad (FHIT) expression induces apoptosis and suppresses tumorigenicity in lung and cervical cancer cell lines.** by Roz L, Gramegna M, Ishii H, Croce CM, Sozzi G.; 2002 Mar 19; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=122572
- **Screening for cervical cancer: Should we test for infection with high-risk HPV?** by Meijer CJ, Snijders PJ, Brule A.; 2000 Sep 5; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=80460
- **Simultaneous Assessment of Loss of Heterozygosity at Multiple Microsatellite Loci Using Semi-Automated Fluorescence-Based Detection: Subregional Mapping of Chromosome 4 in Cervical Carcinoma.** by Hampton GM, Larson AA, Baergen RN, Sommers RL, Kern S, Cavenee WK.; 1996 Jun 25; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=39090

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- **Variable Oncogene Promoter Activity of Human Papillomavirus Type 16 Cervical Cancer Isolates from Australia.** by Watts KJ, Thompson CH, Cossart YE, Rose BR.; 2001 May; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=88072

The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine.[6] The advantage of PubMed over previously mentioned sources is that it covers a greater number of domestic and foreign references. It is also free to use. If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

To generate your own bibliography of studies dealing with cervical cancer, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "cervical cancer" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for cervical cancer (hyperlinks lead to article summaries):

- **A community approach to addressing excess breast and cervical cancer mortality among women of African descent in Boston.**
  Author(s): Bigby J, Ko LK, Johnson N, David MM, Ferrer B; REACH Boston 2010 Breast and Cervical Cancer Coalition.
  Source: Public Health Reports (Washington, D.C. : 1974). 2003 July-August; 118(4): 338-47.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12815081&dopt=Abstract

- **A disease-specific Medicaid expansion for women. The Breast and Cervical Cancer Prevention and Treatment Act of 2000.**
  Author(s): Lantz PM, Weisman CS, Itani Z.
  Source: Women's Health Issues : Official Publication of the Jacobs Institute of Women's Health. 2003 May-June; 13(3): 79-92.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12867087&dopt=Abstract

[6] PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at Web sites of participating publishers. Publishers that participate in PubMed supply NLM with their citations electronically prior to or at the time of publication.

- **A major constituent of green tea, EGCG, inhibits the growth of a human cervical cancer cell line, CaSki cells, through apoptosis, G(1) arrest, and regulation of gene expression.**
  Author(s): Ahn WS, Huh SW, Bae SM, Lee IP, Lee JM, Namkoong SE, Kim CK, Sin JI.
  Source: Dna and Cell Biology. 2003 March; 22(3): 217-24.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12804120&dopt=Abstract

- **A new approach for the detection of cervical cancer in Thai women.**
  Author(s): Sindhuphak R, Issaravanich S, Udomprasertgul V, Srisookho P, Warakamin S, Sindhuphak S, Boonbundarlchai R, Dusitsin N.
  Source: Gynecologic Oncology. 2003 July; 90(1): 10-4.
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- **A phase II study of multimodality treatment for locally advanced cervical cancer: neoadjuvant carboplatin and paclitaxel followed by radical hysterectomy and adjuvant cisplatin chemoradiation.**
  Author(s): Duenas-Gonzalez A, Lopez-Graniel C, Gonzalez-Enciso A, Cetina L, Rivera L, Mariscal I, Montalvo G, Gomez E, de la Garza J, Chanona G, Mohar A.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2003 August; 14(8): 1278-84.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12881393&dopt=Abstract

- **A prospective randomized study comparing retroperitoneal drainage with no drainage and no peritonization following radical hysterectomy and pelvic lymphadenectomy for invasive cervical cancer.**
  Author(s): Srisomboon J, Phongnarisorn C, Suprasert P, Cheewakriangkrai C, Siriaree S, Charoenkwan K.
  Source: The Journal of Obstetrics and Gynaecology Research. 2002 June; 28(3): 149-53.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12214830&dopt=Abstract

- **A relationship between Matrix metalloproteinase-1 (MMP-1) promoter polymorphism and cervical cancer progression.**
  Author(s): Nishioka Y, Sagae S, Nishikawa A, Ishioka S, Kudo R.
  Source: Cancer Letters. 2003 October 8; 200(1): 49-55.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14550952&dopt=Abstract

- **A relationship between methylenetetrahydrofolate reductase variants and the development of invasive cervical cancer.**
  Author(s): Gerhard DS, Nguyen LT, Zhang ZY, Borecki IB, Coleman BI, Rader JS.
  Source: Gynecologic Oncology. 2003 September; 90(3): 560-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=13678724&dopt=Abstract

- **A systematic literature review of the effectiveness of community-based strategies to increase cervical cancer screening.**
  Author(s): Black ME, Yamada J, Mann V.
  Source: Canadian Journal of Public Health. Revue Canadienne De Sante Publique. 2002 September-October; 93(5): 386-93. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12353463&dopt=Abstract

- **Abnormal fragile histidine triad expression in advanced cervical cancer and evaluation of its utility as a prognostic factor.**
  Author(s): Machida S, Ohwada M, Saga Y, Suzuki M.
  Source: Oncology. 2003; 65(1): 89-93.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12837987&dopt=Abstract

- **Accuracy of frozen section examination of pelvic lymph nodes in patients with FIGO stage IB1 to IIB cervical cancer.**
  Author(s): Scholz HS, Lax SF, Benedicic C, Tamussino K, Winter R.
  Source: Gynecologic Oncology. 2003 September; 90(3): 605-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=13678733&dopt=Abstract

- **ACS guideline for the early detection of cervical cancer.**
  Author(s): Mahoney MC, Saslow D, Cohen CJ; ACS.
  Source: American Family Physician. 2003 April 15; 67(8): 1677-8, 1680; Discussion 1680.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12725446&dopt=Abstract

- **An audit of delays before and during radical radiotherapy for cervical cancer--effect on tumour cure probability.**
  Author(s): Coles CE, Burgess L, Tan LT.
  Source: Clin Oncol (R Coll Radiol). 2003 April; 15(2): 47-54.
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- **An examination of sociocultural factors associated with cervical cancer screening among low-income Latina immigrants of reproductive age.**
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CHAPTER 2. NUTRITION AND CERVICAL CANCER

Overview

In this chapter, we will show you how to find studies dedicated specifically to nutrition and cervical cancer.

Finding Nutrition Studies on Cervical Cancer

The National Institutes of Health's Office of Dietary Supplements (ODS) offers a searchable bibliographic database called the IBIDS (International Bibliographic Information on Dietary Supplements; National Institutes of Health, Building 31, Room 1B29, 31 Center Drive, MSC 2086, Bethesda, Maryland 20892-2086, Tel: 301-435-2920, Fax: 301-480-1845, E-mail: ods@nih.gov). The IBIDS contains over 460,000 scientific citations and summaries about dietary supplements and nutrition as well as references to published international, scientific literature on dietary supplements such as vitamins, minerals, and botanicals.[7] The IBIDS includes references and citations to both human and animal research studies.

As a service of the ODS, access to the IBIDS database is available free of charge at the following Web address: **http://ods.od.nih.gov/databases/ibids.html**. After entering the search area, you have three choices: (1) IBIDS Consumer Database, (2) Full IBIDS Database, or (3) Peer Reviewed Citations Only.

Now that you have selected a database, click on the "Advanced" tab. An advanced search allows you to retrieve up to 100 fully explained references in a comprehensive format. Type "cervical cancer" (or synonyms) into the search box, and click "Go." To narrow the search, you can also select the "Title" field.

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[7] Adapted from **http://ods.od.nih.gov**. IBIDS is produced by the Office of Dietary Supplements (ODS) at the National Institutes of Health to assist the public, healthcare providers, educators, and researchers in locating credible, scientific information on dietary supplements. IBIDS was developed and will be maintained through an interagency partnership with the Food and Nutrition Information Center of the National Agricultural Library, U.S. Department of Agriculture.

The following information is typical of that found when using the "Full IBIDS Database" to search for "cervical cancer" (or a synonym):

- **A case report of recurrent cervical cancer which responded to a combination of biological therapies.**
  Author(s): Biotechnology Research Center, Teikyo University, Kanagawa, Japan.
  Source: Goto, S Sakai, S Kera, J Suma, Y Soma, G I Takeuchi, S Eur-J-Gynaecol-Oncol. 1994; 15(3): 235-40 0392-2936
- **Anticarcinogenic activity of strawberry, blueberry, and raspberry extracts to breast and cervical cancer cells.**
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- **Anti-tumour activity of a panel of taxanes toward a cellular model of human cervical cancer.**
  Author(s): Laboratory of Antineoplastic Pharmacology, Department of Obstetrics and Gynaecology, Universita Cattolica del Sacro Cuore, Largo A. Gemelli 8, I-00168 Rome, Italy.
  Source: Gallo, D Ferlini, C Distefano, M Cantelmo, F Gaggini, C Fattorossi, A Riva, A Bombardelli, E Proietti, E Mancuso, S Scambia, G Cancer-Chemother-Pharmacol. 2000; 45(2): 127-32 0344-5704
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  Author(s): Department of Therapeutic Radiology, University of Minnesota Hospital, Minneapolis 55455.
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- **Chemotherapy with paclitaxel, ifosfamide, and cisplatin for the treatment of squamous cell cervical cancer: the experience of Monza.**
  Author(s): Department of Obstetrics and Gynecology, San Gerardo Hospital, Monza, Italy.
  Source: Zanetta, G Fei, F Mangioni, C Semin-Oncol. 2000 February; 27(1 Suppl 1): 23-7 0093-7754
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  Author(s): Department of Obstetrics and Gynecology, Kinki University School of Medicine, Osaka.
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- **Combination therapy with irinotecan and cisplatin as neoadjuvant chemotherapy in locally advanced cervical cancer.**
  Author(s): Department of Obstetrics and Gynecology, Kurume University School of Medicine, Kurume City, Japan.
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- **Comparative study of bulky stage IB and IA cervical cancer patients treated by radical hysterectomy with and without neoadjuvant chemotherapy: long-term follow-up.**
  Author(s): Department of Obstetrics and Gynecology, Bangkok Metropolitan Medical College and Vajira Hospital, Thailand.

Source: Manusirivithaya, S Chareoniam, V Pantusart, A Isariyodom, P Srisomboon, J J-Med-Assoc-Thai. 2001 November; 84(11): 1550-7 0125-2208

- **Correlation of cervical cancer mortality with reproductive and dietary factors, and serum markers in China.**
  Author(s): Cancer Institute, Chinese Academy of Medical Sciences, Beijing, People's Republic of China.
  Source: Guo, W D Hsing, A W Li, J Y Chen, J S Chow, W H Blot, W J Int-J-Epidemiol. 1994 December; 23(6): 1127-32 0300-5771

- **Cure of cervical cancer using 252Cf neutron brachytherapy.**
  Author(s): Department of Radiation Medicine, University of Kentucky Medical Center, Lexington.
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  Author(s): Environmental Epidemiology Branch, National Cancer Institute, Bethesda, MD.
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  Author(s): Department of Family and Preventive Medicine, University of Utah School of Medicine, Salt Lake City 84132.
  Source: Slattery, M L Abbott, T M Overall, J C Robison, L M French, T K Jolles, C Gardner, J W West, D W Epidemiology. 1990 January; 1(1): 8-15 1044-3983

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  Author(s): Institute of Cytology and Preventive Oncology (ICMR), Maulana Azad Medical College, New Delhi, India. icpo@icmricpo.ren.nic.in
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  Author(s): Department of Gynecology/Obstetrics, Catholic University, Rome, Italy.
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  Author(s): Department of Obstetrics and Gynecology, Georgetown University Medical Center, USA.
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  Source: Robb Nicholson, C Harv-Womens-Health-Watch. 1998 September; 6(1): 8 1070-910X

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  Author(s): Institute of Oncology and Radiology, Beograd, Yugoslavia.
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  Author(s): Department of Anatomy, Kanazawa Medical University, Uchinada, Ishikawa, Japan.
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  Author(s): Division of Radiation Medicine, National Institute of Radiological Sciences, Chiba-shi, Japan.
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  Author(s): Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA.
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  Author(s): Faculty of Science, Department of Biochemistry, Annamalai University, Tamil Nadu, India. manshi2001in@yahoo.com
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  Author(s): Gynecology Clinic, Health Services. University of California, Santa Barbara, CA 93106, USA. cox-t@ucsb.edu
  Source: Cox, J T Obstet-Gynecol-Clin-North-Am. 2002 December; 29(4): 751-85 0889-8545

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  Author(s): Institute of Carcinogenesis, Cancer Research Center, Kashirskoye shosse 24, Moscow 115478, Russia. tan_ivanova@mail.ru
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  Author(s): Division of Radiation Oncology, Department of Radiology, The University of Iowa College of Medicine, Iowa City, Iowa 52242, USA.
  Source: Mayr, N A Hawighorst, H Yuh, W T Essig, M Magnotta, V A Knopp, M V J-Magn-Reson-Imaging. 1999 September; 10(3): 267-76 1053-1807

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  Author(s): Pengiran Arak Puteri Rashidah Sa'adatol Bolkiah College of Nursing, Gadong, Brunei.
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  Author(s): Biochemistry Department, University of Liverpool, UK.
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  Author(s): Department of Oncology, Albert Einstein College of Medicine, Bronx, New York, USA.
  Source: Wadler, S Schwartz, E L Anderson, P Runowicz, C D Chuang, L Del Priore, G Hochster, H Goldberg, G Fields, A Loewen, G Haynes, H Cancer-J-Sci-Am. 1999 May-June; 5(3): 165-70 1081-4442

- **Randomized trial of neoadjuvant cisplatin, vincristine, bleomycin, and radical hysterectomy versus radiation therapy for bulky stage IB and IIA cervical cancer.**
  Author(s): Departments of Obstetrics and Gynecology (Division of Gynecologic Oncology), Pathology, Radiation Oncology, and Diagnostic Radiology, and Biostatistics Consulting Center, Chang Gung Memorial Hospital Linkou Medical Center, Taoyuan, Taiwan.
  Source: Chang, T C Lai, C H Hong, J H Hsueh, S Huang, K G Chou, H H Tseng, C J Tsai, C S Chang, J T Lin, C T Chang, H H Chao, P J Ng, K K Tang, S G Soong, Y K J-Clin-Oncol. 2000 April; 18(8): 1740-7 0732-183X
- **Randomized trial radiotherapy with and without concomitant 13-cis-retinoic acid plus interferon-alpha for locally advanced cervical cancer: a preliminary report.**
  Author(s): Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.
  Source: Veerasarn, V Sritongchai, C Tepmongkol, P Senapad, S J-Med-Assoc-Thai. 1996 July; 79(7): 439-47 0125-2208
- **Remission of recurrent cervical cancer with paclitaxel and carboplatin: a case report and review of literature.**
  Author(s): Chulalongkorn University Hospital, Bangkok, Thailand.
  Source: Termrungruanglert, W Kudelka, A P Piamsomboon, S Edwards, C L Verschraegen, C F Loyer, E Kavanagh, J J Eur-J-Gynaecol-Oncol. 1996; 17(6): 493-6 0392-2936
- **Retention of cell adhesion and growth capability in human cervical cancer cells deprived of cell anchorage.**
  Author(s): Laboratory of Molecular Cell Biology, Kanagawa Cancer Center Research Institute, Yokohama. kkikuchi@yk.rim.or.jp
  Source: Kikuchi, K Yasumoto, S Jpn-J-Cancer-Res. 1999 August; 90(8): 867-73 0910-5050
- **Schedule in Cf-252 neutron brachytherapy: complications after delayed implant therapy for cervical cancer in a phase II trial.**
  Author(s): Radiation Therapy Oncology Center, University of Kentucky Medical Center, Lexington 40536.
  Source: Maruyama, Y van Nagell, J R Yoneda, J Gallion, H H DePriest, P Feola, J M Wierzbicki, J Am-J-Clin-Oncol. 1993 April; 16(2): 168-74 0277-3732
- **Serum selenium and the risk of cervical cancer among women in the United States.**
  Author(s): National Cancer Institute, Division of Cancer Control and Population Sciences, Applied Research Program, Risk Factor Monitoring and Methods Branch, EPN 4016, 6130 Executive Blvd, MSC 7344, Bethesda, MD 20892-7344, USA.
  Source: Thompson, F E Patterson, B H Weinstein, S J McAdams, M Spate, V L Hamman, R F Levine, R S Mallin, K Stolley, P D Brinton, L A Morris, J S Ziegler, R G Cancer-Causes-Control. 2002 August; 13(6): 517-26 0957-5243
- **Skin relapse from cervical cancer.**
  Author(s): Department of Gynaecology, University of Rome Campus Biomedico, Via Longoni 69, 00155 Rome, Italy.
  Source: Palaia, I Angioli, R Cutillo, G Manci, N Panici, P B Gynecol-Oncol. 2002 October; 87(1): 155-6 0090-8258
- **Smoking and dietary risk factors for cervical cancer at different age group in Japan.**
  Author(s): Division of Epidemiology, Aichi Cancer Center Research Institute, Nagoya, Japan.
  Source: Hirose, K Hamajima, N Takezaki, T Kuroishi, T Kuzuya, K Sasaki, S Tokudome, S Tajima, K J-Epidemiol. 1998 March; 8(1): 6-14 0917-5040

- **Smoking, dietary, and breast and cervical cancer screening knowledge and screening practices of employees in an urban medical center.**
  Author(s): Department of Epidemiology and Social Medicine, Albert Einstein College of Medicine, Bronx, New York, USA.
  Source: Hyman, R B Greenwald, E S Hacker, S J-Cancer-Educ. 1995 Summer; 10(2): 82-7 0885-8195

- **The differential inhibitory effects of genistein on the growth of cervical cancer cells in vitro.**
  Author(s): Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan. eugene@ms2.mmh.org.tw
  Source: Wang, S Y Yang, K W Hsu, Y T Chang, C L Yang, Y C Neoplasma. 2001; 48(3): 227-33 0028-2685

- **The effects of thiophosphoric acid (Ukrain) on cervical cancer, stage IB bulky.**
  Author(s): Department of Obstectrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Thailand.
  Source: Pengsaa, P Wongpratoom, W Vatanasapt, V Udomthavornsuk, B Mairieng, E Tangvorapongchai, V Pesi, M Krusan, S Boonvisoot, V Nowicky, J W Drugs-Exp-Clin-Res. 1992; 18 Suppl69-72 0378-6501

- **Utilization of the human genome sequence localizes human papillomavirus type 16 DNA integrated into the TNFAIP2 gene in a fatal cervical cancer from a 39-year-old woman.**
  Author(s): Division of Gynecologic Oncology, Department of Obstetrics and Gynecology and Women's Health, Albert Einstein College of Medicine/Montefiore Medical Center, 1300 Morris Park Avenue, Bronx, NY 10461, USA.
  Source: Einstein, Mark H Cruz, Yvette El Awady, Mustafa K Popescu, Nicolas C DiPaolo, Joseph A van Ranst, Marc Kadish, Anna S Romney, Seymour Runowicz, Carolyn D Burk, Robert D Clin-Cancer-Res. 2002 February; 8(2): 549-54 1078-0432

- **Weekly carboplatin and docetaxel for locally advanced primary and recurrent cervical cancer: a phase I study.**
  Author(s): Department of Gynecology and Obstetrics, University of Dusseldorf, Postfach 10 10 07, 40001 Dusseldorf, Germany. rein@med.uni-duesseldorf.de
  Source: Rein, D T Kurbacher, C M Breidenbach, M Schondorf, T Schmidt, T Konig, E Gohring, U J Blohmer, J U Mallmann, P Gynecol-Oncol. 2002 October; 87(1): 98-103 0090-8258

Federal Resources on Nutrition

In addition to the IBIDS, the United States Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) provide many sources of information on general nutrition and health. Recommended resources include:

- healthfinder®, HHS's gateway to health information, including diet and nutrition: **http://www.healthfinder.gov/scripts/SearchContext.asp?topic=238&page=0**
- The United States Department of Agriculture's Web site dedicated to nutrition information: **www.nutrition.gov**
- The Food and Drug Administration's Web site for federal food safety information: **www.foodsafety.gov**

- The National Action Plan on Overweight and Obesity sponsored by the United States Surgeon General: **http://www.surgeongeneral.gov/topics/obesity/**
- The Center for Food Safety and Applied Nutrition has an Internet site sponsored by the Food and Drug Administration and the Department of Health and Human Services: **http://vm.cfsan.fda.gov/**
- Center for Nutrition Policy and Promotion sponsored by the United States Department of Agriculture: **http://www.usda.gov/cnpp/**
- Food and Nutrition Information Center, National Agricultural Library sponsored by the United States Department of Agriculture: **http://www.nal.usda.gov/fnic/**
- Food and Nutrition Service sponsored by the United States Department of Agriculture: **http://www.fns.usda.gov/fns/**

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering food and nutrition. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=174&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/med_nutrition.html**
- Google: **http://directory.google.com/Top/Health/Nutrition/**
- Healthnotes: **http://www.healthnotes.com/**
- Open Directory Project: **http://dmoz.org/Health/Nutrition/**
- Yahoo.com: **http://dir.yahoo.com/Health/Nutrition/**
- WebMD®Health: **http://my.webmd.com/nutrition**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**

The following is a specific Web list relating to cervical cancer; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **Vitamins**

  Vitamin C
  Source: Prima Communications, Inc.www.personalhealthzone.com

- **Minerals**

  Folate
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Sulfur
  Source: Integrative Medicine Communications; www.drkoop.com

CHAPTER 3. ALTERNATIVE MEDICINE AND CERVICAL CANCER

Overview

In this chapter, we will begin by introducing you to official information sources on complementary and alternative medicine (CAM) relating to cervical cancer. At the conclusion of this chapter, we will provide additional sources.

National Center for Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (**http://nccam.nih.gov/**) has created a link to the National Library of Medicine's databases to facilitate research for articles that specifically relate to cervical cancer and complementary medicine. To search the database, go to the following Web site: **http://www.nlm.nih.gov/nccam/camonpubmed.html**. Select "CAM on PubMed." Enter "cervical cancer" (or synonyms) into the search box. Click "Go." The following references provide information on particular aspects of complementary and alternative medicine that are related to cervical cancer:

- **A breast and cervical cancer project in a native Hawaiian community: Wai'anae cancer research project.**
  Author(s): Banner RO, DeCambra H, Enos R, Gotay C, Hammond OW, Hedlung N, Issell BF, Matsunaga DS, Tsark JA.
  Source: Preventive Medicine. 1995 September; 24(5): 447-53.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8524718&dopt=Abstract

- **A case report of recurrent cervical cancer which responded to a combination of biological therapies.**
  Author(s): Goto S, Sakai S, Kera J, Suma Y, Soma GI, Takeuchi S.
  Source: Eur J Gynaecol Oncol. 1994; 15(3): 235-40.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7957329&dopt=Abstract

- **A comparison of MRI and PET scanning in surgically staged loco-regionally advanced cervical cancer: potential impact on treatment.**
  Author(s): Narayan K, Hicks RJ, Jobling T, Bernshaw D, McKenzie AF.
  Source: International Journal of Gynecological Cancer : Official Journal of the International Gynecological Cancer Society. 2001 July-August; 11(4): 263-71.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11520363&dopt=Abstract

- **A major constituent of green tea, EGCG, inhibits the growth of a human cervical cancer cell line, CaSki cells, through apoptosis, G(1) arrest, and regulation of gene expression.**
  Author(s): Ahn WS, Huh SW, Bae SM, Lee IP, Lee JM, Namkoong SE, Kim CK, Sin JI.
  Source: Dna and Cell Biology. 2003 March; 22(3): 217-24.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12804120&dopt=Abstract

- **A phase II study of multimodality treatment for locally advanced cervical cancer: neoadjuvant carboplatin and paclitaxel followed by radical hysterectomy and adjuvant cisplatin chemoradiation.**
  Author(s): Duenas-Gonzalez A, Lopez-Graniel C, Gonzalez-Enciso A, Cetina L, Rivera L, Mariscal I, Montalvo G, Gomez E, de la Garza J, Chanona G, Mohar A.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2003 August; 14(8): 1278-84.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12881393&dopt=Abstract

- **Adjuvant cytotoxic chemotherapy following Wertheim radical hysterectomy for cervical cancer.**
  Author(s): Sivanesaratnam V, Sen DK, Jayalakshmi P.
  Source: The Australian & New Zealand Journal of Obstetrics & Gynaecology. 1987 August; 27(3): 231-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2449159&dopt=Abstract

- **Adjuvant immunotherapy: two randomized controlled studies of patients with cervical cancer.**
  Author(s): Okamura K, Hamazaki Y, Yajima A, Noda K.
  Source: Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie. 1989; 43(3): 177-81.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2528386&dopt=Abstract

- **American Indian women's talking circle. A cervical cancer screening and prevention project.**
  Author(s): Hodge FS, Fredericks L, Rodriguez B.
  Source: Cancer. 1996 October 1; 78(7 Suppl): 1592-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8839577&dopt=Abstract

- **Antitumor activity of Langerhans cells in radiation therapy for cervical cancer and its modulation with SPG administration.**
  Author(s): Nakano T, Oka K, Sugita T, Tsunemoto H.
  Source: In Vivo. 1993 May-June; 7(3): 257-63.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8357967&dopt=Abstract

- **Anti-tumour activity of a panel of taxanes toward a cellular model of human cervical cancer.**
  Author(s): Gallo D, Ferlini C, Distefano M, Cantelmo F, Gaggini C, Fattorossi A, Riva A, Bombardelli E, Proietti E, Mancuso S, Scambia G.
  Source: Cancer Chemotherapy and Pharmacology. 2000; 45(2): 127-32.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10663627&dopt=Abstract

- **Assessing tumor hypoxia in cervical cancer by positron emission tomography with 60Cu-ATSM: relationship to therapeutic response-a preliminary report.**
  Author(s): Dehdashti F, Grigsby PW, Mintun MA, Lewis JS, Siegel BA, Welch MJ.
  Source: International Journal of Radiation Oncology, Biology, Physics. 2003 April 1; 55(5): 1233-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12654432&dopt=Abstract

- **Augmentation of immune responses of pelvic lymph node lymphocytes in patients with cervical cancer by sizofiran.**
  Author(s): Shimizu Y, Chen JT, Hirai Y, Nakayama K, Hamada T, Fujimoto I, Hasumi K, Masubuchi K.
  Source: Nippon Sanka Fujinka Gakkai Zasshi. 1989 December; 41(12): 2013-4. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2531784&dopt=Abstract

- **Augmenting effect of sizofiran on the immunofunction of regional lymph nodes in cervical cancer.**
  Author(s): Shimizu Y, Hasumi K, Masubuchi K.
  Source: Cancer. 1992 March 1; 69(5): 1184-94.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1739919&dopt=Abstract

- **Bleomycin, vincristine, and mitomycin C (BOM) as second-line treatment after failure of cis-platinum-based combination chemotherapy for recurrent cervical cancer.**
  Author(s): Wheelock JB, Krebs HB, Goplerud DR.
  Source: Gynecologic Oncology. 1990 April; 37(1): 21-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1691126&dopt=Abstract

- **Breast and cervical cancer among lesbians.**
  Author(s): Rankow EJ.

Source: Women's Health Issues : Official Publication of the Jacobs Institute of Women's Health. 1995 Fall; 5(3): 123-9.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7549490&dopt=Abstract

- **Chemotherapy with paclitaxel, ifosfamide, and cisplatin for the treatment of squamous cell cervical cancer: the experience of Monza.**
  Author(s): Zanetta G, Fei F, Mangioni C.
  Source: Seminars in Oncology. 2000 February; 27(1 Suppl 1): 23-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10697040&dopt=Abstract

- **Circulating nucleosomes and response to chemotherapy: an in vitro, in vivo and clinical study on cervical cancer patients.**
  Author(s): Trejo-Becerril C, Perez-Cardenas E, Trevino-Cuevas H, Taja-Chayeb L, Garcia-Lopez P, Segura-Pacheco B, Chavez-Blanco A, Lizano-Soberon M, Gonzalez-Fierro A, Mariscal I, Wegman-Ostrosky T, Duenas-Gonzalez A.
  Source: International Journal of Cancer. Journal International Du Cancer. 2003 May 10; 104(6): 663-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12640671&dopt=Abstract

- **Clinical effect of sizofiran combined with irradiation in cervical cancer patients: a randomized controlled study. Cooperative Study Group on SPG for Gynecological Cancer.**
  Author(s): Noda K, Takeuchi S, Yajima A, Akiya K, Kasamatsu T, Tomoda Y, Ozawa M, Sekiba K, Sugimori H, Hashimoto S, et al.
  Source: Japanese Journal of Clinical Oncology. 1992 February; 22(1): 17-25.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1573785&dopt=Abstract

- **Clinical evaluation of sizofiran combined with irradiation in patients with cervical cancer. A randomized controlled study; a five-year survival rate.**
  Author(s): Okamura K, Suzuki M, Chihara T, Fujiwara A, Fukuda T, Goto S, Ichinohe K, Jimi S, Kasamatsu T, Kawai N, et al.
  Source: Biotherapy (Dordrecht, Netherlands). 1989; 1(2): 103-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2534912&dopt=Abstract

- **Combination chemotherapy followed by surgery or radiotherapy in patients with locally advanced cervical cancer.**
  Author(s): Kirsten F, Atkinson KH, Coppleson JV, Elliott PM, Green D, Houghton R, Murray JC, Russell P, Solomon HJ, Friedlander M, et al.
  Source: British Journal of Obstetrics and Gynaecology. 1987 June; 94(6): 583-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2441736&dopt=Abstract

- **Combination therapy with irinotecan and cisplatin as neoadjuvant chemotherapy in locally advanced cervical cancer.**

Author(s): Sugiyama T, Nishida T, Kumagai S, Nishio S, Fujiyoshi K, Okura N, Yakushiji M, Hiura M, Umesaki N.
Source: British Journal of Cancer. 1999 September; 81(1): 95-8.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10487618&dopt=Abstract

- **Comparative study of bulky stage IB and IA cervical cancer patients treated by radical hysterectomy with and without neoadjuvant chemotherapy: long-term follow-up.**
  Author(s): Manusirivithaya S, Chareoniam V, Pantusart A, Isariyodom P, Srisomboon J.
  Source: J Med Assoc Thai. 2001 November; 84(11): 1550-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11853297&dopt=Abstract

- **Concurrent radiation therapy and irinotecan in stage IIIB cervical cancer.**
  Author(s): Suntornpong N, Pattaranutaporn P, Chanslip Y, Thephamongkhol K.
  Source: J Med Assoc Thai. 2003 May; 86(5): 430-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12859099&dopt=Abstract

- **Contribution of whole-body 18FDG PET imaging in the management of cervical cancer.**
  Author(s): Belhocine T, Thille A, Fridman V, Albert A, Seidel L, Nickers P, Kridelka F, Rigo P.
  Source: Gynecologic Oncology. 2002 October; 87(1): 90-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12468348&dopt=Abstract

- **Detecting para-aortic lymph nodal metastasis by positron emission tomography of 18F-fluorodeoxyglucose in advanced cervical cancer with negative magnetic resonance imaging findings.**
  Author(s): Yeh LS, Hung YC, Shen YY, Kao CH, Lin CC, Lee CC.
  Source: Oncol Rep. 2002 November-December; 9(6): 1289-92.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12375036&dopt=Abstract

- **Detection of early recurrence with 18F-FDG PET in patients with cervical cancer.**
  Author(s): Ryu SY, Kim MH, Choi SC, Choi CW, Lee KH.
  Source: Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine. 2003 March; 44(3): 347-52.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12620999&dopt=Abstract

- **Diagnosis of recurrent uterine cervical cancer: computed tomography versus positron emission tomography.**
  Author(s): Park DH, Kim KH, Park SY, Lee BH, Choi CW, Chin SY.
  Source: Korean Journal of Radiology : Official Journal of the Korean Radiological Society. 2000 January-March; 1(1): 51-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11752929&dopt=Abstract

- **Dialectic classification of syndrome diagnosis in traditional Chinese medicine used as new criterion for evaluating prognosis of patients with cervical cancer.**
  Author(s): Yu SY, Zhang LA, Yang JX, Qian ZK, Peng YW.
  Source: J Tongji Med Univ. 1991; 11(2): 123-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1816417&dopt=Abstract

- **Early diagnosis and evaluation of therapy in postoperative recurrent cervical cancers by positron emission tomography.**
  Author(s): Umesaki N, Tanaka T, Miyama M, Tokuyama O, Kawamura N, Ogita S, Kawabe J, Okamura T, Koyama K, Ochi H.
  Source: Oncol Rep. 2000 January-February; 7(1): 53-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10601591&dopt=Abstract

- **Effect of bitter melon (Momordica charantia Linn) on level and function of natural killer cells in cervical cancer patients with radiotherapy.**
  Author(s): Pongnikorn S, Fongmoon D, Kasinrerk W, Limtrakul PN.
  Source: J Med Assoc Thai. 2003 January; 86(1): 61-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12678140&dopt=Abstract

- **Effects of concomitant use of doxifluridine, radiotherapy and immunotherapy in patients with advanced cervical cancer.**
  Author(s): Yamamoto K, Noda K, Hatae M, Kudo T, Hasegawa K, Nishimura R, Honjo H, Yajima A, Sato S, Mizutani K, Yakushiji M, Terashima Y, Ochiai K, Sasaki H, Ozaki M.
  Source: Oncol Rep. 2001 March-April; 8(2): 273-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11182039&dopt=Abstract

- **Elevated topoisomerase I activity in cervical cancer as a target for chemoradiation therapy.**
  Author(s): Chen BM, Chen JY, Kao M, Lin JB, Yu MH, Roffler SR.
  Source: Gynecologic Oncology. 2000 November; 79(2): 272-80.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11063656&dopt=Abstract

- **Emodin induces apoptosis of human cervical cancer cells through poly(ADP-ribose) polymerase cleavage and activation of caspase-9.**
  Author(s): Srinivas G, Anto RJ, Srinivas P, Vidhyalakshmi S, Senan VP, Karunagaran D.
  Source: European Journal of Pharmacology. 2003 July 25; 473(2-3): 117-25.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12892828&dopt=Abstract

- **Evidence of an association between human papillomavirus and impaired chemotherapy-induced apoptosis in cervical cancer cells.**
  Author(s): Padilla LA, Leung BS, Carson LF.

Source: Gynecologic Oncology. 2002 April; 85(1): 59-66.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11925121&dopt=Abstract

- **Health promotion in cervical cancer prevention among the Yakama Indian women of the Wa'Shat Longhouse.**
  Author(s): Strickland CJ, Squeoch MD, Chrisman NJ.
  Source: Journal of Transcultural Nursing : Official Journal of the Transcultural Nursing Society / Transcultural Nursing Society. 1999 July; 10(3): 190-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10693405&dopt=Abstract

- **Hemolytic-uremic syndrome associated with neoadjuvant chemotherapy in the treatment of advanced cervical cancer.**
  Author(s): Angiola G, Bloss JD, DiSaia PJ, Warner AS, Manetta A, Berman ML.
  Source: Gynecologic Oncology. 1990 November; 39(2): 214-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1699855&dopt=Abstract

- **Holistic care of the patient with cervical cancer.**
  Author(s): McMullin M.
  Source: Nurs Clin North Am. 1992 December; 27(4): 847-58. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1448360&dopt=Abstract

- **Human cervical cancer cells use Ca2+ signalling, protein tyrosine phosphorylation and MAP kinase in regulatory volume decrease.**
  Author(s): Shen MR, Chou CY, Browning JA, Wilkins RJ, Ellory JC.
  Source: The Journal of Physiology. 2001 December 1; 537(Pt 2): 347-62.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11731569&dopt=Abstract

- **Human papillomaviruses and cervical cancer in Bangkok. III. The role of husbands and commercial sex workers.**
  Author(s): Thomas DB, Ray RM, Kuypers J, Kiviat N, Koetsawang A, Ashley RL, Qin Q, Koetsawang S.
  Source: American Journal of Epidemiology. 2001 April 15; 153(8): 740-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11296145&dopt=Abstract

- **Immunological modulation of lymphocyte subpopulation in cervical cancer tissue by sizofiran and OK-432.**
  Author(s): Gorai I, Yanagibashi T, Minaguchi H.
  Source: Gynecologic Oncology. 1992 February; 44(2): 137-46.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1371977&dopt=Abstract

- **Impact on survival following successful neoadjuvant chemotherapy and radical surgery for Stage IIb bulky and Stage IIIb cervical cancer.**
  Author(s): Sugiyama T, Hasuo Y, Nishida T, Kamura T.

Source: Gynecologic Oncology. 2001 May; 81(2): 330-1.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11330973&dopt=Abstract

- **Implications for breast and cervical cancer control for Latinas in the rural South: a review of the literature.**
  Author(s): Mayo RM, Erwin DO, Spitler HD.
  Source: Cancer Control : Journal of the Moffitt Cancer Center. 2003 September-October; 10(5 Suppl): 60-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14581906&dopt=Abstract

- **Improved prognostic value of 18F-FDG PET using a simple visual analysis of tumor characteristics in patients with cervical cancer.**
  Author(s): Miller TR, Pinkus E, Dehdashti F, Grigsby PW.
  Source: Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine. 2003 February; 44(2): 192-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12571208&dopt=Abstract

- **In vitro synergistic effects of some novel Cu(II) complexes in combination with epirubicin and mitomycin C against HeLa-S3 cervical cancer cell line.**
  Author(s): Geromichalos GD, Katsoulos GA, Hadjikostas CC, Kortsaris AH, Kyriakidis DA.
  Source: Anti-Cancer Drugs. 1996 June; 7(4): 469-75.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8826615&dopt=Abstract

- **Induced apoptosis and necrosis by 2-methylfuranonaphthoquinone in human cervical cancer HeLa cells.**
  Author(s): Pan J, Simamura E, Koyama J, Shimada H, Hirai KI.
  Source: Cancer Detection and Prevention. 2000; 24(3): 266-74.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10975289&dopt=Abstract

- **Induction chemotherapy followed by radical surgery in cervical cancer.**
  Author(s): Dottino PR, Plaxe SC, Beddoe AM, Johnston C, Cohen CJ.
  Source: Gynecologic Oncology. 1991 January; 40(1): 7-11.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1703509&dopt=Abstract

- **Intracavitary brachytherapy and cervical cancer.**
  Author(s): Grigsby PW.
  Source: Cancer Journal (Sudbury, Mass.). 2000 November-December; 6(6): 362-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11131484&dopt=Abstract

- **Intratumoral administration of sizofiran activates Langerhans cell and T-cell infiltration in cervical cancer.**
  Author(s): Nakano T, Oka K, Hanba K, Morita S.

Source: Clinical Immunology and Immunopathology. 1996 April; 79(1): 79-86.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8612354&dopt=Abstract

- **Involvement of JNK-mediated pathway in EGF-mediated protection against paclitaxel-induced apoptosis in SiHa human cervical cancer cells.**
Author(s): Liu B, Fang M, Lu Y, Lu Y, Mills GB, Fan Z.
Source: British Journal of Cancer. 2001 July 20; 85(2): 303-11.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11461094&dopt=Abstract

- **Involvement of PKC-alpha in regulatory volume decrease responses and activation of volume-sensitive chloride channels in human cervical cancer HT-3 cells.**
Author(s): Chou CY, Shen MR, Hsu KS, Huang HY, Lin HC.
Source: The Journal of Physiology. 1998 October 15; 512 (Pt 2): 435-48.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9763633&dopt=Abstract

- **Irinotecan for the treatment of cervical cancer.**
Author(s): Verschraegen CF.
Source: Oncology (Huntingt). 2002 May; 16(5 Suppl 5): 32-4. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12109804&dopt=Abstract

- **Irinotecan in cervical cancer.**
Author(s): Kavanagh JJ, Verschraegen CF, Kudelka AP.
Source: Oncology (Huntingt). 1998 August; 12(8 Suppl 6): 94-8. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9726099&dopt=Abstract

- **Measurement of tumor volume by PET to evaluate prognosis in patients with advanced cervical cancer treated by radiation therapy.**
Author(s): Miller TR, Grigsby PW.
Source: International Journal of Radiation Oncology, Biology, Physics. 2002 June 1; 53(2): 353-9.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12023139&dopt=Abstract

- **Mitochondrial damage by a new antitumour agent furanonaphthoquinone derivative in human cervical cancer HeLa cells.**
Author(s): Pan J, Hirai KI, Simamura E, Koyama J, Shimada H, Kuwabara S.
Source: Journal of Electron Microscopy. 1997; 46(2): 181-7.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9180033&dopt=Abstract

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Author(s): Shen MR, Chou CY, Hsu KF, Hsu KS, Wu ML.

Source: Acta Physiologica Scandinavica. 1999 November; 167(3): 215-25.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10606823&dopt=Abstract

- **Multimodal therapy including neoadjuvant methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) for stage IIB to IV cervical cancer.**
  Author(s): Dowdy SC, Boardman CH, Wilson TO, Podratz KC, Hartmann LC, Long HJ.
  Source: American Journal of Obstetrics and Gynecology. 2002 June; 186(6): 1167-73.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12066092&dopt=Abstract

- **Neoadjuvant chemotherapy followed by radiotherapy should not be a standard approach for locally advanced cervical cancer.**
  Author(s): Shueng PW, Hsu WL, Jen YM, Wu CJ, Liu HS.
  Source: International Journal of Radiation Oncology, Biology, Physics. 1998 March 1; 40(4): 889-96.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9531375&dopt=Abstract

- **Neoadjuvant chemotherapy with cisplatin, ifosfamide and paclitaxel for locally advanced squamous-cell cervical cancer.**
  Author(s): Zanetta G, Lissoni A, Pellegrino A, Sessa C, Colombo N, Gueli-Alletti D, Mangioni C.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 1998 September; 9(9): 977-80.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9818071&dopt=Abstract

- **Neoadjuvant chemotherapy with vincristine and cisplatin followed by radical hysterectomy and pelvic lymphadenectomy for FIGO stage IB bulky cervical cancer: a Gynecologic Oncology Group pilot study.**
  Author(s): Eddy GL, Manetta A, Alvarez RD, Williams L, Creasman WT.
  Source: Gynecologic Oncology. 1995 June; 57(3): 412-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7774847&dopt=Abstract

- **Neoadjuvant intraarterial infusion chemotherapy with a combination of mitomycin-C, vincristine, and cisplatin for locally advanced cervical cancer: a preliminary report.**
  Author(s): Itoh N, Sawairi M, Hanabayashi T, Mori H, Yamawaki Y, Tamaya T.
  Source: Gynecologic Oncology. 1992 December; 47(3): 391-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1473755&dopt=Abstract

- **Paclitaxel, ifosfamide and cisplatin (TIP) chemotherapy for recurrent or persistent squamous-cell cervical cancer.**
  Author(s): Zanetta G, Fei F, Parma G, Balestrino M, Lissoni A, Gabriele A, Mangioni C.

Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 1999 October; 10(10): 1171-4.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10586332&dopt=Abstract

- **Paclitaxel: a radiation sensitizer of human cervical cancer cells.**
  Author(s): Rodriguez M, Sevin BU, Perras J, Nguyen HN, Pham C, Steren AJ, Koechli OR, Averette HE.
  Source: Gynecologic Oncology. 1995 May; 57(2): 165-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7729728&dopt=Abstract

- **Phase I study of combination chemotherapy using irinotecan hydrochloride and nedaplatin for advanced or recurrent cervical cancer.**
  Author(s): Machida S, Ohwada M, Fujiwara H, Konno R, Takano M, Kita T, Kikuchi Y, Komiyama S, Mikami M, Suzuki M.
  Source: Oncology. 2003; 65(2): 102-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12931014&dopt=Abstract

- **Phase I trial of taxol as a radiation sensitizer with cisplatin in advanced cervical cancer.**
  Author(s): Chen MD, Paley PJ, Potish RA, Twiggs LB.
  Source: Gynecologic Oncology. 1997 November; 67(2): 131-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9367695&dopt=Abstract

- **Phase II clinical study of irinotecan and cisplatin as first-line chemotherapy in metastatic or recurrent cervical cancer.**
  Author(s): Chitapanarux I, Tonusin A, Sukthomya V, Charuchinda C, Pukanhapan N, Lorvidhaya V.
  Source: Gynecologic Oncology. 2003 June; 89(3): 402-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12798702&dopt=Abstract

- **Phase II study of irinotecan and cisplatin as first-line chemotherapy in advanced or recurrent cervical cancer.**
  Author(s): Sugiyama T, Yakushiji M, Noda K, Ikeda M, Kudoh R, Yajima A, Tomoda Y, Terashima Y, Takeuchi S, Hiura M, Saji F, Takahashi T, Umesaki N, Sato S, Hatae M, Ohashi Y.
  Source: Oncology. 2000; 58(1): 31-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10644938&dopt=Abstract

- **Physiologic FDG-PET three-dimensional brachytherapy treatment planning for cervical cancer.**
  Author(s): Malyapa RS, Mutic S, Low DA, Zoberi I, Bosch WR, Laforest R, Miller TR, Grigsby PW.

Source: International Journal of Radiation Oncology, Biology, Physics. 2002 November 15; 54(4): 1140-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12419441&dopt=Abstract

- **Pilot study on induction chemotherapy with cisplatin, epirubicin, etoposide and bleomycin in cervical cancer stage Ib, IIa and IIb.**
  Author(s): Panetta A, Angelelli B, Martoni A.
  Source: Anticancer Res. 1999 January-February; 19(1B): 765-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10216490&dopt=Abstract

- **Positron emission tomography for evaluating para-aortic nodal metastasis in locally advanced cervical cancer before surgical staging: a surgicopathologic study.**
  Author(s): Rose PG, Adler LP, Rodriguez M, Faulhaber PF, Abdul-Karim FW, Miraldi F.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1999 January; 17(1): 41-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10458216&dopt=Abstract

- **Posttherapy surveillance monitoring of cervical cancer by FDG-PET.**
  Author(s): Grigsby PW, Siegel BA, Dehdashti F, Mutch DG.
  Source: International Journal of Radiation Oncology, Biology, Physics. 2003 March 15; 55(4): 907-13.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12605968&dopt=Abstract

- **Preoperative adjuvant chemotherapy in the treatment of cervical cancer stage Ib, IIa, and IIb with bulky tumor.**
  Author(s): Kim DS, Moon H, Hwang YY, Cho SH.
  Source: Gynecologic Oncology. 1988 March; 29(3): 321-32.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2450055&dopt=Abstract

- **Prognostic value of positron emission tomography using F-18-fluorodeoxyglucose in patients with cervical cancer undergoing radiotherapy.**
  Author(s): Nakamoto Y, Eisbruch A, Achtyes ED, Sugawara Y, Reynolds KR, Johnston CM, Wahl RL.
  Source: Gynecologic Oncology. 2002 February; 84(2): 289-95.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11812089&dopt=Abstract

- **Prognostic value of thymidine phosphorylase immunostaining in patients with uterine cervical cancer treated concurrently with doxifluridine, radiotherapy and immunotherapy.**
  Author(s): Sato S, Yajima A, Sasaki H, Mizutani K, Honjo H, Yamamoto K, Ozaki M, Hasegawa K, Kudo T, Yakushiji M, Hatae M, Noda K.

Source: Oncol Rep. 2001 March-April; 8(2): 239-44.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11182033&dopt=Abstract

- **Randomized trial of neoadjuvant cisplatin, vincristine, bleomycin, and radical hysterectomy versus radiation therapy for bulky stage IB and IIA cervical cancer.**
  Author(s): Chang TC, Lai CH, Hong JH, Hsueh S, Huang KG, Chou HH, Tseng CJ, Tsai CS, Chang JT, Lin CT, Chang HH, Chao PJ, Ng KK, Tang SG, Soong YK.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 2000 April; 18(8): 1740-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10764435&dopt=Abstract

- **Remission of recurrent cervical cancer with paclitaxel and carboplatin: a case report and review of literature.**
  Author(s): Termrungruanglert W, Kudelka AP, Piamsomboon S, Edwards CL, Verschraegen CF, Loyer E, Kavanagh JJ.
  Source: Eur J Gynaecol Oncol. 1996; 17(6): 493-6. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8971525&dopt=Abstract

- **Role of the nurse practitioner in breast and cervical cancer prevention.**
  Author(s): Leslie NS.
  Source: Cancer Nursing. 1995 August; 18(4): 251-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7664252&dopt=Abstract

- **Skin relapse from cervical cancer.**
  Author(s): Palaia I, Angioli R, Cutillo G, Manci N, Panici PB.
  Source: Gynecologic Oncology. 2002 October; 87(1): 155-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12468360&dopt=Abstract

- **Stressful events, pessimism, natural killer cell cytotoxicity, and cytotoxic/suppressor T cells in HIV+ black women at risk for cervical cancer.**
  Author(s): Byrnes DM, Antoni MH, Goodkin K, Efantis-Potter J, Asthana D, Simon T, Munajj J, Ironson G, Fletcher MA.
  Source: Psychosomatic Medicine. 1998 November-December; 60(6): 714-22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9847030&dopt=Abstract

- **Surgical management of early stage cervical cancer: ten years experience from one Greek health region.**
  Author(s): Paraskevaidis E, Kalantaridou SN, Kaponis A, Chouliara S, Agnantis NJ, Dousias V, Zikopoulos K, Paschopoulos M, Stamatopoulos P, Lolis DE.
  Source: Eur J Gynaecol Oncol. 2002; 23(4): 341-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12214740&dopt=Abstract

- **Ten-year survival of patients with locally advanced, stage ib-iib cervical cancer after neoadjuvant chemotherapy and radical hysterectomy.**
  Author(s): Hwang YY, Moon H, Cho SH, Kim KT, Moon YJ, Kim SR, Kim DS.
  Source: Gynecologic Oncology. 2001 July; 82(1): 88-93.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11426967&dopt=Abstract

- **The differential inhibitory effects of genistein on the growth of cervical cancer cells in vitro.**
  Author(s): Wang SY, Yang KW, Hsu YT, Chang CL, Yang YC.
  Source: Neoplasma. 2001; 48(3): 227-33.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11583294&dopt=Abstract

- **The effects of thiophosphoric acid (Ukrain) on cervical cancer, stage IB bulky.**
  Author(s): Pengsaa P, Wongpratoom W, Vatanasapt V, Udomthavornsuk B, Mairieng E, Tangvorapongchai V, Pesi M, Krusan S, Boonvisoot V, Nowicky JW.
  Source: Drugs Exp Clin Res. 1992; 18 Suppl: 69-72.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1305048&dopt=Abstract

- **The role of focus groups in health education for cervical cancer among minority women.**
  Author(s): Dignan M, Michielutte R, Sharp P, Bahnson J, Young L, Beal P.
  Source: Journal of Community Health. 1990 December; 15(6): 369-75.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2280036&dopt=Abstract

- **The role of neoadjuvant chemotherapy for squamous cell cervical cancer (Ib-IIIb): a long-term randomized trial.**
  Author(s): Napolitano U, Imperato F, Mossa B, Framarino ML, Marziani R, Marzetti L.
  Source: Eur J Gynaecol Oncol. 2003; 24(1): 51-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12691318&dopt=Abstract

- **The role of topotecan in the treatment of advanced cervical cancer.**
  Author(s): Fiorica JV.
  Source: Gynecologic Oncology. 2003 September; 90(3 Pt 2): S16-21. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=13129491&dopt=Abstract

- **Therapy monitoring using FDG-PET in metastatic cervical cancer.**
  Author(s): Dose J, Hemminger GE, Bohuslavizki KH.
  Source: The Lancet Oncology. 2000 October; 1: 106.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11905661&dopt=Abstract

- **Treatment of advanced cervical cancer by a combination of peplomycin, vincristine, mitomycin-C, and cisplatin.**
  Author(s): Sugimori H, Iwasaka T, Fukuda K, Hayashi Y, Hachisuga T.

Source: Gynecologic Oncology. 1989 August; 34(2): 180-2.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2473949&dopt=Abstract

- **Two-year survival: preoperative adjuvant chemotherapy in the treatment of cervical cancer stages Ib and II with bulky tumor.**
  Author(s): Kim DS, Moon H, Kim KT, Hwang YY, Cho SH, Kim SR.
  Source: Gynecologic Oncology. 1989 May; 33(2): 225-30.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2467848&dopt=Abstract

- **Vaginal radical hysterectomy for uterine cervical cancer.**
  Author(s): Zhang QB.
  Source: Chinese Medical Journal. 1990 September; 103(9): 743-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2123775&dopt=Abstract

- **Value of whole body 18F-fluoro-2-deoxyglucose positron emission tomography in the evaluation of recurrent cervical cancer.**
  Author(s): Sun SS, Chen TC, Yen RF, Shen YY, Changlai SP, Kao A.
  Source: Anticancer Res. 2001 July-August; 21(4B): 2957-61.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11712793&dopt=Abstract

- **Weekly carboplatin and docetaxel for locally advanced primary and recurrent cervical cancer: a phase I study.**
  Author(s): Rein DT, Kurbacher CM, Breidenbach M, Schondorf T, Schmidt T, Konig E, Gohring UJ, Blohmer JU, Mallmann P.
  Source: Gynecologic Oncology. 2002 October; 87(1): 98-103.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12468349&dopt=Abstract

- **Wertheim's hysterectomy after neoadjuvant carboplatin-based chemotherapy in patients with cervical cancer stage IIB and IIIB.**
  Author(s): Meden H, Fattahi-Meibodi A, Osmers R, Krauss T, Kuhn W.
  Source: Anticancer Res. 1998 November-December; 18(6B): 4575-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9891521&dopt=Abstract

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering CAM and related topics. The following is a representative sample:

- Alternative Medicine Foundation, Inc.: **http://www.herbmed.org/**
- AOL: **http://search.aol.com/cat.adp?id=169&layer=&from=subcats**
- Chinese Medicine: **http://www.newcenturynutrition.com/**
- drkoop.com®: **http://www.drkoop.com/InteractiveMedicine/IndexC.html**

- Family Village: **http://www.familyvillage.wisc.edu/med_altn.htm**
- Google: **http://directory.google.com/Top/Health/Alternative/**
- Healthnotes: **http://www.healthnotes.com/**
- MedWebPlus: **http://medwebplus.com/subject/Alternative_and_Complementary_Medicine**
- Open Directory Project: **http://dmoz.org/Health/Alternative/**
- HealthGate: **http://www.tnp.com/**
- WebMD®Health: **http://my.webmd.com/drugs_and_herbs**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**
- Yahoo.com: **http://dir.yahoo.com/Health/Alternative_Medicine/**

The following is a specific Web list relating to cervical cancer; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **General Overview**

  Abnormal Pap Smear
  Source: Healthnotes, Inc.; www.healthnotes.com

  AIDS and HIV
  Source: Integrative Medicine Communications; www.drkoop.com

  Breast Cancer
  Source: Healthnotes, Inc.; www.healthnotes.com

  Cancer Prevention (reducing the Risk)
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Cervical Dysplasia
  Source: Integrative Medicine Communications; www.drkoop.com

  Cervical Dysplasia
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Warts
  Source: Healthnotes, Inc.; www.healthnotes.com

- **Herbs and Supplements**

  Beta-carotene
  Source: Prima Communications, Inc.www.personalhealthzone.com

  Carotenoids
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com

Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,763,00.html

Gamma-linolenic Acid (gla)
Source: Integrative Medicine Communications; www.drkoop.com

Gla
Source: Integrative Medicine Communications; www.drkoop.com

Indole-3-carbinol
Source: Healthnotes, Inc.; www.healthnotes.com

Oral Contraceptives
Source: Healthnotes, Inc.; www.healthnotes.com

General References

A good place to find general background information on CAM is the National Library of Medicine. It has prepared within the MEDLINEplus system an information topic page dedicated to complementary and alternative medicine. To access this page, go to the MEDLINEplus site at **http://www.nlm.nih.gov/medlineplus/alternativemedicine.html**. This Web site provides a general overview of various topics and can lead to a number of general sources.

CHAPTER 4. DISSERTATIONS ON CERVICAL CANCER

Overview

In this chapter, we will give you a bibliography on recent dissertations relating to cervical cancer. We will also provide you with information on how to use the Internet to stay current on dissertations. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical dissertations that use the generic term "cervical cancer" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on cervical cancer, we have not necessarily excluded non-medical dissertations in this bibliography.

Dissertations on Cervical Cancer

ProQuest Digital Dissertations, the largest archive of academic dissertations available, is located at the following Web address: **http://wwwlib.umi.com/dissertations**. From this archive, we have compiled the following list covering dissertations devoted to cervical cancer. You will see that the information provided includes the dissertation's title, its author, and the institution with which the author is associated. The following covers recent dissertations found when using this search procedure:

- **A Population-based Study of the Management of Cervical Cancer in Ontario, 1982--1991** by Strang, Barbara Kathleen; Msc from Queen's University at Kingston (canada), 2002, 146 pages
  http://wwwlib.umi.com/dissertations/fullcit/MQ73090
- **Adoption of Liquid-based Cervical Cancer Screening Test and Other Technologies in Primary Care** by Rappaport, Karen M.; Phd from The Johns Hopkins University, 2002, 288 pages
  http://wwwlib.umi.com/dissertations/fullcit/3046543
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CHAPTER 5. CLINICAL TRIALS AND CERVICAL CANCER

Overview

In this chapter, we will show you how to keep informed of the latest clinical trials concerning cervical cancer.

Recent Trials on Cervical Cancer

The following is a list of recent trials dedicated to cervical cancer.[8] Further information on a trial is available at the Web site indicated.

- **A Clinical Trial of the P-Glycoprotein Antagonist, Tariquidar (XR9576), in Combination With Docetaxel in Patients With Lung, Ovarian, and Cervical Cancer: Analysis of the Interaction Between Tariquidar and Docetaxel**

  Condition(s): Lung Neoplasms; Ovarian Neoplasms; Cervix Neoplasms

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI)

  Purpose - Excerpt: Intrinsic and acquired drug resistance remain major obstacles in the treatment of cancer. Accumulating evidence indicates that in some malignancies Pglycoprotein (Pgp) can confer resistance, and that its reversal can improve therapeutic outcome. Clinical trials investigating Pgp antagonists have been hampered by the occurrence of unpredictable pharmacokinetic interactions, which have required dose reductions of the chemotherapeutic agents to avert excessive toxicity. Tariquidar (XR9576) is a new Pgp antagonist that is more potent and has prolonged activity. Phase I trials with paclitaxel, vinorelbine, and doxorubicin have demonstrated that tariquidar (XR9576) has minimal pharmacokinetic interactions while surrogate studies have confirmed in vivo inhibition of Pgp-mediated drug transport. This study seeks to determine the pharmacokinetic interaction, if any, between docetaxel and tariquidar and to evaluate the potential for activity in lung, ovarian, and cervical cancers. The secondary goal is to evaluate the impact of tariquidar on uptake of (99m)Tc-sestamibi in recurrent or metastatic tumors of patients with lung, ovarian, or cervical cancer.

  Phase(s): Phase II

[8] These are listed at **www.ClinicalTrials.gov**.

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00069160

- **Antineoplaston Therapy in Treating Patients With Stage IV Cancer of the Cervix and/or Vulva**

  Condition(s): stage IV cervical cancer; recurrent cervical cancer; stage IV vulvar cancer; recurrent vulvar cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Burzynski Research Institute

  Purpose - Excerpt: RATIONALE: Antineoplastons are naturally occurring substances found in urine. Antineoplastons may inhibit the growth of cancer cells. PURPOSE: Phase II trial to study the effectiveness of antineoplaston therapy in treating patients with stage IV cancer of the cervix and/or vulva.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00003525

- **Bevacizumab in Treating Patients With Persistent or Recurrent Cancer of the Cervix**

  Condition(s): recurrent cervical cancer; cervical squamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Monoclonal antibodies such as bevacizumab can locate tumor cells and either kill them or deliver tumor-killing substances to them without harming normal cells. PURPOSE: Phase II trial to study the effectiveness of bevacizumab in treating patients who have persistent or recurrent cancer of the cervix.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00025233

- **Capecitabine in Treating Patients With Persistent or Recurrent Cervical Cancer**

  Condition(s): recurrent cervical cancer; cervical adenocarcinoma; cervical adenosquamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. PURPOSE: Phase II trial to study the effectiveness of capecitabine in treating patients who have persistent or recurrent cervical cancer.

  Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00039442

- **Chemotherapy and Radiation Therapy With or Without Surgery in Treating Patients With Stage I Cancer of the Cervix**

  Condition(s): cervical adenocarcinoma; cervical adenosquamous cell carcinoma; cervical squamous cell carcinoma; stage IB cervical cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Radiation therapy uses high-energy x-rays to damage tumor cells. Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. It is not yet known which regimen of radiation therapy combined with chemotherapy, with or without surgery, is more effective in treating early cancer of the cervix. PURPOSE: Randomized phase III trial to compare the effectiveness of surgery followed by different regimens of radiation therapy and chemotherapy with that of chemotherapy and radiation therapy alone in treating patients who have stage I cancer of the cervix.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00054067

- **Chemotherapy Followed By Surgery Compared With Radiation Therapy Plus Chemotherapy in Treating Patients With Stage IB or Stage II Cervical Cancer**

  Condition(s): stage IB cervical cancer; stage IIB cervical cancer; stage IIA cervical cancer; cervical squamous cell carcinoma; cervical adenocarcinoma; cervical adenosquamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): EORTC Gynecological Cancer Cooperative Group

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Giving chemotherapy drugs before surgery may shrink the tumor so that it can be removed during surgery. Radiation therapy uses high-energy x-rays to kill tumor cells. Combining radiation therapy with chemotherapy may kill more tumor cells. It is not yet known whether chemotherapy is more effective followed by surgery or combined with radiation therapy in treating cervical cancer. PURPOSE: Randomized phase III trial to compare the effectiveness of chemotherapy followed by radical hysterectomy with that of chemotherapy plus radiation therapy in treating patients who have stage IB or stage II cervical cancer.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00039338

- **Comparison of Three Chemotherapy Regimens in Treating Patients With Stage IVB, Recurrent, or Persistent Cervical Cancer**

  Condition(s): recurrent cervical cancer; stage IVB cervical cancer; cervical squamous cell carcinoma; cervical adenocarcinoma; cervical adenosquamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI); Eastern Cooperative Oncology Group

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining more than one drug may kill more tumor cells. It is not yet known which chemotherapy regimen is more effective for cervical cancer. PURPOSE: Randomized phase III trial to compare the effectiveness of three different chemotherapy regimens in treating patients with stage IVB, recurrent, or persistent cervical cancer.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00003945

- **Docetaxel in Treating Patients With Persistent or Recurrent Cervical Cancer**

  Condition(s): recurrent cervical cancer; cervical squamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. PURPOSE: Phase II trial to study the effectiveness of docetaxel in treating patients who have persistent or recurrent cervical cancer.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00041093

- **EF5 to Detect Tumor Hypoxia in Patients With Stage IIB, Stage IIIB, or Stage IVA Cervical Cancer**

  Condition(s): cervical adenocarcinoma; cervical adenosquamous cell carcinoma; cervical squamous cell carcinoma; stage IIB cervical cancer; stage III cervical cancer; stage IVA cervical cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Knowing the level of oxygen in tumor tissue may help predict the effectiveness of anticancer therapy. EF5 may be effective in measuring oxygen in tumor tissue and helping to predict the effectiveness of anticancer therapy. PURPOSE: Diagnostic trial to study the effectiveness of EF5 in detecting tumor hypoxia in patients who have stage IIB, stage IIIB, or stage IVA cervical cancer.

  Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00049231

- **Epoetin beta in Treating Anemia in Patients With Cervical Cancer**

  Condition(s): Anemia; Cervical Cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): AGO Ovarian Cancer Study Group

  Purpose - Excerpt: RATIONALE: Epoetin beta may stimulate red blood cell production to prevent or control anemia in patients treated with chemotherapy and radiation therapy. PURPOSE: Randomized phase IV trial to determine the effectiveness of epoetin beta in treating anemia in patients who are receiving cisplatin and radiation therapy for stage IIB, stage III, or stage IVA cervical cancer.

  Phase(s): Phase IV

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00046969

- **Erlotinib in Treating Patients With Persistent or Recurrent Cancer of the Cervix**

  Condition(s): recurrent cervical cancer; cervical squamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Biological therapies such as erlotinib may interfere with the growth of tumor cells and slow the growth of the tumor. PURPOSE: Phase II trial to study the effectiveness of erlotinib in treating patients who have persistent or recurrent cancer of the cervix.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00031993

- **Healing Touch and Immunity in Advanced Cervical Cancer Patients**

  Condition(s): Cervical Cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Center for Complementary and Alternative Medicine (NCCAM)

  Purpose - Excerpt: Healing touch is a therapy classified by NIH as a "biofield" therapy as its effects are proposed to be the result of manipulation of hypothesized "energy fields" around the body of a patient. Although HT is frequently used as a complementary treatment by cancer patients undergoing chemotherapy and radiation to reduce toxic side effects of treatment and to maintain immunocompetence, effects of this treatment during cancer chemotherapy and radiation have not been investigated. Additionally, little is known about physiological mechanisms by which HT may work. A recent meta-analysis has demonstrated relatively large effects of HT on well-being and on physiological parameters, even from brief treatments. This study is designed to examine

effects of HT on cellular immune function and short-term side effects of treatment among women with advanced cervical cancer who are receiving a standard 5-week course of external radiation therapy and concurrent chemotherapy.Although combined chemotherapy and radiation treatment is potentially curative in 69% of cases, many patients experience both acute and late side effects of radiation. Severe immune compromise has also been reported following intensive radiation. Identification of interventions that could reduce side effects and help maintain immunocompetence in advanced cervical cancer patients undergoing treatment is a critical health problem. There are no data on the effects of healing touch on immune function among cancer patients undergoing chemotherapy and radiation. Therefore this study is designed as an exploratory trial to determine whether such immune effects exist, and if so, what immune parameters are most likely to be affected. Effects of healing touch on mood and treatment-specific side-effects will also be examined. The significance of this study is that it will provide preliminary data on the impact, if any, of HT on various parameters of cellular immune function, beginning information on mechanisms of action, and whether the magnitude of the impact is large enough to be of sufficient clinical significance to be examined in larger clinical trials.

Phase(s): Phase I; Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00065091

- **Imiquimod in Preventing Cervical Cancer in Women With Cervical Neoplasia**

  Condition(s): Cervical Cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): North Central Cancer Treatment Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Chemoprevention therapy is the use of certain substances to try to prevent the development of cancer. Applying topical imiquimod before abnormal cervical cells are removed may be effective in preventing cervical cancer. PURPOSE: Randomized phase II trial to study the effectiveness of applying topical imiquimod before abnormal cervical cells are removed in preventing cervical cancer in patients who have recurrent or persistent cervical neoplasia.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00031759

- **Liposomal Doxorubicin in Treating Patients With Persistent or Recurrent Cancer of the Cervix**

  Condition(s): recurrent cervical cancer; stage IVB cervical cancer; cervical squamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. PURPOSE: Phase II trial to

study the effectiveness liposomal doxorubicin in treating patients who have persistent or recurrent cancer of the cervix.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00030472

- **Oxaliplatin and Paclitaxel in Treating Patients With Locally Recurrent or Metastatic Cervical Cancer**

  Condition(s): recurrent cervical cancer; stage IVA cervical cancer; stage IVB cervical cancer; cervical adenosquamous cell carcinoma; cervical squamous cell carcinoma; cervical adenocarcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Cornell University Medical College; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining more than one drug may kill more tumor cells. PURPOSE: Phase II trial to study the effectiveness of combining oxaliplatin with paclitaxel in treating patients who have locally recurrent or metastatic cervical cancer.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00057863

- **Paclitaxel and Cisplatin Compared With Vinorelbine and Cisplatin in Treating Patients With Stage IVB, Recurrent, or Persistent Cancer of the Cervix**

  Condition(s): cervical adenocarcinoma; cervical adenosquamous cell carcinoma; cervical squamous cell carcinoma; recurrent cervical cancer; stage IVB cervical cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy such as paclitaxel, cisplatin, and vinorelbine use different ways to stop tumor cells from dividing so they stop growing or die. It is not yet known whether cisplatin is more effective when combined with paclitaxel or vinorelbine in treating **cervical cancer.** PURPOSE: Randomized phase III trial to compare the effectiveness of cisplatin combined with either paclitaxel or vinorelbine in treating women who have stage IVB, recurrent, or persistent cancer of the cervix.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00064077

- **Peripheral Stem Cell Transplantation, White Blood Cell Infusions, Chemotherapy, and Radiation Therapy in Treating Patients With Recurrent Metastatic Cervical or Vaginal Cancer**

  Condition(s): Cervical Cancer; Vaginal Cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Fred Hutchinson Cancer Research Center; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Donor peripheral stem cell transplantation and donor white blood cell infusions may be able to replace immune cells that were destroyed by chemotherapy or radiation therapy used to kill tumor cells. Sometimes the transplanted cells are rejected by the body's normal tissues. Mycophenolate mofetil and cyclosporine may prevent this from happening. PURPOSE: Phase II trial to study the effectiveness of donor peripheral stem cell transplantation plus chemotherapy and total-body irradiation followed by donor white blood cell infusion in treating patients who have recurrent metastatic or locally advanced cancer of the cervix or vagina that is associated with human papillomavirus.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00005941

- **Photodynamic Therapy Using Lutetium Texaphyrin in Treating Patients With Cervical Intraepithelial Neoplasia**

  Condition(s): Cervical Cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): University of Pittsburgh Cancer Institute; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Photodynamic therapy uses light and drugs such as lutetium texaphyrin that make abnormal cells more sensitive to light and may kill abnormal cells in the cervix and prevent the development of **cervical cancer.** PURPOSE: Phase I trial to study the effectiveness of photodynamic therapy with lutetium texaphyrin in treating patients who have cervical intraepithelial neoplasia.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00005808

- **Pilot Study of ZD1839 (Iressa, Gefitinib) in Patients with Advanced Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer, or Cervical Cancer**

  Condition(s): Ovarian Neoplasms; Cervix Neoplasms

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI)

  Purpose - Excerpt: This study will evaluate the safety and effectiveness of the experimental drug ZD1839 (also known as Iressa(r) (Registered Trademark) or gefitinib) for treating patients with advanced ovarian or cervical cancer with or without fallopian tube or primary peritoneal cancer. ZD1839 attacks a group of proteins called epidermal

growth factor receptor (EGFR) proteins. These proteins are found on the surface of some cancer cells and some normal cells and may help tumor cells grow and spread to other parts of the body. In laboratory experiments, ZD1839 slowed the growth of certain cancers, and in preliminary studies in humans, a small number of women with ovarian cancer who took ZD1839 had no tumor growth for the period of time they received the drug. This study will determine whether ZD1839 can cause tumors to shrink or stabilize in some patients with ovarian or cervical cancer. It will also look for tumor characteristics that may indicate which ones are more likely to respond to treatment with ZD1839. Women 18 years of age or older with ovarian or cervical cancer whose cancer persists or has relapsed after undergoing at least one operation and one course of chemotherapy or radiotherapy may be eligible for this study. Patients with fallopian tube or primary peritoneal cancer may also participate. Candidates will be screened with a medical history, physical examination, blood and urine tests, and a computerized tomography (CT) scan to locate the tumor and determine biopsy sites (see below). Participants will take ZD1839 tablets by mouth once a day. They will keep a diary of when they take the medicine and record any side effects they may experience. In addition, they will have the following tests and procedures: - CT scan before starting treatment and again every 8 weeks to monitor tumor size. - Tumor biopsies before starting treatment and about 4 weeks into the study to look for characteristics unique to the patient's tumor that might make it more likely to respond to ZD1839. Tumor biopsies will be done using a needle or by direct visualization using laparoscopy. For the needle biopsy, the area of the procedure is anesthetized and a small needle is inserted through the skin into the tumor. A piece of tissue smaller than the size of a pin is withdrawn through the needle. The needle biopsy is done under CT guidance, allowing the radiologist to see exactly where to place the needle. Laparoscopy is a surgical procedure, performed under sedation or general anesthesia, that is done if the tumor is in a place that cannot be reached with a needle through the skin. It requires making two small holes in the skin through which tubes are inserted to locate the tumor and cut out a small piece of tissue. - Skin biopsies before starting treatment and about 4 weeks into the study to determine the effect of ZD1839 on EGFR. The skin biopsies use a cookie cutter-like instrument to obtain two pieces of skin the size of a grain of rice. - Follow-up visits every 4 weeks or more often, as needed, for a physical examination and blood tests, and review of laboratory studies and drug side effects. Patients whose tumor stops growing or shrinks and who do not have serious drug side effects may continue to receive treatment. Those whose cancer worsens or who develop severe drug side effects will be taken off the study, referred back to their local physician, and counseled about other NCI trials for which they may be eligible or options outside NCI that may be available to them.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00046007

- **Protein Expression as a Potential Diagnostic Biomarker of Cervical Dysplasia and/or Cancer**

  Condition(s): stage 0 cervical cancer; Precancerous Condition

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

Purpose - Excerpt: RATIONALE: The presence of specific proteins may allow a doctor to determine whether a patient has cervical dysplasia and/or cancer. PURPOSE: Diagnostic trial to evaluate the effectiveness of the presence of a specific protein as a potential biomarker of cervical dysplasia and/or cancer.

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00003384

- **Radiation Therapy and Cisplatin With or Without Amifostine in Treating Patients With Stage IIIB or Stage IVA Cancer of the Cervix**

  Condition(s): radiation toxicity; stage III cervical cancer; stage IVA cervical cancer; cervical squamous cell carcinoma; cervical adenocarcinoma; cervical adenosquamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Radiation Therapy Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy, such as cisplatin, use different ways to stop tumor cells from dividing so they stop growing or die. Radiation therapy uses high-energy x-rays to damage tumor cells. Combining radiation therapy with chemotherapy may kill more tumor cells. Drugs such as amifostine may protect normal cells from the side effects of radiation therapy. PURPOSE: Phase I/II trial to study the effectiveness of combining cisplatin and radiation therapy with or without amifostine in treating patients who have stage IIIB or stage IVA cancer of the cervix.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00012012

- **Radiation Therapy Plus Celecoxib, Fluorouracil, and Cisplatin in Patients With Locally Advanced Cervical Cancer**

  Condition(s): Cervical Cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Radiation Therapy Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Radiation therapy uses high-energy x-rays to damage tumor cells. Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Giving radiation therapy in different ways and combining it with chemotherapy may kill more tumor cells. Celecoxib may slow the growth of cervical cancer by stopping blood flow to the tumor. PURPOSE: Phase I/II trial to study the effectiveness of radiation therapy plus celecoxib, fluorouracil, and cisplatin in treating patients who have locally advanced cervical cancer.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00023660

- **Radiation Therapy Plus Paclitaxel and Cisplatin in Treating Patients With Cervical Cancer**

  Condition(s): Cervical Cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Radiation therapy uses high-energy x-rays to damage tumor cells. Paclitaxel and cisplatin may increase the effectiveness of radiation therapy by making the tumor cells more sensitive to radiation. Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining radiation therapy with chemotherapy may kill more tumor cells. PURPOSE: Phase I/II trial to study the effectiveness of radiation therapy to the pelvis plus paclitaxel and cisplatin in treating patients who have cervical cancer.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00003379

- **Radiation Therapy, Paclitaxel, and Cisplatin in Treating Patients With Cancer of the Cervix**

  Condition(s): stage III cervical cancer; stage IVA cervical cancer; cervical squamous cell carcinoma; cervical adenocarcinoma; cervical adenosquamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Radiation therapy uses high-energy x-rays to damage tumor cells. Paclitaxel and cisplatin may increase the effectiveness of radiation therapy by making the tumor cells more sensitive to the radiation. Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining radiation therapy with chemotherapy may kill more tumor cells. PURPOSE: Phase I/II trial to study the effectiveness of radiation therapy plus paclitaxel and cisplatin in treating patients who have cancer of the cervix that has spread to the lymph nodes in the pelvis and abdomen.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00003377

- **SGN-00101 in Treating Patients With Cervical Intraepithelial Neoplasia**

  Condition(s): Cervical Cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Brigham and Women's Hospital; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Chemoprevention therapy is the use of certain drugs to try to prevent the development of or treat early cancer. SGN-00101 may be effective in preventing the development of **cervical cancer** in patients with cervical intraepithelial neoplasia. PURPOSE: Randomized phase II trial to study the effectiveness of SGN-00101

in preventing **cervical cancer** in patients who have cervical intraepithelial neoplasia and human papillomavirus.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00060099

- **Surgery and Vaccine Therapy in Treating Patients With Early Cervical Cancer**

  Condition(s): stage IB cervical cancer; stage IIA cervical cancer; cervical squamous cell carcinoma; cervical adenocarcinoma; cervical adenosquamous cell carcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): EORTC New Drug Development Group

  Purpose - Excerpt: RATIONALE: Vaccines made from human papillomavirus may make the body build an immune response to and kill cervical cancer cells. Combining vaccine therapy with surgery may be a more effective treatment for cervical cancer. PURPOSE: Phase II trial to study the effectiveness of vaccine therapy made from human papillomavirus plus surgery in treating patients with early cervical cancer.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002916

- **Topotecan and Paclitaxel in Treating Patients With Recurrent or Metastatic Cancer of the Cervix**

  Condition(s): recurrent cervical cancer; stage IVB cervical cancer; stage IVA cervical cancer; cervical squamous cell carcinoma; cervical adenocarcinoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Herbert Irving Comprehensive Cancer Center

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining more than one drug may kill more tumor cells. PURPOSE: Phase II trial to study the effectiveness of topotecan and paclitaxel in treating patients who have recurrent or metastatic cancer of the cervix.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00003065

- **Vaginal Changes and Sexual Function in Patients With Cervical Cancer**

  Condition(s): sexuality and reproductive issues; stage IB cervical cancer

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

Purpose - Excerpt: RATIONALE: Vaginal changes that may effect sexual function occur in patients undergoing treatment for cervical cancer. PURPOSE: Clinical trial to determine the type of vaginal changes such as vaginal dryness that occur in patients receiving treatment for cervical cancer and the effect these changes have on sexual function.

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00053261

- **Whole Body Hyperthermia Combined With Chemotherapy in Treating Patients With Metastatic Breast, Ovarian, Endometrial, or Cervical Cancer**

  Condition(s): Breast Cancer; Cervical Cancer; Endometrial Cancer; Male Breast Cancer; ovarian epithelial cancer; ovarian germ cell tumor

  Study Status: This study is currently recruiting patients.

  Sponsor(s): University of Texas

  Purpose - Excerpt: RATIONALE: Hyperthermia therapy kills tumor cells by heating them to several degrees above body temperature. Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining chemotherapy with hyperthermia may kill more tumor cells. PURPOSE: Phase II trial to study the effectiveness of fluorouracil and liposomal doxorubicin combined with systemic hyperthermia in treating patients with metastatic breast, ovarian, endometrial, or cervical cancer.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00003135

- **Will Radiation/Chemotherapy Treatment of Cervical Cancer Work Better With Medication That May Improve Anemia?**

  Condition(s): Anemia; Cervix Neoplasms

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Amgen

  Purpose - Excerpt: This is a clinical trial (a type of research study) designed to describe the efficacy (effectiveness) and toxicity (safety) of a new medical treatment, NESP (Novel Erythropoiesis Stimulating Protein). This study will be offered to patients with cervical cancer undergoing a combination of chemotherapy and radiation. This treatment may lower your red blood cells. The use of NESP may stimulate the body to produce more red blood cells. Our hypothesis is that higher red blood cells will be beneficial to the patient during treatment for cervical cancer.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00039884

- **Celecoxib in Treating Patients With High-Grade Squamous Intraepithelial Lesions of the Cervix**

  Condition(s): stage 0 cervical cancer; high-grade squamous intraepithelial lesion

  Study Status: This study is not yet open for patient recruitment.

  Sponsor(s): Southwest Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Chemoprevention therapy is the use of certain drugs to try to prevent the development of cancer. Celecoxib may be effective in preventing **cervical cancer.** PURPOSE: Randomized phase II trial to study the effectiveness of celecoxib in preventing **cervical cancer** in patients who have high-grade squamous intraepithelial lesions of the cervix.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00072540

- **Lymph Node Mapping and Sentinel Lymph Node Identification in Patients With Stage IB1 Cervical Cancer**

  Condition(s): cervical adenocarcinoma; cervical adenosquamous cell carcinoma; cervical squamous cell carcinoma; stage I cervical cancer

  Study Status: This study is not yet open for patient recruitment.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Diagnostic procedures, such as lymph node mapping and sentinel lymph node identification, performed before and during surgery, may improve the ability to detect lymph node metastases in patients who have cervical cancer. PURPOSE: Diagnostic trial to study the effectiveness of lymph node mapping and sentinel lymph node identification before and during surgery in detecting lymph node metastases in patients who have stage IB1 cervical cancer.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00070317

- **Radiation Therapy and Chemotherapy in Treating Patients With Locally Advanced Cervical Cancer**

  Condition(s): cervical adenocarcinoma; Cervical Cancer; cervical squamous cell carcinoma

  Study Status: This study is not yet open for patient recruitment.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Radiation therapy uses high-energy x-rays to damage tumor cells. Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining radiation therapy with chemotherapy may kill more tumor cells. PURPOSE: Phase I trial to study the effectiveness of combining radiation therapy with chemotherapy in treating patients who have locally advanced cervical cancer.

  Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00054444

- **Radiation Therapy Plus Cisplatin and Gemcitabine in Treating Patients With Cervical Cancer**

  Condition(s): Cervical Cancer

  Study Status: This study is not yet open for patient recruitment.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Radiation therapy uses high-energy x-rays to damage tumor cells. Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining cisplatin with gemcitabine may make the tumor cells more sensitive to radiation therapy and may kill more tumor cells. PURPOSE: Phase I trial to study the effectiveness of combining radiation therapy with cisplatin and gemcitabine in treating patients who have cervical cancer that has not spread beyond the pelvis.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00068549

- **Vaccine Therapy in Preventing Cervical Cancer in Patients With Cervical Intraepithelial Neoplasia**

  Condition(s): Cervical Cancer

  Study Status: This study is not yet open for patient recruitment.

  Sponsor(s): Gynecologic Oncology Group; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Vaccines made from antigens may make the body build an immune response to kill abnormal cervical cells and may be effective in preventing cervical cancer. PURPOSE: Randomized phase II trial to study the effectiveness of vaccine therapy in preventing cervical cancer in patients who have cervical intraepithelial neoplasia.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00054041

Keeping Current on Clinical Trials

The U.S. National Institutes of Health, through the National Library of Medicine, has developed ClinicalTrials.gov to provide current information about clinical research across the broadest number of diseases and conditions.

The site was launched in February 2000 and currently contains approximately 5,700 clinical studies in over 59,000 locations worldwide, with most studies being conducted in the United States. ClinicalTrials.gov receives about 2 million hits per month and hosts approximately 5,400 visitors daily. To access this database, simply go to the Web site at **http://www.clinicaltrials.gov/** and search by "cervical cancer" (or synonyms).

While ClinicalTrials.gov is the most comprehensive listing of NIH-supported clinical trials available, not all trials are in the database. The database is updated regularly, so clinical trials are continually being added. The following is a list of specialty databases affiliated with the National Institutes of Health that offer additional information on trials:

- For clinical studies at the Warren Grant Magnuson Clinical Center located in Bethesda, Maryland, visit their Web site: **http://clinicalstudies.info.nih.gov/**
- For clinical studies conducted at the Bayview Campus in Baltimore, Maryland, visit their Web site: **http://www.jhbmc.jhu.edu/studies/index.html**
- For cancer trials, visit the National Cancer Institute: **http://cancertrials.nci.nih.gov/**
- For eye-related trials, visit and search the Web page of the National Eye Institute: **http://www.nei.nih.gov/neitrials/index.htm**
- For heart, lung and blood trials, visit the Web page of the National Heart, Lung and Blood Institute: **http://www.nhlbi.nih.gov/studies/index.htm**
- For trials on aging, visit and search the Web site of the National Institute on Aging: **http://www.grc.nia.nih.gov/studies/index.htm**
- For rare diseases, visit and search the Web site sponsored by the Office of Rare Diseases: **http://ord.aspensys.com/asp/resources/rsch_trials.asp**
- For alcoholism, visit the National Institute on Alcohol Abuse and Alcoholism: **http://www.niaaa.nih.gov/intramural/Web_dicbr_hp/particip.htm**
- For trials on infectious, immune, and allergic diseases, visit the site of the National Institute of Allergy and Infectious Diseases: **http://www.niaid.nih.gov/clintrials/**
- For trials on arthritis, musculoskeletal and skin diseases, visit newly revised site of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health: **http://www.niams.nih.gov/hi/studies/index.htm**
- For hearing-related trials, visit the National Institute on Deafness and Other Communication Disorders: **http://www.nidcd.nih.gov/health/clinical/index.htm**
- For trials on diseases of the digestive system and kidneys, and diabetes, visit the National Institute of Diabetes and Digestive and Kidney Diseases: **http://www.niddk.nih.gov/patient/patient.htm**
- For drug abuse trials, visit and search the Web site sponsored by the National Institute on Drug Abuse: **http://www.nida.nih.gov/CTN/Index.htm**
- For trials on mental disorders, visit and search the Web site of the National Institute of Mental Health: **http://www.nimh.nih.gov/studies/index.cfm**
- For trials on neurological disorders and stroke, visit and search the Web site sponsored by the National Institute of Neurological Disorders and Stroke of the NIH: **http://www.ninds.nih.gov/funding/funding_opportunities.htm#Clinical_Trials**

CHAPTER 6. PATENTS ON CERVICAL CANCER

Overview

Patents can be physical innovations (e.g. chemicals, pharmaceuticals, medical equipment) or processes (e.g. treatments or diagnostic procedures). The United States Patent and Trademark Office defines a patent as a grant of a property right to the inventor, issued by the Patent and Trademark Office.[9] Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

In this chapter, we show you how to locate information on patents and their inventors. If you find a patent that is particularly interesting to you, contact the inventor or the assignee for further information. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical patents that use the generic term "cervical cancer" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on cervical cancer, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Cervical Cancer

By performing a patent search focusing on cervical cancer, you can obtain information such as the title of the invention, the names of the inventor(s), the assignee(s) or the company that owns or controls the patent, a short abstract that summarizes the patent, and a few excerpts from the description of the patent. The abstract of a patent tends to be more technical in nature, while the description is often written for the public. Full patent descriptions contain much more information than is presented here (e.g. claims, references, figures, diagrams, etc.). We will tell you how to obtain this information later in the chapter. The following is an

[9]Adapted from the United States Patent and Trademark Office: **http://www.uspto.gov/web/offices/pac/doc/general/whatis.htm**.

example of the type of information that you can expect to obtain from a patent search on cervical cancer:

- **Cap-pap test**

  Inventor(s): Markovic; Nenad (259 Congressional La., #602, Rockville, MD 20852), Markovic; Olivera (259 Congressional La., #602, Rockville, MD 20852)

  Assignee(s): none reported

  Patent Number: 6,143,512

  Date filed: June 10, 1999

  Abstract: The CAP-PAP Test is a double-staining, single-slide microscopic method. An in vitro diagnostic medical device for manual and automatic staining and interpreting of the Pap smear for **cervical cancer** screening, cervical dysplasia and for follow-up therapy can be developed using this double-staining, single-slide microscopic method. Abnormal cervical cells are labeled with an intracellular acid phosphatase derived pigment (azo-dye) to improve visibility of abnormal cervical cells on conventionally stained Pap smears. The enzyme marker improves human perception and/or sensitivity of automatic instruments when distinguishing cell a abnormality and interpretation of Pap smears. Increased accuracy of CAP-PAP-vs-Pap test is expected to reduce false negative readings of the conventional Pap test. A rapid manual version of the test that is low cost, does not require additional personnel training and is instantly applicable in all cytopathology laboratories is provided. The invention further provides a diagnostic kit, an automatic stainer and an automatic evaluation device for performing the double-staining, single-slide microscopic method.

  Excerpt(s): The CAP-PAP Test is a new double-staining, single-slide microscopic method that could be developed into an in vitro diagnostic medical device for manual and automatic staining and interpreting of Pap smears for **cervical cancer** screening, diagnosis of cervical dysplasia and follow-up of therapy. Our idea (novelty) is to use acid phosphatase to label abnormal cervical epithelial cells on Pap smears stained by conventional Papanicolaou technique and, by improving visibility of abnormal cells to improve human perception (sensitivity of automatic instruments) of abnormal cells and interpretation (specificity of automatic instruments) of Pap smears. Increasing accuracy (better sensitivity and at least equivalent specificity with Pap test) the CAP-PAP test could reduce false negative readings of the conventional Pap test--an achievement that could be of benefit to many women. We are not aware that anybody else has used our technique for the same purpose. The manual version of the test is a rapid, low cost assay, which does not require additional personnel training, and is instantly applicable in all cytopathology laboratories. The patent protects against infringement of the idea, a process (method, assay) and three products--a diagnostic kit, an automatic processor (stainer) and an automatic evaluation device (digitized image analyzer). Patent protection should cover all rights including manufacture, use and sale.

  Web site: http://www.delphion.com/details?pn=US06143512__

- **Cervical cancer self-screening methods and apparatus**

  Inventor(s): Zwelling-Aamot; Marcy L. (2425 E. Ocean Blvd., Long Beach, CA 90803)

  Assignee(s): none reported

  Patent Number: 6,206,839

  Date filed: January 15, 1999

  Abstract: An insert for the passive, painless, noninvasive self-collection of free endocervical cells by a subject includes a body and a substrate for cell collection. The body has a proximal end for manipulation by the subject and a distal end on which the cell-collecting substrate is disposed. The body is configured so that the substrate is positionable by the subject within the vagina, preferably near the vaginal portion of the cervix, to allow collection of free endocervical cells onto the cell-collection surface. After cells have been collected, the subject may place the cell-retaining substrate into a cell-suspension preservative contained in a sealable receptacle for transport to a laboratory for conventional analysis.

  Excerpt(s): Broadly stated, the present invention relates to cancer screening methods and apparatus. More particularly, the present invention is directed to a simple and accurate method and associated apparatus that will allow a female patient to collect cervical cells in the privacy of her home as part of a cervical cancer-screening test. The apparatus of the present invention is easy and inexpensive to manufacture and, used in accordance with the method of the invention, will enhance patient compliance with recommended cervical cancer-screening protocols. In the early 1900s, **cervical cancer** was the leading cause of cancer death for women. Even today, after nearly 100 years of continued medical research and development, **cervical cancer** continues to be the leading cause of cancer death for women in developing countries. These deaths are completely unnecessary because up to 90% of the most common types of **cervical cancer** may be prevented if identified early and treated. The present invention facilitates this early identification and subsequent treatment. In spite of the ability of modem medical practitioners to effectively eradicate most types of **cervical cancer,** it is estimated that 100,000 new cases of **cervical cancer** in the United States go undetected every five years. The same characteristics of **cervical cancer** that make it relatively easy to treat once identified contribute to the difficulty in its detection. In its early stages of development, **cervical cancer** grows contiguously in localized, defined sites and does not interfere with other normal bodily functions. Thus, at these early stages, **cervical cancer** can be relatively asymptomatic and can continue to grow and progress for years with little indication other than minor, localized bleeding which can be dismissed as normal "spotting." Left unchecked for a year or more, **cervical cancer** can spread beyond the cervix without warning. At this point, once detected, the cancer may be so advanced that it may likely be untreatable and may ultimately lead to the patient's death.

  Web site: http://www.delphion.com/details?pn=US06206839__

- **Cervix-to-rectum measuring device in a radiation applicator for use in the treatment of cervical cancer**

  Inventor(s): Fischell; David R. (Ithaca, NY), Mazique; Jeffrey C. (Mt. Rainier, MD)

  Assignee(s): The United States of America as represented by the Administrator of the (Washington, DC)

  Patent Number: 4,294,264

  Date filed: May 12, 1977

  Abstract: A cervix-to-rectum measuring device to be used in the treatment of **cervical cancer** which includes a handle and a probe pivotably connected to the handle for insertion in the rectum. The measuring device further includes means for coupling the handle to an intrauterine radiation applicator when the latter is positioned in the uterine cervix and the probe is inserted in the rectum to pivot the handle about the probe. A gear is provided which is adapted to pivot with the probe. A pinion pivotably connected to the handle meshes with the gear. A pointer fixed to the pinion is displaced in response to the pivoting of the handle about the probe, and this displacement can be read from a scale on the handle, providing an indication of the cervix-to-rectum distance.

  Excerpt(s): The present invention relates generally to radiation applicators for use in the treatment of cancerous tissue and, more particularly, to such an applicator having a measuring device to indicate the distance between the radiation sources and healthy tissues. U.S. Pat. No. 2,544,939. The major problem with such devices is that they place the source of radioactivity so close to the rectum that it makes the rectal dose of radiation the limiting factor in the internal treatment. Thus, the rectal dose must be measured accurately to avoid over-irradiating the rectal area and harming healthy tissues in the process of treating diseased tissues.

  Web site: http://www.delphion.com/details?pn=US04294264__

- **Chemoprevention and treatment of cervical or vaginal neoplasia**

  Inventor(s): Bell; Maria (562 Tolland Dr., Castle Rock, CO 80104), Schmidt-Grimminger; Delf-Christian (562 Tolland Dr., Castle Rock, CO 80104)

  Assignee(s): none reported

  Patent Number: 6,399,645

  Date filed: March 20, 2000

  Abstract: The invention relates to non-surgical methods for treating cervical or vaginal neoplasia including cervical intraepithelial neoplasia, intraepithelial neoplasia, vulvar intraepithelial neoplasia and ano-genital warts. The treatment, which utilizes an effective amount of indole-3-carbinol and/or diindolylmethane, is effective whether or not the patient is also infected with human papillomavirus, the most common sexually transmitted viral disease in the United States and a known risk factor for both cervical intraepithelial neoplasia and **cervical cancer.**

  Excerpt(s): This invention relates to the treatment of cervical or vaginal neoplasia including cervical intraepithelial neoplasia ("CIN"), intraepithelial neoplasia, vulvar intraepithelial neoplasia and ano-genital warts, and in particular, provides a method of treatment to prevent these conditions from progressing into cancer. Treatment in accordance with the present invention utilizes an effective amount of indole-3-carbinol

("I3C") and/or diindolylmethane ("DIM"). Human papillomavirus ("HPV") infection of the lower genital tract is the most common sexually transmitted viral disease in the United States. (Husseinzadeh, N., et al., "Subclinical Cervicovaginal Human Papillomavirus Infections Associated with Cervical Condylomata and Dysplasia Treatment Outcomes," J. Reprod. Med., Vol. 39, 777-80, (1994)). Most of these viral infections remain dormant and never result in clinically evident disease. However, in some cases, the virus may propagate and cause clinically recognizable HPV-associated changes, including condylomata (genital warts), precancerous lesions of the cervix, as well as invasive **cervical cancer.** Cancer of the cervix is the second most common cancer in women and the seventh most common form of cancer worldwide. (World Health Organization, "The World Health Report," Geneva: WHO, (1997)). The association between HPV infection and genital cancer is well documented. (Richart, R., "Causes and Management of Cervical Intraepithelial Neoplasia," Vol. 60, Cancer, 1951-1959, (1987); Schiffman, M. et al., "Epidemiologic Evidence Showing that Human Papillomavirus Infection Causes Most Cervical Intraepithelial Neoplasia," Vol. 85, J. Nat'l Cancer Inst., 958-964, (1993)). Not all dysplastic lesions develop into cancer. Mildly dysplastic lesions will spontaneously regress without therapy in the majority of patients, and only a small subset of cases actually possess cancerous potential. Less than one half of more severely dysplastic lesions in patients will eventually progress to invasive disease. (Barron, B. & Richart, R., "Statistical Model of the Natural History of **Cervical Carcinoma.** II. Estimates of the Transition Time from Dysplasia to Carcinoma In Situ," Vol. 45, J. Nat'l Cancer Inst., 1025, (1970)). The progression of HPV infection to genital cancer is therefore not absolute, and other factors (e.g., smoking, diet, and immunosuppression) probably contribute to the progression.

Web site: http://www.delphion.com/details?pn=US06399645__

- **DFMO for the treatment or prevention of cervical intraepithelial neoplasia**

  Inventor(s): Follen; Michele (Houston, TX), Hittelman; Walter (Houston, TX), Hong; Wuan K. (Houston, TX), Lotan; Reuben (Kingwood, TX), Nishioka; Kenji (Houston, TX)

  Assignee(s): Board of Regents, The University of Texas System (Austin, TX)

  Patent Number: 6,166,079

  Date filed: December 30, 1996

  Abstract: Methods for treating, preventing, controlling the growth of and/or reducing the risk of developing **cervical cancer,** particularly in patients with cervical intraepithelial neoplasia are provided employing pharmaceutically acceptable preparations of DFMO. Methods for treating a patient having cervical intraepithelial neoplasia, which methods comprise administering DFMO alone or in combination with a cytotoxic or cytostatic agent, are also provided.

  Excerpt(s): The present invention provides a pharmaceutical formulation and a method for its use in the prevention of **cervical cancer.** More specifically, the present invention provides a composition comprising alpha-difluoromethylornithine for treating, preventing, reducing the risk of and/or controlling the growth and progression of cervical intraepithelial neoplasia grade III into malignancy. Despite the advent of the Papanicolaou (Pap) smear, cervical cancers and pre-cancers remain important health problems for women, especially underobserved women in the United States (U.S.) and women in underdeveloped countries (Parkin, 1993). The incidence of both invasive **cervical cancer** and carcinoma-in-situ are increasing in the U.S. The reasons for this increase are unknown. In the U.S., an estimated 2,500,000 women will have abnormal

Pap smears demonstrating atypical cells of uncertain significance and low-grade intraepithelial lesions (lesions of HPV and CIN 1) annually (Kurman, 1994). The exact number of patients with high-grade squamous intraepithelial lesions (CIN II and III), not classified as carcinoma-in-situ, is unknown. A risk factor for **cervical cancer** is HPV. The most common types of HPV are those classified as high risk (HPV 16, 18, 45, and 56), intermediate risk (HPV 31, 33, 35, 51, 52, and 58), and low risk (HPV 6, 11). The high and intermediate risk types have been identified in 77% of high grade cervical intraepithelial neoplasia (CIN) and squamous intraepithelial lesions (SIL) and in 84% of invasive lesions. Cohort studies demonstrate that women with HPV infection have 11-60 times increased risk of developing high grade CIN and 15-50 times increased risk of developing invasive cancer than do women without HPV infection for which the high-risk HPV types include types 16, 18, 45, and 56. This association has been consistent and independent of the HPV assay method employed or epidemiologic study design (Bosch, 1995).

Web site: http://www.delphion.com/details?pn=US06166079__

- **Diagnostic method and apparatus for cervical squamous intraepithelial lesions in vitro and in vivo using fluorescence spectroscopy**

  Inventor(s): Mahadevan-Jansen; Anita (Austin, TX), Mitchell; Michele Follen (Houston, TX), Ramanujam; Nirmala (Philadelphia, PA), Richards-Kortum; Rebecca (Austin, TX)

  Assignee(s): Board of Regents, the University of Texas System (Austin, TX)

  Patent Number: 6,258,576

  Date filed: June 19, 1996

  Abstract: The present invention involves the use of fluorescence spectroscopy in the diagnosis of **cervical cancer** and precancer. Using multiple illumination wavelengths, it is possible to (i) differentiate normal or inflamed tissue from squamous intraepithelial lesions (SILs) and (ii) to differentiate high grade SILs from non-high grade SILs. The detection may be performed in vitro or in vivo. Multivariate statistical analysis was employed to reduce the number of fluorescence excitation-emission wavelength pairs needed to re-develop algorithms that demonstrate a minimum decrease in classification accuracy. Fluorescence at excitation-emission wavelength pairs was used to redevelop and test screening and diagnostic algorithms that have a similar classification accuracy to those that employ fluorescence emission spectra at three excitation wavelengths. Both the full-parameter and reduced-parameter screening algorithms discriminate between SILs and non-SILs with a similar specificity and a substantially improved sensitivity relative to Pap smear screening and differentiate high grade SILs from non-high grade SILs.

  Excerpt(s): The invention relates to optical methods and apparatus used for the diagnosis of cervical precancers. There has been a significant decline in the incidence of advanced **cervical cancer** over the last 40 years, primarily due to the development of organized programs that target early detection of its curable precursor, cervical Squamous Intraepithelial Lesion (SIL) (SILs consist of Cervical Intraepithelial Neoplasia (CIN) and Human Papilloma Viral (HPV) infection) [1]. Even though organized screening (Pap smear) and diagnostic (colposcopy) programs are currently in place, approximately 15,900 new cases of **cervical cancer** and 4,900 **cervical cancer** related deaths were reported in 1995, in the United States alone [2]. Currently, 24.5% of women with **cervical cancer** are under the age of 35 years, and the incidence continues to increase for women in this age group [1]. The continuing morbidity and mortality rate

related to **cervical cancer** necessitates an improvement in the accuracy and efficacy of current detection modalities. The Pap smear is the primary screening tool for the detection of **cervical cancer** and its precursor [3]. In a Pap test, a large number of cells obtained by scraping the cervical epithelium are smeared onto a slide which is then fixed and stained for cytologic examination. Each smear is then examined under a microscope for the presence of neoplastic cells [4]. The Pap smear's reported sensitivity and specificity range from 11-99% and 14-97%, respectively. Like many screening tests in an asymptomatic population, the Pap smear is unable to achieve a concurrently high sensitivity and high specificity [5]. The accuracy of the Pap smear is limited by both sampling and reading errors [6]. Approximately 60% of false-negative smears are attributed to insufficient sampling; the remaining 40% are due to reading errors. Because of the monotony and fatigue associated with reading Pap smears (50,000-300,000 cells per slide), the American Society of Cytology has proposed that a cyto-technologist should be limited to evaluating no more than 12,000 smears annually [7]. As a result, accurate Pap smear screening is labor intensive and requires highly trained professionals.

Web site: http://www.delphion.com/details?pn=US06258576__

- **Formulations containing hyaluronic acid**

  Inventor(s): Asculai; Samuel Simon (Toronto, CA), Falk; Rudolf Edgar (Toronto, CA), Harper; David W. (Oakville, CA), Hochman; David (Thornhill, CA), Klein; Ehud Shmuel (Givat Savyon, IL), Purschke; Don (Toronto, CA)

  Assignee(s): Hyal Pharmaceutical Corp. (CA)

  Patent Number: 6,114,314

  Date filed: December 1, 1994

  Abstract: Topically applied transdermally quick penetrating (best targeting the epidermis and subsequently remaining there for a prolonged period of time) systemic independent acting, combinations and formulations which employ, combine, or incorporate a therapeutically effective non-toxic (to the patient) amount of a drug which inhibits prostaglandin synthesis together with an amount of hyaluronic acid and/or salts thereof (for example the sodium salt) and/or homologues, analogues, derivatives, complexes, esters, fragments, and/or sub units of hyaluronic acid to treat a disease and condition of the skin and exposed tissue for example, basal cell carcinoma, the precancerous, often recurrent, actinic keratoses lesions, fungal lesions, "liver" spots and like lesions (found for the most part in the epidermis), squamous cell tumours, metastatic cancer of the breast to the skin, primary and metastatic melanoma in the skin, genital warts **cervical cancer,** and HPV (Human Papilloma Virus) including HPV of the cervix, psoriasis (both plaque-type psoriasis and nail bed psoriasis), corns on the feet and hair loss on the head of pregnant women and remain in the skin for a prolonged period of time.

  Excerpt(s): This invention also relates to formulations suitable for use in such treatments, the use of such formulations in such treatments, methods of such treatment, and the delivery of drugs for such treatments. Basal cell carcinoma is presently treated by surgery. Each lesion, together with all surrounding and underlying tissue (dermis, epidermis, and subdermis), is cut out. In some instances, surgery, while necessary for the patient's welfare, may put the patient at risk in some other respect (for example, a lesion on a patient's temple whose removal (resection) may jeopardize the patient's health). Squamous cell tumours are also treated the same way as are other forms of

cancer in the skin and exposed tissue. Furthermore, other conditions and diseases of the skin and exposed tissue are treated the same way or in ways that cause discomfort to the patient, for example melanoma, genital warts, **cervical cancer,** HPV (Human Papilloma Virus). Actinic keratoses lesion is dealt with similarly. Additionally, liquid nitrogen has been used to remove the lesion.

Web site: http://www.delphion.com/details?pn=US06114314__

- **Hybridoma cell lines producing monoclonal antibodies directed against cervical cancer cells**

  Inventor(s): Chan; Teh-sheng (League City, TX)

  Assignee(s): Board of Regents, The University of Texas System (Austin, TX)

  Patent Number: 4,618,585

  Date filed: July 16, 1984

  Abstract: Continuous hybrid cell lines for producing monoclonal antibodies, the antibodies specific for an antigenic determinant unique to **cervical cancer** cells, have been developed. The hybrid cell lines were established by fusing differentiated lymphoid cells primed with intact human **cervical cancer** cells with myeloma cells, particularly plasmacytoma cells. The resulting fused hybrid cells were cultured in HAT tissue culture media which included a small concentration of deoxycytidine. Deoxycytidine was found to enhance the growth of the hybrid cells and subsequent yield of monoclonal antibodies secreted therefrom. Hybrid cell lines secreting monoclonal antibodies to antigenic determinants unique for human **cervical cancer** cells can be maintained indefinitely in culture to produce large amounts of homogenous anti-cervical cancer cell antibody.

  Excerpt(s): The present invention relates to the production of monoclonal antibodies; and, in particular, to hybrid cell lines capable of continuously producing monoclonal antibodies directed against the antigenic determinants unique to **cervical cancer** cells. The present invention further relates to tissue culture media for enhanced growth of hybrid cell lines. In recent years, the capability to produce monoclonal antibodies specific for the antigenic and immunogenic determinants of cell surface antigens has provided a new vista of diagnostic and immunotherapeutic agents. For example, monoclonal antibodies have been available for some time now which are specific for an assortment of antigens, including viral antigens, such as rabies, hepatitis and influenza virus; red blood cells; fluorescent dyes; and cell associated antigens including human tumors such as melanoma, colorectal cancer, glioma, choriocarcinoma, renal cancer, breast cancer, lymphoma, and leukemia. Heretofore, as far as applicant is aware, there have been no reports of the production of continuous cell lines of somatic cell hybrids which elaborate monoclonal antibodies to antigenic determinants of **cervical cancer** cells, in particular cell surface exposed antigenic determinants.

  Web site: http://www.delphion.com/details?pn=US04618585__

- **Method and apparatus for reflective glare removal in digital photography useful in cervical cancer detection**

  Inventor(s): Blair; Kerry L. (Overland Park, KS)

  Assignee(s): Medtech Research Corporation (Lenexa, KS)

  Patent Number: 6,088,612

  Date filed: April 4, 1997

  Abstract: An apparatus is disclosed for glare removal in digital imaging of a cervix. The apparatus includes a digital camera operable to create first and second digital images having substantially the same field of view; lights associated with the camera for illuminating the cervix with light pulses emitted from two locations, and a digital processor. The light pulses are synchronized so the cervix is illuminated with a first pulse for the creation of the first image and the cervix is illuminated with a second pulse for the creation of the second image. First glare and first non-glare regions are created by the first pulse in the first image, and second glare and second non-glare regions are created by the second pulse in the second image. The processor creates a glare-free digital composite image by replacing the digital elements of the glare region of the first image with the corresponding digital elements from the non-glare region of the second image.

  Excerpt(s): Present invention relates generally to the detection of **cervical cancer.** More particularly, the present invention relates to an apparatus and method for the visual examination of cervical epithelium by means of a colposcopy assembly capable of producing a digital image of the cervix which is essentially free of reflective glare that otherwise masks or veils cancerous and pre-cancerous tissue. Over the last fifty years, Papanicolaou Smear ("Pap Smear") has become the cornerstone of efforts to reduce **cervical cancer** mortality. Pap Smear is effective because it identifies the latest stages of **cervical cancer.** Current estimates are that 60-70 million Pap Smears are done in the U.S. each year. Pap Smear has, thus, become a norm in the detection of **cervical cancer.** In spite of its broad acceptance in the medical community, studies indicate that Pap Smear screenings will fail to detect from 50%-80% of low grade cancerous lesions, and even 15%-30% of high grade cancerous lesions. When conducting Pap Smear screenings, the gynecologist collects exfoliated cells from the surface of the cervix and places them on slides that are sent to cytologists for further examination. Cytologists then review the cells placed on the slides and look for abnormal cells. If abnormal cells are found, the Pap Smear is considered to be positive. If no abnormal cells are found, the Pap Smear is considered to be negative. It is also possible that Pap Smear slides cannot be properly evaluated by the cytologist because of technical problems associated with the Pap Smear collection process such inadequate cell count, improper slide fixation, etc.

  Web site: http://www.delphion.com/details?pn=US06088612__

- **Method and kit for early cancer prediction**

  Inventor(s): Gyllensten; Ulf (Uppsala, SE), Josefsson; Agnetha (Uppsala, SE), Magnusson; Patrik (Uppsala, SE)

  Assignee(s): Quantovir AB (Uppsala, SE)

  Patent Number: 6,420,106

  Date filed: June 7, 2000

Abstract: The present invention is within the field of early cancer prediction. More closely, the invention relates to a method and kit for predicting virus-associated **cervical cancer** in a human subject. In the method the amount of viral nucleic acid is normalized in relation to the amount of sample from a human subject. Using specific primers and probes in a DNA amplification kit of the invention, a value of relative viral load is obtained which enables prediction of risk of **cervical cancer** several years before any symptoms thereof.

Excerpt(s): The present invention is within the field of early cancer prediction. More closely, the invention relates to a method and kit for predicting virus-associated **cervical cancer** in a human subject. Infection by certain subtypes of human papillomavirus (HPV), in particular HPV 16 and HPV 18, has long been recognized as a major risk factor for **cervical cancer** and about 95% of cancer biopsies contain HPV DNA. While infection with HPV is common in young women in the ages 16-24, only less than 1% of women with oncogenic HPV smears develop **cervical cancer.** Therefore, known methods for testing for presence of HPV has a low predictive value. Within prior art there are two main strategies to predict or diagnose **cervical cancer.** One strategy uses squamous intraepithelial lesion in cytology, or cervical dysplasia, as an indication of progression to **cervical cancer.** The other main strategy is to detect HPV nucleic acid in a patient sample either directly or following amplification of said nucleic acid, wherein the presence of HPV nucleic acid is taken as an indication of possible progression to **cervical cancer.**

Web site: http://www.delphion.com/details?pn=US06420106__

- **Method and portable colposcope useful in cervical cancer detection**

  Inventor(s): Blair; Kerry L. (15390 Monrovia St., Overland Park, KS 66219)

  Assignee(s): none reported

  Patent Number: 6,277,067

  Date filed: April 4, 1997

  Abstract: A method and portable apparatus for the visual examination and grading of cervical epithelium by means of a hand-held colposcopy assembly capable of producing a digital image of the cervix. The present invention enables real-time imaging and archiving of images of the entire cervix for the purpose of detecting cancerous and pre-cancerous tissue and by virtue of computerized image processing suggests an objective diagnosis of the cervical epithelium by means of a low cost, portable, hand-held digital colposcope.

  Excerpt(s): The present invention relates generally to the detection of **cervical cancer,** and more particularly, to a method and portable apparatus for the visual examination and grading of cervical epithelium by means of a hand-held colposcopy assembly capable of producing a digital image of the cervix. Two methods are used for early detection of **cervical cancer** and precancer: cytology and colposcopy. Cytology is a screening method that is practical and economical and colposcopy is a diagnostic method directed to the clinical diagnosis of patients with abnormal cytology. 1.2.2 Conventional Methods and Systems.

  Web site: http://www.delphion.com/details?pn=US06277067__

- **Method for the detection of cellular abnormalities using infrared spectroscopic imaging**

  Inventor(s): Bhandare; Prashant S. (Arlington, MA), Cahn; Frederick R. (Princeton, NJ), Cohenford; Menashi A. (West Warwick, RI), Krishnan; Krishnaswamy (Norwell, MA), Rigas; Basil (White Plains, NY)

  Assignee(s): Bio-Rad Laboratories, Inc. (Hercules, CA)

  Patent Number: 5,976,885

  Date filed: November 12, 1996

  Abstract: This invention teaches a method to identify cellular abnormalities which are associated with disease states. In one aspect, the invention is a method to distinguish premalignant and malignant stages of **cervical cancer** from normal cervical cells. The method utilizes infrared (IR) spectra of exfoliated cervical cells which are dried on an infrared transparent matrix and scanned at the frequency range from 3000-950 cm.sup.-1. The identification of samples is based on establishing a calibration using a representative set of spectra of normal, dysplastic and malignant specimens. During the calibration process, multivariate techniques such as Principal Component Analysis (PCA) and/or Partial Least Squares (PLS) are used. PCA and PLS reduce the data based on maximum variations between the spectra, and generate clusters in a multidimensional space representing the different populations. The utilization of Mahalinobis distances, or linear regression (e.g., Principle Component Regression on the reduced data from PCA) form the basis for the discrimination. This method is simple to use and achieves statistically reliable distinction between the following groups of cervical smears: normal (individuals with no prior history of dysplasia), dysplasia and malignant samples. Further, this invention discloses a method to obtain the IR spectrum of individual cervical cells fixed on an infrared transparent matrix and to use the spectra o the individual cells in the method described above. In an additional aspect, the invention is a method for using vibrational spectroscopic imaging to distinguish between normal and diseased cells.

  Excerpt(s): The detection of premalignant and malignant cells by the Papanicolaou smear (Pap smear) has greatly reduced the high mortality rate due to **cervical cancer.** Nevertheless, the Pap screening process is labor intensive and has remained essentially unchanged since it was first described by Papanicolaou almost 50 years ago. To perform the test, cells are exfoliated from a patient's cervix by scraping using a spatula or brush. The scraping is then smeared on a slide, and the slide is stained and microscopically examined. The microscopic examination is a tedious process, and requires a cytotechnologist to visually scrutinize all the fields within a slide to detect the often few aberrant cells in a specimen. Consequently, the detection of abnormal specimens depends on the level of a cytotechnologist's experience and workload, and also on the quality of the smear preparation. A recent critical evaluation of the Pap smear reported that the error rates associated with the current technique can be startlingly high. For example, the reported false negative rate (sensitivity) ranges from 6% to 55% (see, Shingleton, H. M., et al., CA Cancer J. Clin., 45:305-320 (1995)). As a result of these concerns, attempts have been made to automate the Pap screening process and to standardize the staining procedure. Certain of the available automated systems have been designed to improve the diagnostic yield of the Pap smear by minimizing the content of blood, mucus and other non-diagnostic debris in the examined cervical scrapings. In spite of these changes and the resulting simplification of the sample, the diagnosis of Pap smears continues to be heavily influenced by subjective bias. Thus, efforts are currently being directed towards developing alternative means of diagnosing

Pap smears which are based on objective criteria such as chemical or morphological changes in cervical cells.

Web site: http://www.delphion.com/details?pn=US05976885__

- **Method for the detection of malignant and premalignant stages of cervical cancer**

  Inventor(s): Bhandare; Prashant S. (Arlington, MA), Cahn; Frederick R. (Princeton, NJ), Cohenford; Menashi A. (West Warwick, RI), Krishnan; Krishnaswamy (Norwell, MA), Rigas; Basil (White Plains, NY)

  Assignee(s): Bio-Rad Laboratories, Inc. (Hercules, CA)

  Patent Number: 6,031,232

  Date filed: November 13, 1995

  Abstract: This invention discloses a method to identify premalignant and malignant stages of **cervical cancer** from an infrared (IR) spectrum of exfoliated cervical cells which are dried on an infrared transparent matrix and scanned at the frequency range from 3000-950 cm.sup.-1. The identification of samples is based on establishing a calibration using a representative set of spectra of normal, dysplastic and malignant specimens. During the calibration process, multivariate techniques such as Principal Component Analysis (PCA) and/or Partial Least Squares (PLS) are used. PCA and PLS reduce the data based on maximum variations between the spectra, and generate clusters in a multidimensional space representing the different populations. The utilization of Mahalinobis distances, or linear regression (e.g., Principle Component Regression on the reduced data from PCA) form the basis for the discrimination. This method is simple to use and achieves statistically reliable distinction between the following groups of cervical smears: normal (individuals with no prior history of dysplasia), dysplasia and malignant samples. Lastly, this invention discloses a method to obtain the IR spectrum of individual cervical cells fixed on an infrared transparent matrix.

  Excerpt(s): The detection of premalignant and malignant cells by the Papanicolaou smear (Pap smear) has greatly reduced the high mortality rate due to **cervical cancer.** Nevertheless, the Pap screening process is labor intensive and has remained essentially unchanged since it was first described by Papanicolaou almost 50 years ago. To perform the test, exfoliated cells from a patient's cervix are first scraped using a spatula or brush. The scraping is then smeared on a slide, and the slide is stained and microscopically examined. The microscopic examination is a tedious process, and requires a cytotechnologist to visually scrutinize all the fields within a slide to detect the often few aberrant cells in a specimen. Consequently, the rate in the detection of abnormal specimens depends on the level of a cytotechnologist's experience, quality of the smear preparation, and the work load. As a result of these concerns, attempts have been made both to automate the Pap screening process, and develop other objective alternatives. A number of methods have been explored to detect cytological anomalies, including those using molecular and immunological techniques. One impetus behind the development of new molecular and immunological methods is the detection of the human papilloma virus (HPV). Certain subtypes of HPV have been linked to a high incidence of abnormal lesions, and are implicated in the etiology of **cervical cancer.** Although these techniques are specific and detect cervical specimens at high risk, they are currently cost prohibitive and too labor intensive. Recently, differences have been reported in the Fourier Transform Infrared (FT-IR) spectra of 156 cervical samples, of which, by cytological screening, 136 were normal, 12 had cancer, and 8 had dysplasia (see, Wong et al., Proc. Natl. Acad. Sci. USA, 87:8140-8145 (1991)). This study relied on features of the Mid-IR

region (3000-950 cm.sup.-1) to discriminate between the samples. The spectra of normal samples exhibited a prominent peak at 1025 cm.sup.-1 which appears to be due to glycogen, and other less pronounced bands at 1047 cm.sup.-1, 1082 cm.sup.-1, 1155 cm.sup.-1 and 1244 cm.sup.-1. The spectra of specimens diagnosed with cancer exhibited significant changes in the intensity of the bands at 1025 cm.sup.-1 and 1047 cm.sup.-1, and demonstrated a peak at 970 cm.sup.-1 which was absent in normal specimens. Samples with cancer also showed a significant shift in the normally appearing peaks at 1082 cm.sup.-1, 1155 cm.sup.-1 and 1244 cm.sup.-1. The cervical specimens diagnosed cytologically as dysplasia exhibited spectra intermediate in appearance between normal and malignant. Based on these observations, Wong et al. concluded that FT-IR spectroscopy may provide a reliable and cost effective alternative for screening cervical specimens.

Web site: http://www.delphion.com/details?pn=US06031232__

- **Methods and a diagnostic aid for distinguishing a subset of HPV that is associated with an increased risk of developing cervical dysplasia and cervical cancer**

  Inventor(s): Parmenter; Cheryl A. (Albuquerque, NM), Wheeler; Cosette M. (Placitas, NM)

  Assignee(s): University of New Mexico (Albuquerque, NM)

  Patent Number: 5,679,509

  Date filed: September 30, 1994

  Abstract: Methods and a diagnostic aid for distinguishing a subset of HPV that is associated with an increased risk of developing cervical dysplasia and **cervical cancer.** The method comprises either distinguishing leucine or valine at amino acid position 83 in the HPV-16 E6 open reading frame, or detecting a nucleotide of T or G at nt 350 in the HPV-16 E6 gene.

  Excerpt(s): The present invention relates to methods and a diagnostic aid for distinguishing a subset of HPV that is associated with an increased risk of developing cervical dysplasia and **cervical cancer.** Human papillomavirus (HPV) has been identified previously as an important cofactor in the development of cervical neoplasia and cancer. Infection with HPV is however insufficient to cause **cervical cancer.** That is to say that when conducting random surveys 30-50% of all women are infected with HPV but only 8/100,000 women ever develop **cervical cancer.** This can in part be explained by the fact that women are often treated for precursor dysplastic cervical disease detected at annual Pap smear. Despite the existence of Pap smear screening, epidemiologic investigations continue to implicate HPV as the single greatest risk factor for progression to cervical dysplasia and cancer. Many investigations continue to search for host and/or viral (HPV) markers that will help identify those women infected with HPV who are at risk for cervical dysplasia or invasive **cervical cancer.** Specific host genetics in the HLA Class II locus have been one area recently identified in a subset of patients infected with HPV. Individuals infected with HPV-16 who have specific HLA haplotypes will either be at risk or protected from getting **cervical cancer.** In this case it has been possible to identify genetic markers that predispose a patient with HPV to progress to cancer.

  Web site: http://www.delphion.com/details?pn=US05679509__

- **Methods for detecting cervical cancer**

  Inventor(s): Auer; Gert (Solna, SE), Heselmeyer; Kerstin (Edewecht, DE), Macville; Merryn (Kensington, MD), Ried; Thomas (Bethesda, MD), Schrock; Evelin (Rockville, MD)

  Assignee(s): The United States of America as represented by the Department of Health (Washington, DC)

  Patent Number: 5,919,624

  Date filed: January 10, 1997

  Abstract: The invention provides a method of detecting the presence of invasive **cervical carcinoma** in a subject comprising detecting in a cervical cell from the subject the presence of a chromosome abnormality which is associated with invasive **cervical carcinoma;** the presence of the cervical cell containing the chromosome abnormality indicating the presence of invasive **cervical carcinoma** in the subject. The invention also provides a method of detecting the presence of advanced-stage **cervical carcinoma** in a subject comprising detecting in a cervical cell from the subject the presence of a chromosome abnormality associated with advanced-stage **cervical carcinoma;** the presence of the cervical cell containing the chromosome abnormality indicating the presence of advanced-stage **cervical carcinoma** in the subject. The invention also provides a method of classifying the progression of dysplastic cervical cells from a non-invasive **cervical carcinoma** to an invasive **cervical carcinoma** comprising analyzing the dysplastic cervical cells for the presence of a chromosome abnormality which is associated with invasive **cervical carcinoma,** and classifying the dysplastic cervical cells having the chromosome abnormality as having progressed from a non-invasive **cervical carcinoma** cells to an invasive **cervical carcinoma.** The invention further provides kits comprising nucleic acids that specifically hybridize to chromosome 3q and specifically hybridize to another chromosome, and to compositions comprising nucleic acids.

  Excerpt(s): This invention relates generally to methods of detecting the presence of a **cervical carcinoma.** Specifically, this invention relates to a method of detecting a **cervical carcinoma** by detecting the presence of a chromosome abnormality in a cervical cell that is associated with the **cervical carcinoma.** Cervical carcinomas are the second most common tumors in women worldwide. The tumor incidence shows strong variability, with industrialized countries having lower morbidity and mortality rates than do developing countries (Pisani et al. (1993) "Estimates of the worldwide mortality from eighteen major cancers in 1985. Implications for prevention and projections of future burden" Int J Cancer 55:891-903) which may be attributable to differences in cytologic screening programs (Hakama et al. (1986) "Screening for cancer of the uterine cervix" IARC Scientific Publications No. 76, Lyon, France). Although other factors, such as cigarette smoking, may influence the incidence of **cervical cancer,** infection with human papilloma virus (HPV) can be an initiating event for cervical carcinogenesis. (IARC Monograph, 1995). An HPV infection alone, however, is not sufficient for the progression of the disease from a stage of mild cellular dysplasia to a stage of invasive carcinoma since some HPV infected cervical cells may never progress to the more malignant stage, and in fact, may never progress past a stage of mild dysplasia. The traditional clinical diagnostic test for the presence of dysplastic cells, the Papanicolaou (Pap) smear, does not provide a reliable predictor of the progression of dysplastic cells to cancerous cells since this test is based upon morphological characteristics of the cells which do not reliably reflect the genetic state of the cells. Additionally, the Pap smear analysis is essentially a subjective test which is therefore susceptible to misinterpretation. Polyploidy has been associated with the transition of normal cervical

cells to dysplastic cervical cells, but this crude genetic determination has also not been associated with cells undergoing a transition past a stage of mild dysplasia other than showing a general increase in genetic instability. This genetic instability, as determined by monitoring ploidy levels, appears nonspecific to a particular chromosome and does not provide a correlation to the transition of dysplasia to invasive carcinoma. Therefore some additional process must occur for a transition of the dysplastic cervical cells to the more advances stages of the disease. It is conceivable that specific genetic aberrations are required for the multistep process of cervical cell tumor initiation and progression (Fearon et al. (1990) "A genetic model for colorectal carcinogenesis" Cell 61:759-767 and Zur Hausen, H. (1994) "Disrupted dichotomous intracellular control of human papilloma virus infection in cancer of the cervix" Lancet 343:955-957), but this association has never been discovered, and therefore, a relatively simple genetic determination of cervical cells in the more advanced stages of the disease, such as those entering into or already in the invasive stage, has not yet been possible.

Web site: http://www.delphion.com/details?pn=US05919624__

- **Nuclear inhibitor I-92 and its use for the production of a medicament**

  Inventor(s): Kopun; Marijana (Heidelberg, DE), Napierski; Inge (Heidelberg, DE), Royer; Hans-Dieter (Berlin-Buch, DE), Stohr; Michael (Neckargerach, DE), Weitz; Jurgen (Durham, NC)

  Assignee(s): Dade Behring Marburg GmbH (Marburg, DE)

  Patent Number: 6,045,831

  Date filed: January 19, 1994

  Abstract: The present invention concerns a nuclear inhibitor which specifically inhibits the activity of sequence specific DNA enhancer binding proteins of Human Papilloma Virus (HPV) and the use of this nuclear inhibitor for the production of a medicament for treatment of human **cervical cancer.**

  Excerpt(s): The invention relates to a compound which regulates the activity of a protein which binds to a DNA enhancer sequence of human papillomavirus. Furthermore, the invention embraces the use of this compound for the production of a medicament for treating human **cervical cancer** and kits for the diagnosis of cervical tumors. Cervical cancer represents the second most frequent cancer in females on a worldwide scale. DNA of human papillomaviruses with high oncogenic potential is found in over 90% of **cervical cancer** biopsies. Two proteins E6 and E7 with transforming activity are encoded by viral early genes and their continuous expression is required for maintenance of the proliferative and transformed phenotype (Cancer Res. 48, 3780-3786 (1988); EMBO J, 8, 513-519 (1989)). The transforming activities of E6 and E7 proteins are at least in part explained by the fact that they interact specifically with products of tumor suppressor genes p105.sup.RB and p53. p105.sup.RB is the product of the retinoblastoma susceptibility gene (Cell, 60, 387-396 (1990)). HPV18 early gene expression is under control of the upstream regulatory region (URR), which has three domains, where the most 5'region, adjacent to the L1 gene, is E6 responsive and the most 3'region, which contains the early gene promoter, is E2 responsive (J. Virol., 62, 665-672 (1988)). The enhancer of papillomavirus type 18 consists of two functionally redundant domains, one is partially conserved between HPV18 and HPV16, both mediate strong transcriptional enhancement. The enhancer is located on a 230 nucleotide long RsaI-RsaI fragment, and can be subdivided into two functionally redundant domains of similar size, whose activity depends on cellular transregulatory factors (EMBO J., 6, 1339-1344 (1987); J.

Virol., 61, 134-142 (1987)). After infection of normal cells, viral DNA is episomal and in rare cases viral DNA integrates into the host genome. In the integrates early genes are expressed at low level. In contrast, in cervix cancer cells, viral DNA is usually integrated and the early genes E6 and E7 are invariably expressed at high level. In most cases, the viral genome uses for the integration event coding sequences of the E2 gene, which encodes the viral transregulatory protein E2 (Nature, 314, 111-114 (1985)). Upon integration in E2 coding sequences this protein is inactivated, and the early gene promoter is no longer E2 dependent. It is assumed that the early gene promoter is then predominantly controlled by host cell factors (Cancer Cells, 1, 43-50 (1989)). The understanding of mechanisms which regulate the expression of the transforming genes is of critical importance for the understanding of cervical carcinogenesis and, consequently, important for the production of effective medicaments against **cervical cancer.**

Web site: http://www.delphion.com/details?pn=US06045831__

- **Pap smear apparatus and method**

  Inventor(s): Richards; Michael Owen (P.O. Box 2320, Waldron, AR 72958)

  Assignee(s): none reported

  Patent Number: 6,402,700

  Date filed: November 21, 2000

  Abstract: A personal PAP smear apparatus and method for collecting a non-intrusive cell or tissue sample for medical testing such as **cervical cancer** screening is provided. The apparatus includes an insertion handle, a flexible speculum ring, and a means for movably attaching the speculum ring to the insertion handle. The speculum ring includes two adjacent ring halves circumferentially divided to permit expansion of the collapsed speculum tube housed within the hollow ring halves. The method of the invention includes insertion of the flexible speculum assembly into the user's vagina, movement of the speculum ring to a raised position encircling the user's cervix, separating the ring halves to expand the tube and define the speculum bore, and inserting a sampling tool through the bore until it touches the cervix or surrounding surface areas for tissue sampling.

  Excerpt(s): Not Applicable. This invention relates to gynecological medical devices, and more particularly to a medical tool and method for enabling a woman to collect a personal cervical cell sample for use during a Papanicalou (PAP) test, commonly known as a PAP smear. The PAP smear is an important routine gynecological test usually done annually in sexually active females to screen for **cervical cancer.** The tests known in the art typically require an in office visit with a gynecologist where the doctor takes a sample of the cervix for lab analysis. Current medical practice requires a gynecologist to insert a speculum into the patient's vagina to access the cervix for tissue sample collection. Many women find this method an uncomfortable, intrusive exam, and opt to not have the routine screening performed.

  Web site: http://www.delphion.com/details?pn=US06402700__

- **Process for detecting a variant CD44 gene product**

  Inventor(s): Dall; Peter (Dusseldorf, DE), Heider; Karl-Heinz (Waldbronn-Reichenbach, DE), Herrlich; Peter (Karlsruhe, DE), Pals; Steven T. (Amsterdam, NL), Ponta; Helmut (Linkenheim-Hochstetten, DE)

  Assignee(s): Boehringer Ingelheim International GmbH (DE)

  Patent Number: 6,010,865

  Date filed: June 3, 1996

  Abstract: The invention relates to a process for diagnosing and analysing tumours which is based on detecting the expression of certain variant exons of the CD44-gene. Detection may be carried out at the protein or nucleic acid level. In a preferred embodiment the expression is detected in biopsy material using exon-specific antibodies. Thus, for example, v6-expression is a suitable prognostic parameter for breast cancer, the expression of a transitional epitope which is coded by exons v7 and v8 serves to diagnose **cervical cancer.**

  Excerpt(s): The invention relates to processes for diagnosing and/or analysing tumours by evaluating the expression of variable exons of the CD44-gene, agents for such processes and the use thereof. There is a need for improved methods of diagnosing and/or analysing cancers, particularly on the basis of molecular markers. For example, the haematogenic spread of mammary carcinomas occurs very early in the course of the disease and is connected with the later occurrence of remote metastases (Diel et al., 1992). The molecular mechanisms of metastatic spread are still unknown. The prognostic factors for predicting the risk of metastasis are currently based mainly on pathological criteria, the main factors being the stage of the tumour, differentiation (gradation) and lymph node metastasis (Fisher et al., 1990). However, in individual cases, there are discrepancies between these factors, e.g. where in spite of a highly advance tumour size or low differentiation (high gradation) there are no lymph node metastases. Little investigation has been carried out into a subgroup or patients suffering from lymph-node-negative breast cancer who later develop remote metastases. There is therefore a need for parameters which allow better prediction of the haematogenic tumour spread and better general prognosis. Another example consists of stomach tumours. These can be divided into two main histological categories, the intestinal type and the diffuse type (Lauren, 1965). Tumours of the intestinal type but not of the diffuse type are often accompanied by chronic gastritis B and particularly by intestinal metaplasias, which are regarded as precursors of dysplastic changes and adenocarcinomas of the intestinal type (Jida et Kusama, 1982; Jass, 1983; Kato et al., 1981; Sipponen et al., 1983; Sirula et al., 1974; Strickland et Mackay, 1973). Pathogenetic differences between these two types of adenocarcinoma are also reflected in the observation that patients with tumours of the diffuse type often belong to blood group A, which indicates a possible influence of genetic factors on the risk of cancer (Piper, 1978), whereas environmental factors such as infections with Helicobacter pylori may be important in the development of tumours of the intestinal type (Parsonnet et al., 1991; Nomura et al., 1991). It would be desirable to be able to distinguish between tumours of the intestinal type and those of the diffuse type by means of molecular markers. Finally, **cervical carcinoma** of the uterus may be mentioned as a third example. In spite of a decreasing incidence (Petterson, 1988) the prognosis for patients with advanced stages of cervical carcinomas is poor (Perez et al., 1983; Park et Thigpen, 1993; Brady et al., 1986). Early diagnosis is based on the assessment of early morphological changes in the epithelial cells (cervical smear). Here again it is desirable to discover definite molecular

markers for early cancer detection which can be used for staging and as prognostic factors.

Web site: http://www.delphion.com/details?pn=US06010865__

- **Quinoline derivatives, their production and use**

  Inventor(s): Choh; Nobuo (Tsukuba, JP), Furuya; Shuichi (Tsukuba, JP), Sasaki; Satoshi (Tsukuba, JP)

  Assignee(s): Takeda Chemical Industries Ltd. (Osaka, JP)

  Patent Number: 6,087,503

  Date filed: September 14, 1998

  Abstract: The present compounds are intermediates for the preparation of quinoline derivatives and compositions having gonadotropin-releasing hormone antagonistic activity useful as propylactics or therapeutic agent for the prevention or treatment of several hormone dependent diseases, for example, a sex hormone dependent cancer (e.g. prostatic cancer, uterine or **cervical cancer,** breast cancer, pituitary adenoma), benign prostatic hypertrophy, myoma of the uterus, endometriosis, precocious puberty, amenorrhea, premenstrual syndrome, polycystic ovary syndrome and acne vulgaris; are effective as a fertility controlling agent in both sexes (e.g. a pregnancy controlling agent and a menstrual cycle controlling agent); can be used as a male or female contraceptive, as an ovulation-inducing agent; can be used as an infertility treating agent by using a rebound effect owing to a stoppage of administration thereof; and are useful for modulating estrous cycles in animals in the field of animal husbandry, as agents for improving the quality of edible meat or promoting the growth of animals, and as agents for promoting spawning in fish.

  Excerpt(s): The present invention relates to novel quinoline derivatives and salts thereof. The present invention further relates to methods for manufacturing these quinoline derivatives and the salts thereof, and pharmaceutical compositions containing the quinoline derivatives. Secretion of anterior pituitary hormone is controlled by peripheral hormones secreted from target organs for the respective hormones and by secretion-accelerating or -inhibiting hormones from the hypothalamus, which is the upper central organ of the anterior lobe of the pituitary (in this specification, these hormones are collectively called "hypothalamic hormones"). At the present stage, nine kinds of hormones have been confirmed as hypothalamic hormones, including, for example, thyrotropin releasing hormone (TRH) or gonadotropin releasing hormone {GnRH: sometimes called LH-RH (luteinizing hormone releasing hormone)} (cf. Seirigaku 2, compiled by M. Iriku and K Toyama, published by Bunkohdo, pp.610-618, 1986). These hypothalamic hormones are assumed to show their actions via the receptor which is considered to exist in the anterior lobe of the pituitary (cf. ibid), and studies of receptor genes specific to these hormones, including those of humans, have been developed (Receptor Kiso To Rinsho, compiled by H. Imura, et al., published by Asakura Shoten, pp.297-304, 1993). Accordingly, antagonists or agonists specifically and selectively acting on these receptors control the action of hypothalamic hormone and the secretion of anterior pituitary hormone. As a result, they are expected to be useful as prophylactic and therapeutic agents of anterior pituitary hormone dependent diseases. As compounds having GnRH antagonistic activity, a number of compounds including, for example, derivatives of GnRH such as straight-chain peptides, (U.S. Pat. No. 5,140,009 and No. 5,171,835), cyclic hexapeptide derivatives [Japanese Patent

Application Laid-open No. 61(1986)-191698) or bicyclic peptide derivatives [Journal of medicinal chemistry, Vol.36, pp.3265-3273, 1993] have been disclosed.

Web site: http://www.delphion.com/details?pn=US06087503__

- **Recombinant virus vectors encoding human papillomavirus proteins**

  Inventor(s): Boursnell; Michael E. (Cambridge, GB3), Inglis; Stephen C. (Cambridge, GB3), Munro; Alan J. (Cambridge, GB3)

  Assignee(s): Cantab Pharmaceuticals Research Limited (Cambridge, GB)

  Patent Number: 5,719,054

  Date filed: November 8, 1993

  Abstract: The invention provides a recombinant virus vector for use as an immunotherapeutic or vaccine. The recombinant virus vector comprises at least one pair of nucleotide sequences heterologous to the virus and which have sufficient sequence homology that recombination between them might be expected. The pair of nucleotide sequences are arranged in the virus vector such that they are inverted with respect to each other. The virus vector is able to infect a mammalian host cell and express as polypeptide the heterologous nucleotide sequences in the host cell. For infection thought to be caused by HPV infection, the pair of nucleotide sequences encode part or all of human papillomavirus (HPV) wild-type proteins or mutant proteins immunologically cross-reactive therewith. For an immunotherapeutic or vaccine against **cervical cancer,** the recombinant virus vector encodes part or all of the HPV wild-type proteins HPV16E7 and HPV18E7 or mutant proteins immunologically cross-reactive therewith.

  Excerpt(s): This invention relates to recombinant virus vectors. In particular, it relates to recombinant virus vectors designed to overcome the problem of recombination between homologous nucleotide sequences. It also relates to recombinant virus vectors encoding human papillomavirus proteins; to immunotherapeutics and vaccines for conditions associated with HPV infection; to the production of a virus (e.g. vaccinia virus) engineered to express antigens encoded by human papillomavirus types 16 and 18 and to immunotherapeutics and vaccines for **cervical cancer.** In recent years, strong evidence has been adduced for a link between **cervical carcinoma** and infection with certain types of human papillomavirus (HPV), particularly with types 16, 18, 31, 33 and 35 (Gissman et al., Cancer Cells 5,275, 1987). This is based on hybridisation studies which have indicated that more than 85-90% of biopsies from cervical tumours can be shown to contain papillomavirus DNA. HPV16 DNA is most commonly found (in about 60% of tumours) with HPV18 the next most frequent (about 20%) and the other types accounting for a further 5-10%. In many instances, tumour cells from the biopsies do not however, contain the complete genome, but rather a deleted form. The extent and location of the deleted information within the virus genome is variable, but a general feature is the retention of the part of the genome encoding the E7 protein (Schwarz et al., Nature 314, 111, 1985). In addition, the adjacent E6-encoding region is usually present. The ubiquitous presence of the E7-encoding region in tumour cells suggests that the protein product of this gene might play a role in the induction or maintenance of the transformed phenotype. Indeed in most cell lines established from tumour biopsies, expression of the E7 gene can be detected (Smotkin & Wettstein, PNAS, 83, 4680, 1986). Furthermore, it has been shown that the E7 gene product can bind to the retinoblastoma (Rb) gene product, a recognised "anti-oncogene" in normal human cells (Munger et al., EMBO J. 8,4099, 1989). This strengthens the belief that E7 is directly involved in cell

transformation. The presence and expression of the E7 and E6 genes in tumour cells derived from **cervical carcinoma** biopsies, suggests the possibility that these proteins could be potential targets for the immunological recognition of the tumour cells. It is well known that viral proteins produced inside mammalian cells can be processed through a host cell pathway to short peptides, which then form a complex with host Major Histocompatibility Complex (MHC) Class 1 molecules and are transported to the cell surface. These complexes may then present a target for recognition by the host immune system. Interaction of the complex with the receptor molecule on the surface of cytotoxic T cells (the T cell receptor) can then lead to activation of the T cells to proliferate or to destroy the recognised cell. It is possible, therefore, that the presence in the body of a population of cytotoxic T lymphocytes (CTLs) which are capable of recognising cells expressing the HPV E6 and/or E7 proteins could afford protection against the development and proliferation of cervical tumours. Indeed it has been reported that normally oncogenic mouse cells engineered to express the HPV E7 protein are unable to form tumours in mice which have been previously immunised with non-tumorigenic E7-expressing cells, and that this rejection is mediated by CD8+lymphocytes (CTLs) (Chen et al., PNAS 88, 110, 1991). Further, the generation of an active population of such cells subsequent to tumour initiation could result in regression of the tumour.

Web site: http://www.delphion.com/details?pn=US05719054__

- **Screening method for determining individuals at risk of developing diseases associated with different polymorphic forms of wildtype P53**

  Inventor(s): Banks; Lawrence (Gallo, IT), Matlashewski; Greg J. (St-Lazare, CA), Storey; Alan (St. Neots, GB)

  Assignee(s): Imperial Cancer Research Technology (London, GB), International Center for Genetic Engineering and Biotechnology (Trieste, IT), McGill University (Montreal, CA)

  Patent Number: 6,489,105

  Date filed: March 1, 2000

  Abstract: The present invention relates to a screening method to identify individuals at risk of developing diseases associated with different polymorphic forms of wildtype p53; which comprises the steps of: a) obtaining a biological sample from said patients; and b) determining the presence of p53pro or p53arg wildtype alleles in said sample; wherein the allele pattern of patients selected from the group consisting of p53pro/p53pro, p53arg/p53arg and p53pro/p53arg are indicative of a risk factor for developing disease associated with different polymorphic forms of wildtype p53. Notably, individuals who are p53arg/arg are at greater risk of developing pathologies associated with human papillomavirus infections, including **cervical cancer.**

  Excerpt(s): The invention relates to a screening method of to identify individuals at risk of developing diseases associated with different polymorphic forms of wildtype p53. The cellular tumor suppressor protein, p53, is one of the major regulators of cell proliferation. Depending upon the context of the stimulus, p53 will induce cell growth arrest or programmed cell death (apoptosis). As a consequence this prevents continued proliferation of cells which have acquired DNA mutations and this regulation represents one of the organism's key defenses against cancer. In many human tumors inactivation of p53 is one of the principal factors in the development of the tumor. In Human Papillomavirus (HPV) associated cancers, however, p53 is almost always wild

type. This is due to the activity of the viral E6 protein which labels p53 for ubiquitin mediated degradation and thus overcomes normal p53 functions. For this reason, HPVs are a major carcinogen for the development of **cervical cancer** in women, one of the most common forms of cancer world wide. Two polymorphic forms of p53 exist which can encode either proline or arginine residues at amino acid position 72 of the p53 protein. This polymorphism results in a change in the migration of the p53 protein in polyacrylamide gels but, to date, both forms of p53 appear to have indistinguishable levels of activity. Indeed, numerous epidemiological surveys have been performed over the last 6-7 years in order to determine whether either polymorphism represents a risk factor for the development of several human tumors. Until now, the evidence has been overwhelmingly in favor of the view that the presence of proline or arginine at amino acid position 72 is not a significant risk factor in the development of any particular cancer.

Web site: http://www.delphion.com/details?pn=US06489105__

- **Spatula for collecting cervical cancer cells**

  Inventor(s): Milgrom; Hymen (Chicago, IL)

  Assignee(s): Milex Products, Inc. (Chicago, IL)

  Patent Number: 4,384,587

  Date filed: August 18, 1980

  Abstract: A spatula for collecting cancer cells outside and within the cervix canal includes a scraper head having a laterally extending outer cervix engaging leg projecting from one side of the head. The head further includes a cervical canal entering finger-like portion projecting longitudinally beyond the leg. The finger-like portion has on the same side of the scraping head from which said leg projects a longitudinal inner scraping surface which scrapes cells from the wall of the cervical canal when the spatula is rotated along the longitudinal axis of the spatula. The longitudinal inner surface of the finger-like portion comprises two adjacent longitudinally extending sections, one of which has a rough surface which scrapes cells from the wall of the cervical canal and the other of which has a relatively smooth surface. The smooth surface section is raised so that only it engages the wall of the cervix during the longitudinal movement of the finger-like portion of the scraping head into and out of the cervical canal.

  Excerpt(s): The present invention relates to devices called spatulas used by a physician for collecting cancer cell specimens within the cervical canal and the cervical os. These devices have been heretofore manufactured in a form having a long straight insertion handle terminating in a scraping head comprising a laterally extending positioning leg which limits the insertion depth of a finger-like portion extending longitudinally beyond this leg and positioned in alignment with the handle of the device. These devices are generally made of wood or synthetic plastic material and are sold in sterilized packages at a cost where they are used only once. The finger-like portion of the scraping head is inserted by the physician into the cervical canal as far as the positioning leg will permit, and as a scraping surface on the inner leg-containing side of the finger-like portion thereof is urged against the cervical canal the device is rotated along its longitudinal axis so that the inner longitudinal side of the finger-like portion and the positioning leg of the scraping head collect cell specimens. The cells are transferred to a test slide for microscope examination by tapping and sliding the scraping head against the slide. In the wooden spatula, the wood is porous and some of the cells and fluid collected are absorbed by the porous wooden surface on the scraping

side of the scraping head. It was found that these spatulas have a limited scraping action since the surface of the scraping side of the scraping head is not of sufficient roughness for efficient scraping of surface cells which are especially meaningful to the cytologist reading slides of such specimen. Also, because of the porous nature of the spatulas, cells which are absorbed by the porous wooden surfaces thereof are not easily transferred to a test slide and frequently remain on or in the pores of the scraping heads thereof. The synthetic plastic spatulas were made with grooves in scraping surface of the spatula, which grooves formed pockets for collecting cell specimens which are very readily transferable to the test slides. Because of the narrowness of the scraping surfaces utilized, the grooves were formed in a lateral direction to form a large number of open-ended grooves which provide a better collection and transfer of cell specimens to the test slides. However, the resulting sawtooth-like profile, in the process of longitudinally inserting and removing the scraping head into and from the cervical canal, frequently ruptures surface blood vessels which can cause discomfort and some minor bleeding which results in blood in the cell samples which hinders examination of the cell specimens on the test slide to which the cell samples are transferred and results in needless bleeding of the patient. For these reasons, the physician using this spatula is instructed to press the smooth backside of the scraping head against the cervical canal during the insertion and removal of the spatula from the cervix. Not infrequently, however, the doctor fails to do this and the undesired blood appears with the collected cell specimens. Also in case of a very tight cervical canal it may not be possible for the physician to press down sufficiently on the smooth backside of the scraping head as per instructions and the grooves come in direct contact with the tissue during insertion and removal and as a result traumatize the cervix and make it difficult if not impossible to avoid bleeding.

Web site: http://www.delphion.com/details?pn=US04384587__

- **Treatment of gynecological malignancies with biologically active peptides**

  Inventor(s): Baker; Margaret A. (Philadelphia, PA), Jacob; Leonard S. (Penn Valley, PA), Maloy; W. Lee (Lansdale, PA)

  Assignee(s): Magainin Pharmaceuticals Inc. (Plymouth Meeting, PA)

  Patent Number: 5,635,479

  Date filed: May 2, 1995

  Abstract: A process for treating a gynecological malignancy in a host which comprises administering to the host at least one biologically active amphiphilic peptide or protein. The peptide or protein may be administered intralesionally, intravenously, or intraperitoneally, whereby the peptide or protein may inhibit, prevent, or destroy the growth of the gynecological malignancy, such as an ovarian cancer, uterine cancer, or **cervical cancer.**

  Excerpt(s): This invention relates to the treatment of gynecological malignancies. More particularly, this invention relates to the treatment of gynecological malignancies by administering a biologically active peptide or protein. In accordance with an aspect of the present invention, there is provided a process for treating a gynecological malignancy in a host comprising administering to a host at least one biologically active amphiphilic peptide or protein. The peptide or protein is an ion channel-forming peptide or protein. The peptide or protein is administered in an amount effective to treat a gynecological malignancy in a host. The term "treating a gynecological malignancy" as used herein means that the peptide or protein prevents, inhibits, or destroys the growth

of cancerous or malignant cells of a cancerous or malignant growth found in the female reproductive organs, such as, but not limited to, the ovaries, uterus, and cervix, and/or reduces the size of or eliminates the cancerous growth.

Web site: http://www.delphion.com/details?pn=US05635479__

- **Use of HVP-16 E6 and E7-gene derived peptides to diagnose HPV-16-associated invasive cervical cancer**

  Inventor(s): Gissmann; Lutz (Wiesloch, DE), Muller; Martin (Heidelberg, DE)

  Assignee(s): Behringwerke Aktiengesellschaft (Marburg, DE)

  Patent Number: 5,629,161

  Date filed: December 23, 1994

  Abstract: The present invention relates to the use of human paillomavirus 16 (HPV-16) E7-gene derived peptides for the diagnostic identification of HPV-16-associated invasive **cervical cancer.**

  Excerpt(s): This invention relates to the use of human papillomavirus 16 (HPV-16) E6 and E7-gene derived peptides for the diagnostic identification of HPV-16-associated invasive **cervical cancer.** Furthermore, this invention relates to antibodies with affinity for a specific HPV-16 E6 or E-7-gene derived peptides which may be agents for the production of a medicament for the treatment of HPV-16 invasive cancer. The object of the present invention therefore was the identification of viral structures for the use as reliable diagnostic markers for HPV-16-associated invasive **cervical cancer.** Furthermore, the object of the present invention was to provide specific tools for the therapeutical control of HPV-16-associated invasive cancer.

  Web site: http://www.delphion.com/details?pn=US05629161__

- **Vectors for DNA immunization against cervical cancer**

  Inventor(s): Cao; Shi-Xian (Etobicoke, CA), Gajewczyk; Diane M. (Toronto, CA), Klein; Michel H. (Willowdale, CA), Moingeon; Phillipe (F-Pommiers, FR), Persson; Roy (North York, CA), Rovinski; Benjamin (Thornhill, CA), Tartaglia; James (Schenectady, NY), Yao; Fei-Long (North York, CA)

  Assignee(s): Connaught Laboratories Limited (Toronto, CA)

  Patent Number: 6,235,523

  Date filed: September 3, 1999

  Abstract: Vectors for DNA immunization against **cervical cancer** comprise a nucleic acid molecule encoding at least one non-toxic T-cell epitope of the E6 and/or E7 antigens of a strain of human papilloma virus (HPV) associated with **cervical cancer,** such as HPV-16, and a promoter operatively coupled to the nucleic acid molecule for expression of the nucleic acid molecule in a host to which the vector is administered.

  Excerpt(s): The invention is concerned with immunotherapy of cancer, specifically **cervical cancer.** Cervical cancer is the second most common cause of cancer-related deaths in women worldwide. There is both epidemiological and experimental data which links the etiology of **cervical cancer** to infection with human papilloma virus (HPV) types 16 and 18. The HPV virus is prevalent in 35 to 40% of young women.

Although treatment of early stage disease is relatively successful, recurrent disease is found in 15% of the patients. The outcomes of patients with recurrent disease are relatively poor. Hence, there is a need for a novel therapeutic approach (refs. 1, 2, 3--various references are referred to in parenthesis to more fully describe the state of the art to which this invention pertains. Full bibliographic information for each citation is found at the end of the specification, immediately preceding the claims. The disclosure of these references are hereby incorporated by reference into the present disclosure). The strong association of HPV infection and **cervical cancer** suggests that a viral antigen-specific immunotherapeutic approach may be a feasible strategy in the treatment of **cervical cancer.** The goal of specific immunotherapy is to stimulate the immune response of a tumour-bearing patient to attack and eradicate tumour lesions. This strategy has been made feasible with the identification of tumour associated antigens (TAA). The strong association between HPV-16 infection and **cervical cancer** has made this disease a good candidate for immunotherapeutic intervention (ref. 4).

Web site: http://www.delphion.com/details?pn=US06235523__

Patent Applications on Cervical Cancer

As of December 2000, U.S. patent applications are open to public viewing.[10] Applications are patent requests which have yet to be granted. (The process to achieve a patent can take several years.) The following patent applications have been filed since December 2000 relating to cervical cancer:

- **Approaches for HPV detection and staging by targeting the E6 gene region of the viral genoMen**

  Inventor(s): Molodysky, Eugen; (US)

  Correspondence: Ladas & Parry; 26 West 61st Street; New York; NY; 10023; US

  Patent Application Number: 20020132227

  Date filed: March 27, 2001

  Abstract: The L1/E1 gene region of the HPV virus maybe deleted during integration into the genome of the host cell, but the E6/E7 gene region is always retained. There is a need to detect HPV infection and **cervical cancer** in way that provides information about the stage of infection so that the proper treatment can be undertaken.

  Excerpt(s): Integration of the E6 region of human papillomavirus into the cellular DNA is an important step in the progression to malignancy. This invention involves methods for detecting human papillomavirus in cervical cells and determining the progression of the infection. Infection by HPV involves the passage of the viral DNA into a cell. The HPV viral genome can be divided into 3 regions, upstream regulatory region (URR) or long control region (LCR), the early gene region and the late gene region. These regions control sequences for HPV replication and gene expression, encoding the E2, E6 and E7 genes, and encoding the L1 and L2 genes respectively (Turek, Adv. Virus Res. 44:305-356 (1994)). Initially at least the circular HPV DNA remains free inside the cell in an episomal form. Whereas the episomal form predominates early in infection, this situation may change later, with the subsequent occurrence of integration. Although initially some episomal HPV DNA remains along with the integrated HPV DNA in an

[10] This has been a common practice outside the United States prior to December 2000.

infected cell, ultimately, in a significant proportion of cancers the integrated form not only dominates, but represents the only HPV DNA present. The evidence suggests that integration may be an important step in the progression to malignancy. The viral genomes are exclusively maintained as episomes in benign lesions induced by HPV types such as 6 and 11 (Dowhanick et al, Suppression of cellular proliferation by the papillomavirus E2 protein. J. Virol 1995; 69:7791-7799; Kobayashi et al., Presence of human papillomavirus DNA in pelvic lymph nodes can predict unexpected recurrence of **cervical cancer** in patients with histologically negative lymph nodes. Clin. Cancer Res 1998; 4:979-83). Only episomal HPV is detected in CIN I and integrated sequences are rarely found in CIN II and CIN III (Cullen et al. Analysis of the physical state of different human papillomavirus DNAs in intraepithelial and invasive cervical neoplasms. J. Virol, 1991; 65:606-612; Das et al. "Analysis by polymerase chain reaction of the physical state of human papillomavirus type 16 DNA in cervical preneoplastic and neoplastic lesions. J. Gen. Virol. 1992; 73:2327-2336). In contrast, the viral DNA is usually integrated into the cellular genome in cell lines derived from cervical carcinomas (Boshart et al., "A New Type of papillomavirus DNA, its presence in genital cancer biopsies and in cell lines derived from **cervical cancer.** EMBO J. 1984 3:1151-1157; Howley, P. M. Presence and expression of human papillomavirus sequences in human **cervical carcinoma** cell lines. Am J. Pathol 1985 119:361-366; and Tsunokawa et al., "Presence of human papillomavirus type-16 and type-18 DNA sequences and their expression in cervical cancers and cell lines from Japanese patients. Int. J. Cancer 1986:37:499-503; and Yee et al."Presence and expression of human papillomavirus sequences in human **cervical carcinoma** cell lines. Am. J. Pathol. 1985: 119:361-6). This suggests that integration begins early in cancer development and is an important event in malignant transformation (Bosch et al. "Prevalence of human papillomavirus in cervical cancer: a worldwide perspective. J. National Cancer Inst. 1995; 87:796-802; Cullen, et al. Analysis of the physical state of different human papillomavirus DNAs in intraepithelial and invasive cervical neoplasms. J. Virol 1991; 65:606-612; and Vernon et al. "Association of human papillomavirus type 16 integration in the E2 gene with poor disease-free survival from **cervical cancer.** Int. J. Cancer 1997: 74:50-56). Thus the accurate detection of the L1 versus E6 status of the HPV DNA may be very important in determining **cervical cancer** progression and in assisting in clinical management of those women.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Cancer treatment with Go6976 and its related compounds**

  Inventor(s): Lu, Zhimin; (San Diego, CA), Wang, Keming; (Suzhuu, CN)

  Correspondence: John R. Ross; Ross Patent Law Office; P.O. Box 2138; Del Mar; CA; 92014; US

  Patent Application Number: 20020016352

  Date filed: July 24, 2001

  Abstract: A chemotheraputic cancer treatment in which Go6976 or a compound chemically similar to Go6976 is administered to a mammal for the treatment of the cancer. The chemical compound is targeted to PKC.alpha. activity. Experiments have shown Go6976 and similar compounds to be effective for the treatment of breast cancer, leukemia, lung cancer, bone cancer, skin cancer, prostate cancer, liver cancer, brain tumor, **cervical cancer,** and cancers located in the digestive tract including gastric cancer and colorectal cancers. These treatments may be accomplished utilizing Go6976 and

compounds similar to it alone or in combination with prior art chemotherapy agents or with radiation therapy. In a preferred embodiment Go6976 is used for the treatment of cancer as a preventative drug by preventing cancer cell formation.

Excerpt(s): This application is a continuation-in-part application of Ser. No. 09/370,190 filed Aug. 9, 1999. This invention relates to cancer treatments and especially to cancer treatments directed to protein kinase C.alpha. enzyme. Researchers have recognized that a family of enzymes known as protein kinase C enzymes is associated with a large number of cancers. This family includes at least eleven isoenzymes. A particular member of this family is identified as the protein kinase C alpha enzyme, abbreviated: PKC.alpha. Researches have reported increases in PKC.alpha. activity in human breast tumors (NG et al., Science. 283:2085-2089) and significant increases in PKC.alpha.: expression in prostate cancers (Cornford et al., Am. J. Pathol. 154: 137 -144). Researchers have reported that PKC.alpha. is required for the metastasis of human melanoma (Dennis et al., Cancer Lett. 128:65-70) and that PKC.alpha. is related to the progression of brain tumors (Shen et al., Mol. Pharmacol. 55:396-402). Recently, Muller et al were granted a patent, U.S. Pat. No. 5,744,460, which discloses a cancer treatment utilizing an antisense oligonuclotide targeted to PKC.alpha. combined with a chemotherapeutic agent. U.S. Pat. Nos. 5,882,927 and 5,885,970 issued to Bennett et al also disclose antisense oligonuclotides targeted to PKC.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Cellular collection apparatus and method**

  Inventor(s): Richards, Michael Owen; (Tupelo, MS)

  Correspondence: Charlotte W. Catlett; PO Box 1147; Meridian; ID; 83642; US

  Patent Application Number: 20020111562

  Date filed: April 11, 2002

  Abstract: A personal cellular collection apparatus and method for collecting a nonintrusive cell or tissue sample for medical testing such as **cervical cancer** screening is provided. The apparatus includes a cervical guide ring, an insertion handle, a means for movably attaching the guide ring, and a means for directing a tissue sampling tool to a woman's cervix. The means for movably attaching the guide ring to the insertion handle is a hinge or rachet mechanism having a tab or latch on the ring and a catch on the proximal end of the insertion handle. The method of the invention includes insertion of the collection tool through the introitus of the user's vagina, digital positioning of the guide ring to encircle the user's cervix, guiding a sampling tool to the cervix, wiping the cervix with the sampling tool to collect a tissue sample and removing the sampling tool and cervical guide from the user's vagina.

  Excerpt(s): This application is a continuation-in-part of U.S. utility application Ser. No. 09/721,026, filed on Nov. 21, 2000, entitled Pap Smear Apparatus and Method, now issued as U.S. Pat. No. _____, which is related to the provisional application Serial No. 60/167,099, filed on Nov. 23, 1999, entitled Pap Smear Apparatus and Method. This invention relates to gynecological medical devices, and more particularly to a medical tool and method for enabling a woman to collect a cervical cell or other biological material sample for use during a screening test for cancer and infections of the cervix. The Papanicalou (PAP) test, commonly known as a PAP smear, is an important routine gynecological test usually done annually in sexually active females to screen for **cervical cancer.** The tests known in the art typically require an in office visit with a gynecologist

where the doctor takes a cellular sample of the cervix for lab analysis. Current medical practice requires a gynecologist to insert a speculum into the patient's vagina to access the cervix for tissue sample collection. Many women find this method an uncomfortable, intrusive exam, and opt to not have the routine screening performed.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Cellulose sulfate and other sulfated polysaccharides to prevent and treat papilloma virus infection and other infections**

  Inventor(s): Anderson, Robert A; (Chicago, IL), Usher, Thomas C; (Washington, WA), Zaneveld, Louren J D; (Chicago, IL)

  Correspondence: Eckert Seamans Cherin & Mellott; 600 Grant Street 44th Floor; Pittsburgh; PA; 15219; US

  Patent Application Number: 20030181415

  Date filed: December 19, 2002

  Abstract: A method for treating and preventing various infections, including papilloma virus and fungal and parasitic infections is provided. In particular, an effective amount of a sulfated polysaccharide, such as cellulose sulfate and dextran sulfate are administered to prevent and treat these infections. The invention also relates to use of these compounds for the prevention and inhibition of malignant epithelial lesions associated with papilloma virus, such as **cervical cancer.**

  Excerpt(s): This invention relates to prevention and treatment of various infectious agents and in particular, relates to inhibitory activity of cellulose sulfate and other sulfated polysaccharides against various infectious agents, including papilloma virus and various vaginitis-causing microbes. U.S. Pat. No. 4,840,941 (941) describes inhibitory effects of certain sulfated polysaccharides on the enveloped retrovirus, human T-cell lymphotrophic virus-III (now known as HIV-1 (human immunodeficiency virus-1)). As disclosed in U.S. Pat. No. 5,288,704, sulfated polysaccharides are also known to be effective against various other enveloped viruses and in particular herpes simplex virus (HSV). The 941 patent, however, discloses that the inhibitory characteristics of sulfated polysaccharides against HIV-1 is quite different from the activities of polysaccharide sulfates against herpes virus. Since different viruses can have fundamentally different properties, a sulfated polysaccharide which is effective against one virus may not be effective against a different virus. While the binding of human papilloma virus-like particles (VLP's) to HaCaT cells has been shown to be inhibited by heparin and dextran sulfate (Joyce et al. The L1 Major Capsid Protein of Human Papillomavirus Type 11 Recombinant Virus-like Particles Interacts with Hepariin and Cell-surface Glycosaminoglycans oil Human Keratinocytes. The Journal of Biological Chemisty, 1999, Vol 274, No. 9, February 26, pp. 5810-5822), studies with VLP's do not reflect papilloma virus infection and it is not known that sulfated polysaccharides can inhibit papilloma virus infection. Papilloma virus differs from HSV and HIV in that it does not have an envelope and it differs from retroviruses such as HIV since it is a DNA virus and does not rely on the enzyme reverse transcriptase for replication. This difference may explain the resistance of papilloma virus to nonoxynol-9, a commonly used spermicide, which has been shown to inhibit both HIV and HSV (Hermonat, P. L., Daniel, R. W. and Shah, K. V. The spermicide nonoxynol-9 does not inactivate papillomavirus Sex. Transm. Dis. 1992; 19:203-205).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Expression vector coding p972 gene for cancer therapy and adenovirus producing the saMen**

  Inventor(s): Cho, Won-Kyung; (Taejon, KR), Dae Gun, Kim; (Taejon, KR), Hong, Seung-Suh; (Taejon, KR), Im, Dong-Soo; (Taejon, KR), Jung, Neon-Cheol; (Taejon, KR), Lee, Hyun-Soo; (Seoul, KR), Seong, Young-Rim; (Taejon, KR)

  Correspondence: S Peter Ludwig; Darby & Darby; Post Office Box 5257; New York; NY; 10150-5257; US

  Patent Application Number: 20020165190

  Date filed: May 3, 2002

  Abstract: The present invention relates to a vector comprising P972 (also referred to as Gadd45.gamma., CR6 or OIG37) gene known as a gene producing a cell growth-inhibiting protein for the treatment of cancers, an recombinant adenovirus that encodes P972 gene in the cell, a method of producing the above adenovirus and a method for the treatment of cancers by using the above vector or adenovirus. The recombinant adenovirus of the present invention can be used in the treatment of various cancers including **cervical cancer,** breast cancerand colon cancer.

  Excerpt(s): The present invention relates to a vector comprising a cell growth-inhibiting gene for gene therapy, a recombinant adenovirus that can deliver the above gene into cells and a method of using the above recombinant adenovirus vector for cancer therapy. Gene therapy is a technique for treating cancer or other genetic diseases, which is hard to cure by other conventional methods including those using the chemically synthesized drugs. Gene therapy uses genes, which are selected after investigating the molecular biological and biochemical cause of diseases, as a therapeutic material to produce the gene products in vivo for treatment of disease. Gene therapy has many advantages over the conventional therapy that uses chemically synthesized formulations in terms of the efficacy and the side effects, since gene therapy uses the actual gene products relating to the protection mechanism process against the disease in vivo, not the synthetically prepared drugs. In the early 1970's, scientists have begun to acknowledge the function of the genes. It has been considered that the congenital disease can be fundamentally treated by delivering many genes related to the genetic disease to patient directly. As time passes, people began to realize that the acquired diseases could also be treated by gene therapy. Since the first gene therapy by French Anderson group in the U.S.A. in September 1990 to treat a patient suffering from severe combined immunodeficiency (SCID), more than 2500 patients has been clinically treated by gene therapy up to date (Sci. Am. 263(2), 33-33B, 1990). Anticancer therapy includes surgical operation, radiation or treatment of drug, hormone or immuno-stimulating agent. There has been a desire, however, to find a better and safer therapeutic method since the above-mentioned conventional methods have severe side effects and limited efficacy. Gene therapy that is currently tried for the treatment of cancer includes firstly the method of delivering the suicide gene such as thymidine kinase of herpes simplex virus or cytosine deaminase of E. coli into cancer cells. Nontoxic precursor molecules become cytotoxic molecules activated by the above-mentioned suicide genes. The converted cytotoxic molecules, in turn, inhibit the growth of cancer cells. Secondly, the genes that induce the immune reaction or produce cytokines can be delivered to cells. The delivered genes trigger the immune reaction that can eliminate cancer cells. Thirdly, the genes that prevent angiogenesis can be delivered into cancer cells or the cells that surround the cancer. Cancer cells, as a consequence die due to the lack of oxygen. Fourthly, as a method of using the genes that cause apoptosis of cancer cells, the tumor

suppressor protein, p53 protein is usually used in the current gene therapy protocol. Recently, caspase-3, which is known to be to the programmed cell death, is beginning to be used to cause apoptosis of cancer cells. Since the effectiveness of the p53 protein as a tumor suppressor protein is widely acknowledged, various attempts have been and are being made to develop anticancer gene therapy using p53. Up to now, liposome and many different viruses have been used as gene carriers. The phase I clinical trial is being carried out by the National Cancer Institute in U.S.A. currently. The safety of gene therapy for the treatment of bladder cancer, breast cancer, lung cancer, and ovarian cancer is being tested at present, while the safety of the gene therapy for the carcinoma of the larynx and hepatoma is more or less approved.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Medical screening**

  Inventor(s): Brauns, Timothy A.; (Roslindale, MA), Gelfand, Jeffrey A.; (Cambridge, MA)

  Correspondence: Celia H. Leber; Fish & Richardson P.C.; 225 Franklin Street; Boston; MA; 02110-2804; US

  Patent Application Number: 20020068856

  Date filed: December 6, 2000

  Abstract: Mass medical, e.g., **cervical cancer,** screening is provided to areas of the world where a lack of sufficient laboratory infrastructure and technical skills presently compromises the effectiveness of screening or even makes mass screening impossible. These methods are cost-effective and provide excellent sensitivity and specificity in **cervical cancer** screening.

  Excerpt(s): This invention relates to medical screening. Various medical conditions are the subject of routine screening of populations of patients who are potential candidates for the particular condition. For example, in the United States women are routinely screened for **cervical cancer.** Carcinoma of the cervix is one of the most common malignancies in women. Worldwide, an estimated 470,000 women develop **cervical cancer** each year, with more than 80% of these cancers occurring in the developing world. In general, **cervical cancer** progresses slowly through several well-defined stages, and thus early detection permits the cancerous lesions to be treated with nearly 100% success. The initiation of mass screening has reduced **cervical cancer** mortality in the United States by 50% over the last 30 years (Kavita, et al., Accuracy of the Papanicolaou test in screening for and follow-up of cervical cytologic abnormalities: a systematic review. Ann Int Med 2000; 132(10):810-819). However, many countries lack the medical infrastructure or technical expertise to carry out effective mass screening (Michelow, et al., Simulation of primary **cervical cancer** screening by the PAPNET system in an unscreened, high-risk community. Acta Cytol 1997; 41(1):88-92; Veneti, et al., PAPNET for cervical cytology screening: experience in Greece. Acta Cytol 1999; 43(1):30-33; Denny, et al., Two-stage **cervical cancer** screening: an alternative for resource-poor settings. Am J Obst Gyn 2000,183(2):383-388). As a result, **cervical cancer** is the leading cancer-related cause of death in women of the developing world. (Denny, et al., supra).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method and marker for identification of pre-malignancy and malignancy and therapeutic intervention**

  Inventor(s): Mai, Sabine; (Manitoba, CA)

  Correspondence: Kenneth L Kohn; Kohn & Associates; Suite 410; 30500 Northwestern Highway; Farmington Hills; MI; 48334; US

  Patent Application Number: 20030211491

  Date filed: October 14, 2002

  Abstract: There is provided a method for identifying pre-malignancy, malignancy, and degree of pre-malignancy and malignancy of a cell by detecting extrachromosomal and intrachromosomal gene amplification. Also provided is a marker for the identification of pre-malignancy, malignancy, and degree of pre-malignancy and malignancy of a cell containing extrachromosomal and intrachromosomal gene amplification of a gene. A diagnostic tool for the diagnosis and prognosis or **cervical cancer** containing extrachromosomal and intrachromosomal gene amplification of a gene.

  Excerpt(s): The present invention relates to methods and markers for identification of pre-malignancy and malignancy states utilizing extrachromosomal and intrachromosomal gene amplification. Further the present invention relates to the identification of specific genes which undergo extrachromosomal gene amplification and therapeutic interventions relating to their utility as therapeutic targets. The diagnosis of malignant conditions is approached from multiple directions as for example tissue biopsies, serum levels of specific markers (PSA for prostate as an example), mammography and the like. However, most of these methods do not identify pre-malignant cells where early diagnosis can significantly increase treatment potential. Further the identification of a malignant condition does not necessarily identify an underlying genetic abnormality which can be corrected utilizing gene therapy or suggest other points of therapeutic intervention. Chronic lymphocytic leukemia (CLL), is the commonest leukemia, making up 30% of all cases (O'Brien, et al. 1995), However, the cause of this disease is unknown. The leukemia primarily effects elderly males and is characterized by the accumulation of morphologically mature-appearing B1-lymphocytes in peripheral blood, marrow, spleen and lymph nodes (O'Brien, et al., 1995). Prognosis in CLL is approximately assessed by Rai staging (Table I) and patient survival varies from 2 years (Rai III and IV) to >10 years (Rai 0) (Rai, et al., 1975). However, with each stage there is considerable variation in survival and patients can be further stratified according to the lymphocyte doubling time (Montserrat, et al., 1986). Patients with a short lymphocyte doubling time (<12 months) have a poorer survival rate than those with a longer doubling time (Montserrat, et al., 1986). At the present time, this disease is incurable but remissions can be obtained with alkylating agents, e.g., chlorambucil, or nucleoside analogs, e.g., fludarabine, but relapse and the eventual development of drug resistance is usually observed (O'Brien, et al., 1995).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method for performing a hysterectomy**

  Inventor(s): Samimi, M.D., Darius; (Corona Del Mar, CA)

  Correspondence: Richard E. Bee; P.O. Box 10544; Costa Mesa; CA; 92627; US

  Patent Application Number: 20020096181

  Date filed: January 19, 2001

Abstract: An improved method for performing a hysterectomy wherein the cardinal ligaments and the uterosacral ligaments attached to a uterus are not severed. Also, the wall of the vaginal apex is not cut. This is accomplished by coring through the cervical stroma of the uterus close to the wall of the endocervical canal and transformation zone and removing the endocervical canal and transformation zone from the cervical stroma. The opening left in the cervical stroma after removal of the endocervical canal and transformation zone is closed with sutures. This technique is practically bloodless. The nerve plexuses and the support system of the female internal organs are preserved. The chance of future **cervical cancer** is substantially eliminated. This is truly a technique for the 21.sup.st century.

Excerpt(s): This invention relates to surgical methods for performing hysterectomies on female patients. A hysterectomy involves the removal of the uterus from the abdomen of a female patient. The traditional method of performing a hysterectomy is to sever the uterosacral ligaments, the cardinal ligaments and the uterine vessels attached to the uterus before entering the vaginal fornix. The uterus is then severed from the vagina in a circular fashion at the cervico-vaginal junction. To access this area, the bladder is pushed down and, if necessary, dissected free of any attachments to the uterus. This traditional procedure causes significant damage to the nerves in the Frankenhauser nerve plexus, the vesical nerve plexus and various regional nerves such as the nerves to the clitoris, the urethra and the vestibular bulbs. This traditional procedure also causes a major impairment of the pelvic support system for the vagina and other major complications.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method for treating cervical cancer**

  Inventor(s): Chandrasekher, Yasmin A.; (Mercer Island, WA), McKernan, Patricia A.; (Seattle, WA)

  Correspondence: Paul G. Lunn, ESQ.; Zymogenetics, INC.; 1201 Eastlake Avenue East; Seattle; WA; 98102; US

  Patent Application Number: 20030161811

  Date filed: December 17, 2002

  Abstract: Use of Interleukin-20 for treating **cervical cancer** or cells infected with human papilloma virus. IL-20 can be administered alone or in conjunction with radiation or chemotherapeutic agents or surgical excision of the involved cells or lesions.

  Excerpt(s): This claims the benefit under 35 U.S.C.sctn.119 (e) of U.S. Provisional Application No. 60/341,783 filed on Dec. 17, 2001. According to the American Cancer Society, 12,800 new cases of invasive **cervical cancer** would be diagnosed in the United States in 1999. During the same year, 4800 patients were expected to die of the disease. This represents approximately 1.8% of all cancer deaths in women and 18% of gynecological cancer deaths. However, for women aged 20 to 39 years of age, **cervical cancer** is the second leading cause of cancer deaths. Molecular and epidemiologic studies have demonstrated a strong relationship between human papillomavirus (HPV), cervical intraepithelial neoplasia, (CIN), and invasive carcinoma of the cervix. Thus, there is a need to develop new therapeutic entities for the treatment of human papillomavirus infection, cervical intraepithelial neoplasia and carcinoma of the cervix. The present invention fills this need by administering interleukin-20 (IL-20) to a mammalian having **cervical cancer.** IL-20 can also be used to treat a human papillomavirus infection. The present invention also provides a method for inhibiting

the growth of **cervical cancer** cells by bringing IL-20 into contact with said cancerous cervical cells. Interleukin-20 (formally called Zcyto10) can be produced according to the method described in International Patent Application No. PCT/US98/25228 filed on Nov. 25, 1998. The human IL-20 polypeptide is comprised of a sequence of 176 amino acids with the initial Met as shown in SEQ ID NO: 1 and SEQ ID NO:2. It is believed that amino residues 1-24 are signal sequence, and the mature IL-20 polypeptide is represented by the amino acid sequence comprised of residues 25, a leucine, through amino acid residue 176, a glutamic acid residue, also defined by SEQ ID NO:12. Another embodiment of the present invention is defined by the sequences of SEQ ID NO: 3 and SEQ ID NO: 4. The polypeptide of SEQ ID NO: 4 is comprised of 151 amino acid residues wherein amino acids 1-24 comprise a signal sequence and the mature sequence is comprised of amino acid residues 25, a leucine, through amino acid 151 a glutamic acid, also defined by SEQ ID NO: 13. Another active variant is comprised of amino acid residues 33, a cysteine, through amino acid residue 176 of SEQ ID NO:2. This variant is also defined by SEQ ID NO:26.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method for using thymosin beta-10 for gene therapy of solid malignant tumors**

  Inventor(s): Kim, Seung-Hoon; (Seoul, KR), Lee, Je-Ho; (Seoul, KR)

  Correspondence: Gates & Cooper Llp; Howard Hughes Center; 6701 Center Drive West, Suite 1050; Los Angeles; CA; 90045; US

  Patent Application Number: 20030099617

  Date filed: August 30, 2002

  Abstract: A method for using thymosin.beta.-10 for cancer treatment by expressing thymosin.beta.-10 in solid malignant tumor cells. More precisely, the present invention relates to a cancer treatment method wherein thymosin.beta.-10 is expressed in solid malignant tumor cells by infecting adenovirus including thymosin.beta.-10. The gene therapy for cancer using thymosin.beta.-10 of the present invention is very effective for the treatment of ovarian cancer, **cervical cancer,** stomach cancer and lung cancer.

  Excerpt(s): This application claims the benefit of priority to Korean Patent Application No. 2001-63524, filed Oct. 10, 2001, the entire contents of which are incorporated herein by reference. The present invention relates to a method for using thymosin.beta.-10 for cancer treatment by expressing thymosin.beta.-10 in solid malignant tumor cells. More precisely, the present invention relates to a cancer treatment method wherein thymosin.beta.-10 is expressed in solid malignant tumor cells by infecting adenovirus including thymosin.beta.-10. The gene therapy for cancer using thymosin.beta.-10 of the present invention is very effective for the treatment of ovarian cancer, **cervical cancer,** stomach cancer and lung cancer. Gene therapy is a kind of treatment for genetic diseases and cancers caused by aberration of genes, whose mechanism is to introduce disease-related genes directly to patients in order to normalize the cell function by expressing those genes inside cells. Gene therapy is very effective not only for the treatment of diseases, but also for prevention of many diseases and even more reinforcing the treatment since the therapy can bestow new function on human body by introducing a specific gene.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Methods and apparatus for diagnostic multispectral digital imaging**

  Inventor(s): Follen, Michele; (Houston, TX), MacAuley, Calum; (Cancouver, CA), Richards-Kortum, Rebecca; (Austin, TX), Utzinger, Urs; (Tucson, AZ)

  Correspondence: Matt Bellinger; Fulbright & Jaworski L.L.P.; A Registered Limited Liability Partnership; 600 Congress Avenue, Suite 2400; Austin; TX; 78701; US

  Patent Application Number: 20020065468

  Date filed: March 28, 2001

  Abstract: Methods and apparatus for generating multispectral images of tissue. The multispectral images may be used as a diagnostic tool for conditions such as **cervical cancer** detection and diagnosis. Primary radiation is produced with an illumination source. The primary radiation is filtered to select a first wavelength and a first polarization. Tissue is illuminated with the filtered primary radiation to generate secondary radiation, which is filtered to select a second wavelength and a second polarization. The filtered secondary radiation is collected with a detector, and a plurality of multispectral images of the tissue is generated according to different combinations of first and second wavelengths and first and second polarization with an analysis unit in operable relation with the detector. Apparatus utilizing the invention include endoscopes and colposcopes.

  Excerpt(s): This application claims priority to provisional patent application Ser. No. 60/192,542 filed Mar. 28, 2000, entitled, "Methods and Apparatus for Diagnostic Multispectral Digital Imaging" by Urs Utzinger, Rebecca Richards Kortum, Calum MacAuley, and Michele Follen. The entire text of the above-referenced disclosure is specifically incorporated by reference herein without disclaimer. The present invention relates generally to the fields of diagnostic imaging. More particularly, it concerns methods and apparatus for generating multispectral images that may be used to diagnose various conditions in various tissues. Even more particularly, it concerns methods and apparatus for generating multispectral digital images using fluorescence, reflectance, and polarized reflectance imaging techniques. Over the last fifty years, Papanicolaou Smear ("Pap Smear") has become the cornerstone of efforts to reduce **cervical cancer** mortality. Pap Smear is effective because it identifies the latest stages of **cervical cancer.** Current estimates are that 60-70 million Pap Smears are done in the U.S. each year. Pap Smear has thus become a norm in the detection of **cervical cancer.** In spite of its broad acceptance in the medical community, studies indicate that Pap Smear screenings will fail to detect from 50%-80% of low grade cancerous lesions, and even 15%-30% of high grade cancerous lesions.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **METHODS AND COMPOSITIONS FOR THE DETECTION OF CERVICAL CANCER**

  Inventor(s): KEESEE, SUSAN K.; (HARVARD, MA), OBAR, ROBERT; (WALPOLE, MA), WU, YING-JYE; (FRAMINGHAM, MA)

  Correspondence: Testa, Hurwitz & Thibeault, Llp; High Street Tower; 125 High Street; Boston; MA; 02110; US

  Patent Application Number: 20030157482

  Date filed: May 17, 1999

Abstract: The invention provides a wide range of methods and compositions for detecting and treating **cervical cancer** in an individual. Specifically, the invention provides target cervical cancer-associated proteins, which permit a rapid detection, preferably before metastases occur, of **cervical cancer.** The target cervical cancer-associated protein, may be detected, for example, by reacting the sample with a labeled binding moiety, for example, a labeled antibody capable of binding specifically to the protein. The invention also provides kits useful in the detection of **cervical cancer** in an individual. In addition, the invention provides methods utilizing the cervical cancer-associated proteins either as targets for treating **cervical cancer** or as indicators for monitoring of the efficacy of such a treatment.

Excerpt(s): The present invention relates generally to methods and compositions for the detection of **cervical cancer.** More specifically, the present invention relates to cervical cancer-associated proteins which act as cellular markers useful (i) in detecting **cervical cancer,** and (ii) as molecular targets for **cervical cancer** therapy. The precursor to **cervical cancer** is dysplasia, also known in the art as cervical intraepithelial neoplasia (CIN) or squamous intraepithelial lesions (SIL) (Brinton et al (1992) "Epidemiology of Cervical Cancer: Overview" in "The Epidemiology of **Cervical Cancer** and Human Papillomavirus", Lyon, France: International Agency for Research on Cancer; and Tabbara et al. (1992) "The Bethesda classification for squamous intraepithelial lesions: histologic, cytologic and viral correlates", Obstet. Gynecol. 79: 338-346). While it is not understood how normal cells become transformed, the concept of a continuous spectrum of histopathological change from normal, stratified epithelium through CIN to invasive cancer has been widely accepted for many years (see, for example, Mitchell et al. (1994) "The natural history of cervical intraepithelial neoplasia: an argument of intermediate endpoint biomarkers", Cancer Epidmiol. Biomark. Prev. 3: 619-626). A large body of epidemiological and molecular biological evidence has been gathered that establishes human papillomavirus (HPV) infection as a causative factor in **cervical cancer** (Munoz et al. (1992) in "The Epidemiology of Human Papillomavirus and Cervical Cancer", IRAC publication no. 119, Lyon France: Int. Agency for Research on Cancer, pp 251-261). HPV is found in 85% or more of squamous cell invasive lesions, which represent the most common histologic type seen in **cervical carcinoma** (Cox et al. (1995) Baillierre's Clin. Obstet Gynaecol. 91-37). Additional cofactors include, for example, oncogenes activated by point mutations, and chromosomal translocations of deletions (Spandidos et al. (1989) J. Pathol. 157: 1-10). Cytological examination of Papanicolaou-stained cervical smears (also referred to as Pap smears) currently is the method of choice for detecting **cervical cancer.** Despite the historical success of this test, concerns have arisen regarding its ability to predict reliably the behavior of same preinvasive lesions (Ostor et al. (1993) Int. J. Gynecol. Pathol. 12: 186-192; and Genest et al. (1993) Human Pathol. 24: 730-736). The identification of a cervical cancer-associated tumor marker for reliably detecting early onset of **cervical cancer** and/or providing early prognostic information will greatly aid the management of **cervical cancer.**

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Methods for detecting papillomavirus DNA in blood plasma and serum**

  Inventor(s): Christensen, Neil; (Harrisburg, PA), Gocke, Christopher D.; (Ellicott City, MD)

  Correspondence: Mcdonnell Boehnen Hulbert & Berghoff; 300 South Wacker Drive; Suite 3200; Chicago; IL; 60606; US

  Patent Application Number: 20030175770

  Date filed: December 24, 2002

  Abstract: This invention relates to the detection of extracellular papillomavirus DNA in blood plasma or serum from a human or animal. In particular, the invention relates to the detection, identification, evaluation, or monitoring of neoplastic, premalignant or malignant disease associated with a papillomavirus. The invention thereby provides methods for the identification of individuals at risk for, or having, cervical dysplasia, cervical intraepithelial neoplasia, or **cervical cancer.**

  Excerpt(s): This application is a continuation-in-part of U.S. patent application Ser. No. 09/456,222, filed Dec. 7, 1999, which is a continuation-in-part of U.S. patent application Ser. No. 09/049,234, filed Mar. 27, 1998, which is a continuation-in-part of U.S. patent application Ser. No. 08/818,058, filed Mar. 14, 1997, which is a continuation-in-part of U.S. Provisional Application Serial No. 60/028,180, filed Oct. 15, 1996, which is a continuation-in-part of U.S. Provisional Application Serial No. 60/026,252, filed Sep. 17, 1996, which is a continuation-in-part of U.S. Provisional Application Serial No. 60/013,497, filed Mar. 15, 1996, the entire disclosure of each of the foregoing is hereby incorporated by reference. This invention relates to methods for detecting specific extracellular nucleic acid in plasma or serum fractions of human or animal blood associated with neoplastic or proliferative disease. Specifically, the invention relates to detection of nucleic acid derived from human viruses associated with human neoplasia, and to methods of detecting and monitoring extracellular viral nucleic acids found in the plasma or serum fraction of blood by using nucleic acid amplification with or without enrichment for viral DNA. In particular, the invention relates to the detection, identification, or monitoring of the existence, progression or clinical status of human neoplastic disease caused by or associated with viral infection through detection of viral nucleic acid in plasma or serum fractions. The invention permits the detection of extracellular, viral nucleic acid in the serum or plasma of humans or other animals recognized as having a neoplastic or proliferative disease or in individuals without any prior history or diagnosis of neoplastic or proliferative disease. The invention specifically provides methods for early identification of **cervical carcinoma, cervical carcinoma** in situ, cervical dysplasia, cervical intraepithelial neoplasia (CIN) and penile squamous cell carcinoma associated with infection by oncogenic human papillomavirus subtypes. Cervical carcinoma is a common form of malignancy afflicting women, arising from the squamous epithelium of the cervix. Much is known of the natural history of this disease. The vast majority of cases are attributable, at least in part, to an infection by a papillomavirus of the cervical epithelium. In particular, certain subtypes of human papillomavirus (HPV), including HPV subtypes 16, 18, 31, 33, and 35, are associated with **cervical malignancy,** where HPV infection seems to alter the epithelium to predispose an individual to the development of cancer. This alteration of the epithelium by viral infection initially leads to cervical premalignant states, specifically cervical dysplasia or cervical intraepithelial neoplasia (CIN). Cervical dysplasia/CIN is important for recognizing, diagnosing, and treating women at risk for developing **cervical cancer,** because surgical removal of dysplastic epithelium reduces and may even eliminate the risk of development of **cervical cancer.**

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Methods for determining risk of developing cervical cancer**

  Inventor(s): Mathur, Rajesh S; (Charleston, SC), Mathur, Subbi P; (Charleston, SC)

  Correspondence: Needle & Rosenberg P C; 127 Peachtree Street N E; Atlanta; GA; 30303-1811; US

  Patent Application Number: 20030017505

  Date filed: July 25, 2002

  Excerpt(s): The present invention relates generally to a method of identifying a subject having an increased risk of developing **cervical cancer** based on levels of IGF-II in serum and levels of EGF-R and HPV-E6/E7 in cervical epithelial cells and in serum. Annual pap smear screening in the USA results in 10 to 15% abnormal cytopathology. For low grade cervical epithelial neoplasia (CIN), the need for treatment in all cases is not clear. The ability to identify patients with CIN who are at greater risk for progression to invasive cancer may allow for more selective treatment protocols, and reduce the number of unnecessary treatments. Although cytological screening and treatment protocols have already reduced **cervical cancer** deaths, **cervical cancer** is still the leading cause of death for women in third world countries. It remains the leading gynecological malignancy in this country with 14,500 new cases and 4,800 deaths every year. (Parker S L, et al, CA Cancer J. Clin. 1997;47:1-27.) About 25% of women with histologically proven high-grade intraepithelial neoplasia are not identified to be at risk during routine gynecological examination. (Blomfield, P I, et al. CBJBrit J Obstet Gyn 1998; 105:486-492; Genest D R, et al.; Arch Pathol Lab Med 1998; 122:338-341.) Although surgical therapy is successful most of the time, metastasis into other locations is hard to diagnose until the cancer is well advanced. This is because the imaging techniques utilized in conjunction with clinical staging fail to reliably identify occult lymphatic spread. (Kim, P Y et al., Gyn Onc 69:243-247; 1998.) The ability to assess patients at risk for metastasis of an invasive cancer would allow the implementation of more appropriate treatment protocols with possible reduction of morbidity and mortality.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Novel genes, compositions, kits and methods for identification, assessment, prevention, and therapy of cervical cancer**

  Inventor(s): Chen, Yan; (Cambridge, MA), Gannavarapu, Manjula; (Acton, MA), Glatt, Karen; (Natick, MA), Hoersh, Sebastian; (Arlington, MA), Kamatkar, Shubhangi; (Newton, MA), Monahan, John E.; (Walpole, MA), Schlegel, Robert; (Auburndale, MA), Zhao, Xumei; (Burlington, MA)

  Correspondence: Lahive & Cockfield; 28 State Street; Boston; MA; 02109; US

  Patent Application Number: 20030087270

  Date filed: June 12, 2002

  Abstract: The invention relates to newly discovered nucleic acid molecules and proteins associated with **cervical cancer** including pre-malignant conditions such as dysplasia. Compositions, kits, and methods for detecting, characterizing, preventing, and treating human cervical cancers are provided.

Excerpt(s): The present application claims priority to U.S. provisional patent application serial No. 60/298,159, filed on Jun. 13, 2001, U.S. provisional patent application serial No. 60/298,155, filed on Jun. 13, 2001, and U.S. provisional patent application serial No. 60/335,936, filed on Nov. 14, 2001, all of which are expressly incorporated by reference. The field of the invention is **cervical cancer,** including diagnosis, characterization, management, and therapy of **cervical cancer.** The increased number of cancer cases reported in the United States, and, indeed, around the world, is a major concern. Currently there are only a handful of treatments available for specific types of cancer, and these provide no absolute guarantee of success. In order to be most effective, these treatments require not only an early detection of the malignancy, but a reliable assessment of the severity of the malignancy.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

Keeping Current

In order to stay informed about patents and patent applications dealing with cervical cancer, you can access the U.S. Patent Office archive via the Internet at the following Web address: **http://www.uspto.gov/patft/index.html**. You will see two broad options: (1) Issued Patent, and (2) Published Applications. To see a list of issued patents, perform the following steps: Under "Issued Patents," click "Quick Search." Then, type "cervical cancer" (or synonyms) into the "Term 1" box. After clicking on the search button, scroll down to see the various patents which have been granted to date on cervical cancer.

You can also use this procedure to view pending patent applications concerning cervical cancer. Simply go back to **http://www.uspto.gov/patft/index.html**. Select "Quick Search" under "Published Applications." Then proceed with the steps listed above.

CHAPTER 7. BOOKS ON CERVICAL CANCER

Overview

This chapter provides bibliographic book references relating to cervical cancer. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on cervical cancer include the Combined Health Information Database and the National Library of Medicine. Your local medical library also may have these titles available for loan.

Book Summaries: Federal Agencies

The Combined Health Information Database collects various book abstracts from a variety of healthcare institutions and federal agencies. To access these summaries, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. You will need to use the "Detailed Search" option. To find book summaries, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer. For the format option, select "Monograph/Book." Now type "cervical cancer" (or synonyms) into the "For these words:" box. You should check back periodically with this database which is updated every three months. The following is a typical result when searching for books on cervical cancer:

- **Women's health under 40: What you should know**

  Source: Cincinnati, OH: Betterway Books. 2000. 184 pp.

  Contact: Available from Betterway Books, 1507 Dana Avenue, Cincinnati, OH 45207-1005. $6.99.

  Summary: This illustrated book gives an explanation of some common health issues women age 40 and younger can experience. The information is presented in an easy to read format. Subjects covered include: anatomy; pap smears and **cervical cancer;** abnormal periods; painful periods; vaginal infections; sexually transmitted diseases; birth control; breast cancer; staying healthy; and exercise. There is place to record questions to take to a doctor. A bibliography is included.

- **Reproductive Tract Infections: Challenges for International Health Policy, Programs, and Research**

  Source: Reproductive Tract Infections.

  Contact: US Government Printing Office, PO Box 371954, Pittsburgh, PA, 15250-7954, (202) 512-1800, http://www.access.gpo.gov. Plenum Publishing Corporation, Plenum Medical Book Company, 233 Spring St, New York, NY, 10013-1578, (888) 640-7378, http://www.wkap.nl.

  Summary: This publication examines the demographic, societal, biomedical, and technological developments that affect reproductive tract infections (RTI). It summarizes the human and socioeconomic costs of RTI developing countries, and discusses program and policy implications. It addresses the prevalence of these diseases and their costs in terms of infertility, ectopic pregnancy, **cervical cancer,** adverse outcomes of pregnancy, HIV transmission, and sexually transmitted diseases.

Book Summaries: Online Booksellers

Commercial Internet-based booksellers, such as Amazon.com and Barnes&Noble.com, offer summaries which have been supplied by each title's publisher. Some summaries also include customer reviews. Your local bookseller may have access to in-house and commercial databases that index all published books (e.g. Books in Print®). **IMPORTANT NOTE:** Online booksellers typically produce search results for medical and non-medical books. When searching for "cervical cancer" at online booksellers' Web sites, you may discover non-medical books that use the generic term "cervical cancer" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "cervical cancer" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **21st Century Complete Medical Guide to Cervical Cancer - Authoritative Government Documents and Clinical References for Patients and Physicians with Practical Information on Diagnosis and Treatment Options** by PM Medical Health News; ISBN: 1592480195; http://www.amazon.com/exec/obidos/ASIN/1592480195/icongroupinterna
- **An Afrocentric Approach to Breast and Cervical Cancer Early Detection and Screening: An Educational Program for Undergraduate and Advanced Practice Nursing Students** by Dee Baldwin (Editor), et al; ISBN: 1558101225; http://www.amazon.com/exec/obidos/ASIN/1558101225/icongroupinterna
- **Automated Cervical Cancer Screening** by Heinz K. Grohs, O. A. Nasseem Husain; ISBN: 089640255X; http://www.amazon.com/exec/obidos/ASIN/089640255X/icongroupinterna
- **Cervical Cancer** by Lori J. Klein, Edward L. Trimble (1996); ISBN: 078813342X; http://www.amazon.com/exec/obidos/ASIN/078813342X/icongroupinterna
- **Cervical Cancer** by Janet Chomet, Julian Chomet; ISBN: 0809571129; http://www.amazon.com/exec/obidos/ASIN/0809571129/icongroupinterna
- **Cervical Cancer and How to Stop Worrying About It** by Judith Harvey, et al; ISBN: 0571149847; http://www.amazon.com/exec/obidos/ASIN/0571149847/icongroupinterna

- **Cervical Cancer and Preinvasive Neoplasia** by Stephen C. Rubin (Editor), William J. Hoskins (Editor); ISBN: 0397516452; http://www.amazon.com/exec/obidos/ASIN/0397516452/icongroupinterna
- **Cervical cancer in Australia** by Paul Jelfs; ISBN: 0642224870; http://www.amazon.com/exec/obidos/ASIN/0642224870/icongroupinterna
- **Cervical Cancer Screening in Australia: Options for Change** by Australian Institute Of Health (1991); ISBN: 0644134631; http://www.amazon.com/exec/obidos/ASIN/0644134631/icongroupinterna
- **Cervical cancer screening programmes : managerial guidelines** by A. B. Miller; ISBN: 9241544473; http://www.amazon.com/exec/obidos/ASIN/9241544473/icongroupinterna
- **Cervical Cancer: All You and Your Partner Need to Know About Its Prevention, Detection and Treatment** by Jane, Dr. Chomet, Julian, Dr. Chomet; ISBN: 0722515839; http://www.amazon.com/exec/obidos/ASIN/0722515839/icongroupinterna
- **Cervical Cancer: Is Society Ready For a Preventative Answer? [DOWNLOAD: PDF]** by Datamonitor (Author); ISBN: B0000AUH5U; http://www.amazon.com/exec/obidos/ASIN/B0000AUH5U/icongroupinterna
- **Cytological Screening in the Control of Cervical Cancer: Technical Guidelines: Technical Guidelines**; ISBN: 9241542195; http://www.amazon.com/exec/obidos/ASIN/9241542195/icongroupinterna
- **Early histological diagnosis of cervical cancer Textbook and atlas** by E. Burghardt; ISBN: 3134865017; http://www.amazon.com/exec/obidos/ASIN/3134865017/icongroupinterna
- **Flying in the Face of Fear: Surviving Cervical Cancer (Hypatia Health Monographs)** by Mary Lunnen; ISBN: 1872229190; http://www.amazon.com/exec/obidos/ASIN/1872229190/icongroupinterna
- **Gerson Diet Therapy for Women's Cancers: Breast Cancer, Ovarian Cancer, Cervical Cancer** by Charlotte Gerson (2004); ISBN: 1550823043; http://www.amazon.com/exec/obidos/ASIN/1550823043/icongroupinterna
- **Human Papillomavirus and Cervical Cancer (Iarc Scientific Publications, No 94)** by N. Munoz (Editor), et al; ISBN: 9283211944; http://www.amazon.com/exec/obidos/ASIN/9283211944/icongroupinterna
- **Living for Tomorrow: A Positive Approach to the Treatment of Cervical Cancer** by Margaret Wilson; ISBN: 0855722274; http://www.amazon.com/exec/obidos/ASIN/0855722274/icongroupinterna
- **New Developments in Cervical Cancer Screening and Prevention** by Eduardo Franco (Contributor), Joseph Monsonego (Editor); ISBN: 0632047658; http://www.amazon.com/exec/obidos/ASIN/0632047658/icongroupinterna
- **Prevention of Cervical Cancer: the Patient's View** by Tina Posner, Martin Vessey; ISBN: 1870551036; http://www.amazon.com/exec/obidos/ASIN/1870551036/icongroupinterna
- **Reauthorization of the CDC breast and cervical cancer mortality prevention program : hearing before the Subcommittee on Aging of the Committee on Labor and Human Resources, United States Senate, One Hundred Third Congress, first session, on examining proposed legislation to authorize funds for the Center for Disease Control's breast and cervical cancer mortality prevention program July 15, 1993**; ISBN:

0160413397;
http://www.amazon.com/exec/obidos/ASIN/0160413397/icongroupinterna

- **Second Cancer in Relation to Radiation Treatment for Cervical Cancer: Results of a Cancer Registry Collaboration (Iarc Scientific Publications, 52)** by J.C. Boice (Editor), N. E. Day (Editor); ISBN: 0197230520;
http://www.amazon.com/exec/obidos/ASIN/0197230520/icongroupinterna
- **The Epidemiology of Cervical Cancer and Human Papillomavirus (Iarc Scientific Publications, 119)** by N. Munoz (Editor), et al; ISBN: 9283221192;
http://www.amazon.com/exec/obidos/ASIN/9283221192/icongroupinterna
- **The Official Patient's Sourcebook on Cervical Cancer: A Revised and Updated Directory for the Internet Age** by Icon Health Publications (2002); ISBN: 0597834598;
http://www.amazon.com/exec/obidos/ASIN/0597834598/icongroupinterna
- **Viral Etiology of Cervical Cancer (Banbury Report, 21)** by Richard Peto (Editor) (1986); ISBN: 0879692219;
http://www.amazon.com/exec/obidos/ASIN/0879692219/icongroupinterna
- **Virtually Virgins: Sexual Strategies and Cervical Cancer in Recife, Brazil** by Jessica L. Gregg (2003); ISBN: 0804747563;
http://www.amazon.com/exec/obidos/ASIN/0804747563/icongroupinterna
- **Women's health : what needs to change : a summary of the recommendations of the cervical cancer inquiry & a practical guide to action**; ISBN: 0478040539;
http://www.amazon.com/exec/obidos/ASIN/0478040539/icongroupinterna
- **Women's health, raising awareness of cervical cancer : hearing before the Subcommittee on Health and Environment of the Committee on Commerce, House of Representatives, One Hundred Sixth Congress, first session, March 16, 1999**; ISBN: 0160584078;
http://www.amazon.com/exec/obidos/ASIN/0160584078/icongroupinterna
- **Women's Health: Raising Awareness of Cervical Cancer, Hearing Before the Committee on Commerce, U.S. House of Representatives** by Michael Bilirakis (Editor) (1999); ISBN: 0756700280;
http://www.amazon.com/exec/obidos/ASIN/0756700280/icongroupinterna

The National Library of Medicine Book Index

The National Library of Medicine at the National Institutes of Health has a massive database of books published on healthcare and biomedicine. Go to the following Internet site, **http://locatorplus.gov/**, and then select "Search LOCATORplus." Once you are in the search area, simply type "cervical cancer" (or synonyms) into the search box, and select "books only." From there, results can be sorted by publication date, author, or relevance. The following was recently catalogued by the National Library of Medicine:[11]

[11] In addition to LOCATORPlus, in collaboration with authors and publishers, the National Center for Biotechnology Information (NCBI) is currently adapting biomedical books for the Web. The books may be accessed in two ways: (1) by searching directly using any search term or phrase (in the same way as the bibliographic database PubMed), or (2) by following the links to PubMed abstracts. Each PubMed abstract has a "Books" button that displays a facsimile of the abstract in which some phrases are hypertext links. These phrases are also found in the books available at NCBI. Click on hyperlinked results in the list of books in which the phrase is found. Currently, the majority of the links are between the books and PubMed. In the future, more links will be created between the books and other types of information, such as gene and protein sequences and macromolecular structures. See **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books**.

- **Antibodies to herpesvirus hominis types 1 and 2 among patients with cervical cancer** Author: Pohjonen, Raili.; Year: 1972; Turku [Finland: s.n.], 1972
- **Breast and cervical cancer surveillance in Illinois** Author: Howe, Holly L.; Year: 1981; Springfield, Ill.: Illinois Dept. of Public Health, Division of Epidemiologic Studies, [1993]
- **Cervical cancer: a report by 72 Illinois hospitals on cases diagnosed in 1972-80.** Author: American Cancer Society. Illinois Division.; Year: 1990; Chicago: American
- **Cervical cancer: January 1993 through March 1996: 926 citations** Author: Klein, Lori.; Year: 1988; Bethesda, Md. (8600 Rockville Pike): U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Library of Medicine, Reference Section; Pittsburgh, PA.: Sold by the Supt. of Docs., U.S. G.P.O., 1996
- **Cervical cancer detection through cytology; a public health approach.** Author: Fulghum, James E.,; Year: 1973; Jacksonville, 1967
- **Cervical cancer in developing countries: proceedings of the XI international working party meeting, October 1992** Author: Bhattathiri, V. N.; Year: 1982; Trivandrum: Regional; ISBN: 8185974004
- **Cervical cancer prevention programme** Author: New South Wales State Cancer Council.; Year: 1967; [Sydney]: NSW [State]
- **Colposcopic and cytological diagnosis of cervical cancer and premalignant lesions, by S. Timonen and B. Meyer.** Author: Timonen, Sakari.; Year: 1971; Helsinki, 1967
- **Costs and effectiveness of cervical cancer screening in elderly women** Author: Muller, Charlotte Feldman,; Year: 1967; Washington, DC: Congress of the U.S., Office of Technology Assessment: For sale by the Supt. of Docs., U.S. G.P.O., [1990]
- **Early histological diagnosis of cervical cancer.** Author: Burghardt, E. (Erich); Year: 1956; Philadelphia, Saunders, 1973; ISBN: 0721621759 http://www.amazon.com/exec/obidos/ASIN/0721621759/icongroupinterna
- **Herpes simplex virus type 2 and cervical cancer** Author: Rapp, Fred.; Year: 1987; Chicago: Year Book Medical Publishers, 1981; ISBN: 081519918X http://www.amazon.com/exec/obidos/ASIN/081519918X/icongroupinterna
- **Hormones and cervical cancer; effect of sex hormones and antifertility compounds on chemically induced carcinoma of the mouse uterine cervix; comparative morphological and histochemical [sic] studies. By Eivind Myhre, in cooperation with Knut Björo.** Author: Myhre, Eivind,; Year: 1963; Oslo, Universitetsforlaget, 1971
- **Human papillomaviruses and cervical cancer: biology and immunology** Author: Stern, Peter L.; Year: 1996; Oxford; New York: Oxford University Press, 1994; ISBN: 019854796X
- **Issues in cervical cancer screening and treatment: new technologies and costs of alternative management strategies** Author: Braggett, David.; Year: 1996; Canberra, ACT: Australian Institute of Health; Welfare, [1993]; ISBN: 0644297727
- **Selected abstracts on the viral etiology of cervical cancer** Author: Rapp, Fred.; Year: 1989; [Bethesda, Md.]: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National
- **Technologies for automation in cervical cancer screening: workshop, Heidelberg, Frankfurt, Wetzlar, München, June 13-19, 1976** Author: Goerttler, Klaus.; Year: 1976; [Heidelberg]: DKFZ; [Bethesda, Md.]: National
- **The prevention of cervical cancer.** Author: McLaren, Hugh Cameron.; Year: 1934; London, English Universities Press [1963]

- **The report of the Committee of Inquiry into Allegations Concerning the Treatment of Cervical Cancer at National Women's Hospital and Into Other Related Matters, 1983.** Author: New Zealand. Committee on Inquiry into Allegations Concerning the Treatment of Cervical Cancer at National Women's Hospital and into Other Related Matters.; Year: 1988; Auckland, New Zealand: The Committee, [1988]; ISBN: 0473006642

Chapters on Cervical Cancer

In order to find chapters that specifically relate to cervical cancer, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and cervical cancer using the "Detailed Search" option. Go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find book chapters, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Book Chapter." Type "cervical cancer" (or synonyms) into the "For these words:" box.

CHAPTER 8. MULTIMEDIA ON CERVICAL CANCER

Overview

In this chapter, we show you how to keep current on multimedia sources of information on cervical cancer. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine.

Video Recordings

An excellent source of multimedia information on cervical cancer is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "cervical cancer" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find video productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Videorecording (videotape, videocassette, etc.)." Type "cervical cancer" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on cervical cancer:

- **HIV in Women: Conference Held in Minneapolis, MN, October 15 - 17, 1993**

  Contact: HealthSpan, 2810 57th Ave N Ste 425, Minneapolis, MN, 55430, (612) 628-4800.

  Summary: This series of four videos covers educational sessions on HIV in women, given for health-care workers in Minnesota. The first topic discussed explores the relationship between HIV and human papilloma virus, causative agent of **cervical cancer.** Basic manifestations of HIV disease in women, and the ways in which they differ from symptoms in men, are described next. The need for gender-specific tests, treatments, and AIDS-defining conditions for women are examined. The conference explores transmission issues and women, especially heterosexual transmission; pregnancy; perinatal transmission; counseling women who might become pregnant; and substance abuse. It stresses that HIV in women cannot be successfully treated without involvement of the male partner, and also that transmission through substance abuse should be considered in the context of "sex for drugs" that often occurs. Dr. Patty Wetzel, a physician who became HIV-positive through an accidental needlestick, shares her experiences during and after the exposure. Workplace issues and the health care

worker are discussed, including mandatory testing, privacy, universal precautions, disclosure, and written workplace policies. The conference concludes with a panel discussion of ethical concerns, legal issues, State statues, partner notification, civil and criminal liabilities, the right to health care, and the health care worker's duty to treat.

Audio Recordings

The Combined Health Information Database contains abstracts on audio productions. To search CHID, go directly to the following hyperlink: **http;//chid.nih.gov/detail/detail.html**. To find audio productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Sound Recordings." Type "cervical cancer" (or synonyms) into the "For these words:" box. The following is a typical result when searching for sound recordings on cervical cancer:

- **Lesbian Outreach/Breast & Cancer Programs - #6: 17th National Lesbian & Gay Health Conference; Minneapolis, MN, June 17-21, 1995**

  Contact: NORCOM, PO Box 26172, St. Louis Park, MN, 55426, (612) 927-0050.

  Summary: This audiotape contains the proceedings of a workshop that focuses on Federally-funded/state administered breast and **cervical cancer** prevention programs. Information on the incidence and prevalence of these cancers and their mortality is presented. The speakers represent the Centers for Disease Control and Prevention (CDC) breast and **cervical cancer** prevention program. A history of the CDC program is provided. The CDC program includes four key components: public education, professional education, quality assurance, and surveillance. These components are necessary to effectively implement a breast and **cervical cancer** mortality program. The importance of public education is underscored, and examples of innovative public education and screening strategies aimed at target groups are summarized. Eventually, lesbians became a priority target population for these cancer prevention programs. Demonstration projects in four state health departments are developing, conducting needs assessments, and evaluating outreach programs that will target cancer prevention among lesbians.

- **Gyn Manifestations: National Conference on Women and AIDS/HIV Infection; Washington, D.C., December 13 - 14, 1990**

  Contact: Triad Media Group, PO Box 778, Frederick, MD, 21701, (301) 663-1471.

  Summary: This sound recording offers a presentation from the National Conference on Women and AIDS/HIV Infection held December 13-14, 1990, in Washington, D.C., that deals with gynecological manifestations of H uman immunodeficiency virus (HIV) infection. HIV is the cause of Acquired immunodeficiency syndrome (AIDS). The first speaker explains a variety of fungal infections and treatment for them. The second speaker discusses human papilloma virus and its connection with cervical neoplasia. Pap smears should be done frequently on women who are HIV positive because of the possible increased risk of **cervical cancer.** Colposcopy is seen as an increasingly necessary diagnostic tool for such women. The next speaker analyzes the carcinogenicity of Azidothymidine (AZT) in rats and mice. It appears to increase substantially the number of malignant vaginal tumors. The final speaker describes Sexually transmitted disease (STD) manifestations in women with HIV.

Bibliography: Multimedia on Cervical Cancer

The National Library of Medicine is a rich source of information on healthcare-related multimedia productions including slides, computer software, and databases. To access the multimedia database, go to the following Web site: **http://locatorplus.gov/**. Select "Search LOCATORplus." Once in the search area, simply type in cervical cancer (or synonyms). Then, in the option box provided below the search box, select "Audiovisuals and Computer Files." From there, you can choose to sort results by publication date, author, or relevance. The following multimedia has been indexed on cervical cancer:

- **Breast and cervical cancer update [videorecording]** Source: [presented by] the Medical University of South Carolina, College of Medicine and the Health Communications Network; produced by the Health Communications Network, Division of Television Services, Medic; Year: 1992; Format: Videorecording; Charleston, S.C.: The University, c1992
- **Cervical cancer [videorecording]** Source: Marshfield Medical Foundation, in cooperation with Marshfield Clinic & St. Joseph's Hospital; Year: 1983; Format: Videorecording; Marshfield, WI: Marshfield Regional Video Network, 1983
- **Cervical cancer [videorecording]** Source: a presentation of Films for the Humanities & Sciences; ITV, Information Television Network; Year: 1998; Format: Videorecording; Princeton, N.J.: Films for the Humanities & Sciences, c1998
- **Cervical cancer [videorecording]: success in sight** Source: joint development project of the Early Detection Branch of the National Cancer Institute and the National Library of Medicine; Year: 1992; Format: Videorecording; [Bethesda, Md.: The Library], 1992
- **Cervical cancer, pretreatment [videorecording]** Source: produced as a joint venture of the University of Texas System Cancer Center, M.D. Anderson Hospital & the American Cancer Society, Texas Division; Year: 1983; Format: Videorecording; [Houston]: University of Texas System
- **Cervical cancer, treatment & follow-up [videorecording]** Source: produced as a joint venture of the University of Texas System Cancer Center, M.D. Anderson Hospital & the American Cancer Society, Texas Division; Year: 1983; Format: Videorecording; [Houston]: University of Texas System
- **Detection & diagnosis of cervical cancer [videorecording]** Source: American Cancer Society; [produced by] Milner-Fenwick; Year: 1979; Format: Videorecording; [New York]: The Society, c1979
- **Developing a vaccine to prevent cervical cancer [videorecording]** Source: Medical Arts and Photography Branch; Year: 1997; Format: Videorecording; [Bethesda, Md.: National Institutes of Health, 1997]
- **HPV and cervical cancer [videorecording]: the road from etiological understanding to preventive strategies** Source: Office of Research Services, Medical Arts and Photography Branch; Year: 2002; Format: Videorecording; [Bethesda, Md.: National Institutes of Health, 2002]
- **Pelvic exenteration for cervical cancer [motion picture]** Source: Henry E. Averette, John M. Harper; [made by] Dept. of Medical Illustration, University of Miami, School of Medicine; Year: 1968; Format: Motion picture; Miami, Fla.: Averette; [Danbury, Conn.: for loan by Davis and Geck Film Library; Norwich, N. Y.: for loan by Norwich-Eaton Pharmaceuticals, Film Library, 1968]

- **Taking control of your health [videorecording]: the pap test and cervical cancer** Source: produced by the Nebraska Department of Health in cooperation with the National Cancer Institute; Year: 1992; Format: Videorecording; Bethesda, MD: National
- **The National Breast and Cervical Cancer Early Detection Program [videorecording]: 10th anniversary, 1990-2000.** Year: 2000; Format: Videorecording; Atlanta, GA: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, [2000]

CHAPTER 9. PERIODICALS AND NEWS ON CERVICAL CANCER

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover cervical cancer.

News Services and Press Releases

One of the simplest ways of tracking press releases on cervical cancer is to search the news wires. In the following sample of sources, we will briefly describe how to access each service. These services only post recent news intended for public viewing.

PR Newswire

To access the PR Newswire archive, simply go to **http://www.prnewswire.com/**. Select your country. Type "cervical cancer" (or synonyms) into the search box. You will automatically receive information on relevant news releases posted within the last 30 days. The search results are shown by order of relevance.

Reuters Health

The Reuters' Medical News and Health eLine databases can be very useful in exploring news archives relating to cervical cancer. While some of the listed articles are free to view, others are available for purchase for a nominal fee. To access this archive, go to **http://www.reutershealth.com/en/index.html** and search by "cervical cancer" (or synonyms). The following was recently listed in this archive for cervical cancer:

- **Radical hysterectomy for early cervical cancer tied to lasting sexual problems**
  Source: Reuters Medical News
  Date: November 17, 2003

- **Cervical cancer risk remains high over time after detection of HPV**
  Source: Reuters Medical News
  Date: November 06, 2003
- **UK rolls out liquid-based cytology for cervical cancer**
  Source: Reuters Medical News
  Date: October 22, 2003
- **Findings support less frequent cervical cancer screening in low-risk women**
  Source: Reuters Medical News
  Date: October 15, 2003
- **Visual cervical cancer screening appropriate in developing countries**
  Source: Reuters Medical News
  Date: August 27, 2003
- **HIV infection increases risk of cervical cancer in African women**
  Source: Reuters Medical News
  Date: August 26, 2003
- **Combining HPV vaccination with cervical cancer screening may be cost effective**
  Source: Reuters Medical News
  Date: August 12, 2003
- **Women unaware of viral link to cervical cancer**
  Source: Reuters Health eLine
  Date: August 05, 2003
- **Lower social class linked to higher risk of cervical cancer**
  Source: Reuters Medical News
  Date: July 02, 2003
- **Endometrial cancer can develop after radiation for cervical carcinoma**
  Source: Reuters Medical News
  Date: May 13, 2003
- **Xenova may seek partner for cervical cancer vaccine**
  Source: Reuters Industry Breifing
  Date: April 14, 2003
- **Study: Pill use may raise cervical cancer risk**
  Source: Reuters Health eLine
  Date: April 04, 2003
- **Review confirms link between oral contraceptive use and cervical cancer**
  Source: Reuters Industry Breifing
  Date: April 03, 2003
- **Test, vaccine could stop cervical cancer: expert**
  Source: Reuters Health eLine
  Date: April 02, 2003
- **FDA OKs virus test during cervical cancer screen**
  Source: Reuters Health eLine
  Date: April 01, 2003
- **Study finds riskiest viruses for cervical cancer**
  Source: Reuters Health eLine
  Date: February 10, 2003

- **Risk of cervical cancer associated with 30 HPV types classified**
  Source: Reuters Medical News
  Date: February 05, 2003
- **Childbearing possible following modified surgery for invasive cervical cancer**
  Source: Reuters Medical News
  Date: January 31, 2003
- **Novel oral vaccine may be useful therapy for cervical cancer**
  Source: Reuters Medical News
  Date: January 06, 2003
- **US Hispanic women face higher cervical cancer rate**
  Source: Reuters Health eLine
  Date: November 27, 2002
- **Cervical cancer incidence remains high among Hispanic women in US**
  Source: Reuters Medical News
  Date: November 27, 2002
- **Vaccine aimed at cervical cancer shows promise**
  Source: Reuters Health eLine
  Date: November 20, 2002
- **New guidelines for cervical cancer screening issued**
  Source: Reuters Health eLine
  Date: November 14, 2002
- **American Cancer Society issues new guidelines for cervical cancer screening**
  Source: Reuters Industry Breifing
  Date: November 14, 2002
- **Genital herpes may increase cervical cancer risk**
  Source: Reuters Health eLine
  Date: November 05, 2002
- **Chlamydia infection may boost cervical cancer risk**
  Source: Reuters Health eLine
  Date: October 04, 2002
- **C. trachomatis infection tied to risk of cervical cancer**
  Source: Reuters Medical News
  Date: October 03, 2002
- **Cervical cancer screening can be cost-effective in developing countries**
  Source: Reuters Medical News
  Date: October 01, 2002
- **Smoking ups cervical cancer risk in women with HPV**
  Source: Reuters Health eLine
  Date: September 20, 2002
- **Smoking associated with increased cervical cancer risk in women with HPV**
  Source: Reuters Medical News
  Date: September 18, 2002
- **New technique tested against cervical cancer**
  Source: Reuters Health eLine
  Date: September 05, 2002

- **HPV58 variants linked to cervical cancer in Hong Kong**
  Source: Reuters Medical News
  Date: August 30, 2002
- **More details on cervical cancer - virus link**
  Source: Reuters Health eLine
  Date: July 25, 2002
- **Public funding of Pap tests linked to lower rate of invasive cervical cancer**
  Source: Reuters Medical News
  Date: July 05, 2002
- **US funding for Pap tests cuts cervical cancer rate**
  Source: Reuters Health eLine
  Date: July 03, 2002
- **Number of sex partners key in cervical cancer risk**
  Source: Reuters Health eLine
  Date: May 07, 2002
- **Combined approach most cost-effective cervical cancer screening method**
  Source: Reuters Industry Breifing
  Date: May 07, 2002
- **Circumcision reduces risk of penile HPV infection, cervical cancer in partners**
  Source: Reuters Medical News
  Date: April 10, 2002
- **FDA requests more information on Digene cervical cancer screen**
  Source: Reuters Industry Breifing
  Date: April 02, 2002
- **Cervical cancer risk factors associated with higher Pap test use**
  Source: Reuters Industry Breifing
  Date: April 01, 2002
- **Oral contraceptives raise cervical cancer risk in HPV-infected women**
  Source: Reuters Industry Breifing
  Date: March 26, 2002
- **FDA panel backs cervical cancer screening test**
  Source: Reuters Health eLine
  Date: March 08, 2002
- **FDA advisors back new screening method for cervical cancer**
  Source: Reuters Industry Breifing
  Date: March 08, 2002
- **Dual agents make sentinel node identification reliable in cervical cancer patients**
  Source: Reuters Medical News
  Date: February 25, 2002

The NIH

Within MEDLINEplus, the NIH has made an agreement with the New York Times Syndicate, the AP News Service, and Reuters to deliver news that can be browsed by the public. Search news releases at **http://www.nlm.nih.gov/medlineplus/alphanews_a.html**. MEDLINEplus allows you to browse across an alphabetical index. Or you can search by date

at the following Web page: **http://www.nlm.nih.gov/medlineplus/newsbydate.html**. Often, news items are indexed by MEDLINEplus within its search engine.

Business Wire

Business Wire is similar to PR Newswire. To access this archive, simply go to **http://www.businesswire.com/**. You can scan the news by industry category or company name.

Market Wire

Market Wire is more focused on technology than the other wires. To browse the latest press releases by topic, such as alternative medicine, biotechnology, fitness, healthcare, legal, nutrition, and pharmaceuticals, access Market Wire's Medical/Health channel at **http://www.marketwire.com/mw/release_index?channel=MedicalHealth**. Or simply go to Market Wire's home page at **http://www.marketwire.com/mw/home**, type "cervical cancer" (or synonyms) into the search box, and click on "Search News." As this service is technology oriented, you may wish to use it when searching for press releases covering diagnostic procedures or tests.

Search Engines

Medical news is also available in the news sections of commercial Internet search engines. See the health news page at Yahoo (**http://dir.yahoo.com/Health/News_and_Media/**), or you can use this Web site's general news search page at **http://news.yahoo.com/**. Type in "cervical cancer" (or synonyms). If you know the name of a company that is relevant to cervical cancer, you can go to any stock trading Web site (such as **http://www.etrade.com/**) and search for the company name there. News items across various news sources are reported on indicated hyperlinks. Google offers a similar service at **http://news.google.com/**.

BBC

Covering news from a more European perspective, the British Broadcasting Corporation (BBC) allows the public free access to their news archive located at **http://www.bbc.co.uk/**. Search by "cervical cancer" (or synonyms).

Academic Periodicals covering Cervical Cancer

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to cervical cancer. In addition to these sources, you can search for articles covering cervical cancer that have been published by any of the periodicals listed in previous chapters. To find the latest studies published, go to **http://www.ncbi.nlm.nih.gov/pubmed**, type the name of the periodical into the search box, and click "Go."

If you want complete details about the historical contents of a journal, you can also visit the following Web site: **http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi**. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At **http://locatorplus.gov/**, you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search."

CHAPTER 10. RESEARCHING MEDICATIONS

Overview

While a number of hard copy or CD-ROM resources are available for researching medications, a more flexible method is to use Internet-based databases. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

U.S. Pharmacopeia

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications recommended for cervical cancer. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the U.S. Pharmacopeia (USP). Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400 representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at **http://www.usp.org/**. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient® can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database, located at **http://www.fda.gov/cder/da/da.htm**.

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: **http://www.nlm.nih.gov/medlineplus/druginformation.html**. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopeia (USP).

Below, we have compiled a list of medications associated with cervical cancer. If you would like more information on a particular medication, the provided hyperlinks will direct you to ample documentation (e.g. typical dosage, side effects, drug-interaction risks, etc.). The

following drugs have been mentioned in the Pharmacopeia and other sources as being potentially applicable to cervical cancer:

Vinorelbine

- **Systemic - U.S. Brands:** Navelbine
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203542.html

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. Or, you may be able to access these sources from your local medical library.

Mosby's Drug Consult™

Mosby's Drug Consult™ database (also available on CD-ROM and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Subscription information is available at the following hyperlink: **http://www.mosbysdrugconsult.com/**.

PDR*health*

The PDR*health* database is a free-to-use, drug information search engine that has been written for the public in layman's terms. It contains FDA-approved drug information adapted from the Physicians' Desk Reference (PDR) database. PDR*health* can be searched by brand name, generic name, or indication. It features multiple drug interactions reports. Search PDR*health* at **http://www.pdrhealth.com/drug_info/index.html**.

Other Web Sites

Drugs.com (**www.drugs.com**) reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. (**http://www.medletter.com/**) which allows users to download articles on various drugs and therapeutics for a nominal fee.

Researching Orphan Drugs

Although the list of orphan drugs is revised on a daily basis, you can quickly research orphan drugs that might be applicable to cervical cancer by using the database managed by the National Organization for Rare Disorders, Inc. (NORD), at **http://www.rarediseases.org/**. Scroll down the page, and on the left toolbar, click on "Orphan Drug Designation Database." On this page (**http://www.rarediseases.org/search/noddsearch.html**), type "cervical cancer" (or synonyms) into the search box, and click "Submit Query." When you receive your results, note that not all of the drugs may be relevant, as some may have been withdrawn from orphan status. Write down or print out the name of each drug and the relevant contact

information. From there, visit the Pharmacopeia Web site and type the name of each orphan drug into the search box at **http://www.nlm.nih.gov/medlineplus/druginformation.html**. You may need to contact the sponsor or NORD for further information.

NORD conducts "early access programs for investigational new drugs (IND) under the Food and Drug Administration's (FDA's) approval 'Treatment INDs' programs which allow for a limited number of individuals to receive investigational drugs before FDA marketing approval." If the orphan product about which you are seeking information is approved for marketing, information on side effects can be found on the product's label. If the product is not approved, you may need to contact the sponsor.

The following is a list of orphan drugs currently listed in the NORD Orphan Drug Designation Database for cervical cancer:

- **Recombinant vaccinia (human papillomavirus) (trade name: TA-HPV)**
  http://www.rarediseases.org/nord/search/nodd_full?code=403
- **Porfiromycin (trade name: Promycin)**
  http://www.rarediseases.org/nord/search/nodd_full?code=836

If you have any questions about a medical treatment, the FDA may have an office near you. Look for their number in the blue pages of the phone book. You can also contact the FDA through its toll-free number, 1-888-INFO-FDA (1-888-463-6332), or on the World Wide Web at **www.fda.gov**.

APPENDICES

APPENDIX A. PHYSICIAN RESOURCES

Overview

In this chapter, we focus on databases and Internet-based guidelines and information resources created or written for a professional audience.

NIH Guidelines

Commonly referred to as "clinical" or "professional" guidelines, the National Institutes of Health publish physician guidelines for the most common diseases. Publications are available at the following by relevant Institute[12]:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://www.cancer.gov/cancerinfo/list.aspx?viewid=5f35036e-5497-4d86-8c2c-714a9f7c8d25**
- National Eye Institute (NEI); guidelines available at **http://www.nei.nih.gov/order/index.htm**
- National Heart, Lung, and Blood Institute (NHLBI); guidelines available at **http://www.nhlbi.nih.gov/guidelines/index.htm**
- National Human Genome Research Institute (NHGRI); research available at **http://www.genome.gov/page.cfm?pageID=10000375**
- National Institute on Aging (NIA); guidelines available at **http://www.nia.nih.gov/health/**

[12] These publications are typically written by one or more of the various NIH Institutes.

- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at **http://www.niaaa.nih.gov/publications/publications.htm**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); fact sheets and guidelines available at **http://www.niams.nih.gov/hi/index.htm**
- National Institute of Child Health and Human Development (NICHD); guidelines available at **http://www.nichd.nih.gov/publications/pubskey.cfm**
- National Institute on Deafness and Other Communication Disorders (NIDCD); fact sheets and guidelines at **http://www.nidcd.nih.gov/health/**
- National Institute of Dental and Craniofacial Research (NIDCR); guidelines available at **http://www.nidr.nih.gov/health/**
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); guidelines available at **http://www.niddk.nih.gov/health/health.htm**
- National Institute on Drug Abuse (NIDA); guidelines available at **http://www.nida.nih.gov/DrugAbuse.html**
- National Institute of Environmental Health Sciences (NIEHS); environmental health information available at **http://www.niehs.nih.gov/external/facts.htm**
- National Institute of Mental Health (NIMH); guidelines available at **http://www.nimh.nih.gov/practitioners/index.cfm**
- National Institute of Neurological Disorders and Stroke (NINDS); neurological disorder information pages available at **http://www.ninds.nih.gov/health_and_medical/disorder_index.htm**
- National Institute of Nursing Research (NINR); publications on selected illnesses at **http://www.nih.gov/ninr/news-info/publications.html**
- National Institute of Biomedical Imaging and Bioengineering; general information at **http://grants.nih.gov/grants/becon/becon_info.htm**
- Center for Information Technology (CIT); referrals to other agencies based on keyword searches available at **http://kb.nih.gov/www_query_main.asp**
- National Center for Complementary and Alternative Medicine (NCCAM); health information available at **http://nccam.nih.gov/health/**
- National Center for Research Resources (NCRR); various information directories available at **http://www.ncrr.nih.gov/publications.asp**
- Office of Rare Diseases; various fact sheets available at **http://rarediseases.info.nih.gov/html/resources/rep_pubs.html**
- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/publications.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[13] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[14]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[13] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[14] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

The Combined Health Information Database

A comprehensive source of information on clinical guidelines written for professionals is the Combined Health Information Database. You will need to limit your search to one of the following: Brochure/Pamphlet, Fact Sheet, or Information Package, and "cervical cancer" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For the publication date, select "All Years." Select your preferred language and the format option "Fact Sheet." Type "cervical cancer" (or synonyms) into the "For these words:" box. The following is a sample result:

- **Human Papilloma Virus and Cervical Cancer Issues for Women With HIV and AIDS**

  Contact: Voices of Positive Women, PO Box 471 Ste C, Toronto, (416) 324-8703, http://webhome.idirect.com/~vopw/.

  Summary: This paper covers basic information about Human Papilloma Virus and cervical cancer, both common opportunistic conditions in women with Acquired immunodeficiency syndrome (AIDS). It looks at diagnostic and treatment procedures for the two conditions, and outlines followup and prevention policies.

The NLM Gateway[15]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing one-stop searching for many of NLM's information resources or databases.[16] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "cervical cancer" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

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[15] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[16] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

Results Summary

Category	Items Found
Journal Articles	36489
Books / Periodicals / Audio Visual	856
Consumer Health	911
Meeting Abstracts	209
Other Collections	23
Total	38488

HSTAT[17]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[18] These documents include clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[19] Simply search by "cervical cancer" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

Coffee Break: Tutorials for Biologists[20]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[21] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[22] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

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[17] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[18] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[19] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services' *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

[20] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[21] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[22] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

The Genome Project and Cervical Cancer

In the following section, we will discuss databases and references which relate to the Genome Project and cervical cancer.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[23] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "cervical cancer" (or synonyms) into the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. In particular, the option "Database Links" will search across technical databases that offer an abundance of information. The following is an example of the results you can obtain from the OMIM for cervical cancer:

- **Cervical Cancer**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?603956

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by system of the body. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to revisit it from time to time. The following systems and associated disorders are addressed:

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[23] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

- **Cancer:** Uncontrolled cell division.
  Examples: Breast and ovarian cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Cancer.html**
- **Immune System:** Fights invaders.
  Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe combined immunodeficiency.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Immune.html**
- **Metabolism:** Food and energy.
  Examples: Adreno-leukodystrophy, atherosclerosis, Best disease, Gaucher disease, glucose galactose malabsorption, gyrate atrophy, juvenile-onset diabetes, obesity, paroxysmal nocturnal hemoglobinuria, phenylketonuria, Refsum disease, Tangier disease, Tay-Sachs disease.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Metabolism.html**
- **Muscle and Bone:** Movement and growth.
  Examples: Duchenne muscular dystrophy, Ellis-van Creveld syndrome, Marfan syndrome, myotonic dystrophy, spinal muscular atrophy.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Muscle.html**
- **Nervous System:** Mind and body.
  Examples: Alzheimer disease, amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease, Prader-Willi syndrome, Rett syndrome, spinocerebellar atrophy, Williams syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Brain.html**
- **Signals:** Cellular messages.
  Examples: Ataxia telangiectasia, Cockayne syndrome, glaucoma, male-patterned baldness, SRY: sex determination, tuberous sclerosis, Waardenburg syndrome, Werner syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Signals.html**
- **Transporters:** Pumps and channels.
  Examples: Cystic fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Transporters.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**

- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**
- **Nucleotide Sequence Database (Genbank):**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide**
- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**
- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**
- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Taxonomy:** Organisms in GenBank,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome**, and then select the database that you would like to search. The databases available are listed in the drop box next to "Search." Enter "cervical cancer" (or synonyms) into the search box and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[24]

This online resource has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually limited or completely omitted in existing reference sources due to space limitations of the printed form.

At **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html**, you can search across syndromes using an alphabetical index**.** Search by keywords at **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

[24] Adapted from the National Library of Medicine:
http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html.

The Genome Database[25]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "cervical cancer" (or synonyms) into the search box, and review the results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms).

[25] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html - mission**.

APPENDIX B. PATIENT RESOURCES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines written with the patient in mind. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. Since new guidelines on cervical cancer can appear at any moment and be published by a number of sources, the best approach to finding guidelines is to systematically scan the Internet-based services that post them.

Patient Guideline Sources

The remainder of this chapter directs you to sources which either publish or can help you find additional guidelines on topics related to cervical cancer. Due to space limitations, these sources are listed in a concise manner. Do not hesitate to consult the following sources by either using the Internet hyperlink provided, or, in cases where the contact information is provided, contacting the publisher or author directly.

The National Institutes of Health

The NIH gateway to patients is located at **http://health.nih.gov/**. From this site, you can search across various sources and institutes, a number of which are summarized below.

Topic Pages: MEDLINEplus

The National Library of Medicine has created a vast and patient-oriented healthcare information portal called MEDLINEplus. Within this Internet-based system are "health topic pages" which list links to available materials relevant to cervical cancer. To access this system, log on to **http://www.nlm.nih.gov/medlineplus/healthtopics.html**. From there you can either search using the alphabetical index or browse by broad topic areas. Recently, MEDLINEplus listed the following when searched for "cervical cancer":

- Guides on cervical cancer

  Cancer
  http://www.nlm.nih.gov/medlineplus/cancer.html

- Other guides

  Breast Cancer
  http://www.nlm.nih.gov/medlineplus/breastcancer.html

  Cervical Cancer
  http://www.nlm.nih.gov/medlineplus/cervicalcancer.html

  HPV
  http://www.nlm.nih.gov/medlineplus/hpv.html

  Neurofibromatosis
  http://www.nlm.nih.gov/medlineplus/neurofibromatosis.html

  Ovarian Cancer
  http://www.nlm.nih.gov/medlineplus/ovariancancer.html

  Prostate Cancer
  http://www.nlm.nih.gov/medlineplus/prostatecancer.html

  Uterine Cancer
  http://www.nlm.nih.gov/medlineplus/uterinecancer.html

  Uterine Fibroids
  http://www.nlm.nih.gov/medlineplus/uterinefibroids.html

  Vaginal Cancer
  http://www.nlm.nih.gov/medlineplus/vaginalcancer.html

  Vulvar Cancer
  http://www.nlm.nih.gov/medlineplus/vulvarcancer.html

Within the health topic page dedicated to cervical cancer, the following was listed:

- General/Overviews

  What Is Cervical Cancer?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_1x_what_is_cervical_cancer_8.asp?sitearea=cri

- Diagnosis/Symptoms

  Colposcopy
  http://www.nlm.nih.gov/medlineplus/tutorials/colposcopyloader.html

  Colposcopy
  Source: American Academy of Family Physicians
  http://familydoctor.org/handouts/082.html

  How Is Cervical Cancer Diagnosed?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_3x_how_is_cervical_cancer_

diagnosed_8.asp?sitearea=cri

How Is Cervical Cancer Staged?
Source: American Cancer Society
http://www.cancer.org/docroot/cri/content/cri_2_4_3x_how_is_cervical_cancer_staged_8.asp?sitearea=cri

- Treatment

  Cervical Cancer (PDQ): Treatment
  Source: National Cancer Institute
  http://www.cancer.gov/cancerinfo/pdq/treatment/cervical/patient/

  Dilation and Curettage
  http://www.nlm.nih.gov/medlineplus/tutorials/dilationandcurettageloader.html

  Loop Electrosurgical Excision Procedure (LEEP)
  Source: American College of Obstetricians and Gynecologists
  http://www.medem.com/medlb/article_detaillb.cfm?article_ID=ZZZD6NJ687C&sub_cat=2006

- Coping

  Active Coping Helps Gynecologic Cancer Patients' Quality of Life: Lowers Anxiety, Depression, and Confusion
  Source: American Cancer Society
  http://www.cancer.org/docroot/NWS/content/NWS_2_1x_Active_Coping_Helps_Gynecologic_Cancer_Patients_Quality_of_Life.asp

  Female Sexuality After Cancer: What You and Your Partner Need to Know
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=SA00071

  Where to Seek Professional Help: Sexuality and Cancer
  Source: American Cancer Society
  http://www.cancer.org/docroot/mit/content/mit_7_2x_where_to_seek_professional_help_women.asp

- Specific Conditions/Aspects

  Cervical Cancer and Specific Populations
  Source: National Center for Chronic Disease Prevention and Health Promotion
  http://www.cdc.gov/cancer/nbccedp/cc-strategies/index.htm

  Cervical Cancer in Pregnancy
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_4x_cervical_cancer_in_pregnancy_8.asp?sitearea=cri

  Cervical Dysplasia
  Source: American Medical Association
  http://www.medem.com/MedLB/article_detaillb.cfm?article_ID=ZZZIY13X59C&sub_cat=9

DES: Questions and Answers
Source: National Cancer Institute
http://cis.nci.nih.gov/fact/3_4.htm

Human Papillomaviruses and Cancer
Source: National Cancer Institute
http://cis.nci.nih.gov/fact/3_20.htm

Known Health Effects for DES (Diethylstilbestrol) Daughters
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/DES/consumers/about/effects_daughters.html

Oral Contraceptives and Cancer Risk
Source: National Cancer Institute
http://cis.nci.nih.gov/fact/3_13.htm

What Should You Ask Your Doctor about Cervical Cancer?
Source: American Cancer Society
http://www.cancer.org/docroot/cri/content/cri_2_4_5x_what_should_you_ask_your_doctor_about_cervical_cancer_8.asp?sitearea=cri

- From the National Institutes of Health

  What You Need to Know about Cancer of the Cervix
  Source: National Cancer Institute
  http://www.cancer.gov/cancerinfo/wyntk/cervix

- Latest New

  Experts Advise Young Women to Get HPV Test
  Source: 11/03/2003, New York Times Syndicate
  http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_14515.html

  Study Links Obesity to Cervical Cancer, Excess Weight May Be a Co-factor, Along with HPV
  Source: 09/12/2003, American Cancer Society
  http://www.cancer.org/docroot/NWS/content/NWS_1_1x_Study_Links_Obesity_to_Cervical_Cancer.asp

- Law and Polic

  Guidance and Summary of Actions on the Breast and Cervical Cancer Prevention and Treatment Act of 2000
  Source: National Center for Chronic Disease Prevention and Health Promotion
  http://www.cdc.gov/cancer/nbccedp/law106-354.htm

- Organizations

  American Cancer Society
  http://www.cancer.org/

  National Cancer Institute
  http://www.cancer.gov/

- Prevention/Screening

  Cervical Cancer (PDQ): Prevention
  Source: National Cancer Institute
  http://www.cancer.gov/cancerinfo/pdq/prevention/cervical/patient/

  Cervical Cancer (PDQ): Screening
  Source: National Cancer Institute
  http://www.cancer.gov/cancerinfo/pdq/screening/cervical/patient/

  Cervical Cancer Questionnaire
  Source: Harvard Center for Cancer Prevention
  http://www.yourcancerrisk.harvard.edu/hccpquiz.pl?func=start&quiz=cervical

  Having a Pelvic Exam and Pap Test
  Source: National Cancer Institute
  http://www.cancer.gov/cancerinfo/having-a-pelvic-exam

  National Breast and Cervical Cancer Early Detection Program: Reducing Mortality Through Screening
  Source: National Center for Chronic Disease Prevention and Health Promotion
  http://www.cdc.gov/cancer/nbccedp/about.htm

  Pap Smear
  http://www.nlm.nih.gov/medlineplus/tutorials/papsmearloader.html

  PAP Test
  Source: National Women's Health Information Center
  http://www.4woman.gov/faq/pap.htm

  Pap Test: Questions and Answers
  Source: National Cancer Institute
  http://cis.nci.nih.gov/fact/5_16.htm

  Task Force Announces New Cervical Cancer Screening Guidelines
  Source: National Cancer Institute
  http://www.cancer.gov/newscenter/pressreleases/cervicalscreen

  What Are the Risk Factors for Cervical Cancer?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_2x_what_are_the_risk_factors_for_cervical_cancer_8.asp?sitearea=cri

- Research

  Study Links Obesity to Cervical Cancer, Excess Weight May Be a Co-factor, Along with HPV
  Source: American Cancer Society
  http://www.cancer.org/docroot/NWS/content/NWS_1_1x_Study_Links_Obesity_to_Cervical_Cancer.asp

  What's New in Cervical Cancer Research and Treatment?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_6x_whats_new_in_cervical_cancer_research_and_treatment_8.asp?sitearea=cri

- Statistics

  CDC Releases First Cervical Cancer Detection Rates by Race and Ethnicity
  Source: Centers for Disease Control and Prevention
  http://www.cdc.gov/od/oc/media/pressrel/r010116a.htm

  Cervical Cancer Facts
  Source: American Society for Clinical Pathology
  http://www.ascp.org/general/pub_resources/papsmear/facts.asp

  What Are the Key Statistics for Cervical Cancer?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_1x_what_are_the_key_statistics_for_cervical_cancer_8.asp?sitearea=cri

You may also choose to use the search utility provided by MEDLINEplus at the following Web address: **http://www.nlm.nih.gov/medlineplus/**. Simply type a keyword into the search box and click "Search." This utility is similar to the NIH search utility, with the exception that it only includes materials that are linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on cervical cancer. CHID offers summaries that describe the guidelines available, including contact information and pricing. CHID's general Web site is **http://chid.nih.gov/**. To search this database, go to **http://chid.nih.gov/detail/detail.html**. In particular, you can use the advanced search options to look up pamphlets, reports, brochures, and information kits. The following was recently posted in this archive:

- **HPV and Cervical Cancer Screening**

  Contact: American Social Health Association, PO Box 13827, Research Triangle Park, NC, 27709, (919) 361-8400.

  Summary: This brochure presents women with information about the human papillomavirus (HPV) and its relationship to cervical cancer. HPV includes a group of viruses generally known to cause warts on the body. Genital HPV types are sexually transmitted and cause genital warts or cause cell changes on the cervix that increase a woman's risk for cervical cancer. The brochure makes recommendations about how to cope with and prevent HPV. HPV is generally detected using a Pap smear. When Pap smears detect abnormal cells, further exams are usually needed such as a biopsy, colposcopy, or endocervical curettage. The types of HPV that cause genital warts are categorized by their risks for cervical cancer. The brochure provides a table to help individuals understand the meaning of their Pap smear results. The HPV testing process is discussed. Some of the options available to women to help them to manage growths of genital warts include cryosurgery, laser removal, electro-cauterization, and a cone biopsy. The brochure provides contact information for services from which individuals can learn more about HPV and other sexually transmitted diseases (STDs).

- **HPV and Cervical Cancer**

  Contact: Education Training and Research Associates, PO Box 1830, Santa Cruz, CA, 95061-1830, (800) 321-4407, http://www.etr.org.

  Summary: This brochure, for women, discusses the facts about the human papillomavirus (HPV) and its connection to cervical cancer. It discusses HPV transmission, how it is often asymptomatic, and how it may develop into genital warts and cause cell changes in women's cervical walls. The brochure distinguishes between low- and high-risk types of HPV and recommends regular and frequent Pap smear tests for all women with HPV. The brochure identifies ways that women can help reduce their risks for contracting HPV and developing cervical cancer.

- **Cervical Cancer**

  Contact: Community AIDS Treatment Information Exchange, PO Box 1104, Toronto, (416) 203-7122, http://www.catie.ca.

  Summary: This fact sheet for women discusses cervical cancer; an abnormal growth of cells on the cervix, the opening of the uterus that leads into the vagina, which can develop slowly from a pre-cancerous condition, called cervical dysplasia. Cervical cancer has been linked to the sexually transmitted disease (STD) human papillomavirus (HPV, by immune system suppression due to medical drug use, or as a result of the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS). Practicing safer sex with condoms or having non-penetrative sex are ways to reduce the risk of contracting HIV or HPV. Often, there are no symptoms for cervical cancer other than genital warts that indicate exposure to HPV, particularly in the early stages. In the advanced stages there may be pain in the lower abdomen or back, pain during intercourse, unusual vaginal discharge, or bleeding between menstrual periods. Cervical cancer and its precursory conditions can often be detected using Pap smears or colposcopies, both of which are described in the fact sheet. These tests will determine if abnormal cells exist on the cervix but do not determine if they are cancerous. Treatment for cervical cancer varies depending on the location and size of the cancer, and whether or not it has spread to other parts of the body. The treatments for cervical cancer are outlined in the fact sheet. Although cervical cancer can be treated, HIV-positive women are at risk for recurrences. Cervical cancer is an AIDS-defining condition in HIV-positive women.

- **HPV and Cervical Cancer : Questions and Answers**

  Summary: This pamphlet discusses the relationship between the sexually transmitted disease (STD), human papillomavirus (HPV), and cancer. The pamphlet describes HPV, how it is spread, and its symptoms. It discusses how women can help to prevent HPV by practicing sexual abstinence or practicing safer sex with condoms. The pamphlet examines the relationship between HPV as a pre-determinant for cervical cancer. It explains the Pap test, which is used to diagnose abnormal cell changes and cervical cancer, and what an abnormal result indicates.

- **Human Papillomavirus Testing.: Improving Cervical Cancer Screening: What You Need to Know**

  Contact: Digene Corporation, 1201 Clopper Rd, Gaithersburg, MD, 20878, (301) 944-7000, http://www.digene.com.

Summary: This pamphlet discusses the sexually transmitted disease (STD) human papilloma virus (HPV), which is the leading cause of cervical cancer. The pamphlet explains the signs of HPV infection in the form of bumps called genital warts, transmission, testing, and prevention. A new test called the Hybrid Capture HPV DNA Assay can indicate the presence and type of HPV. The use of latex condoms may reduce the risk of HPV, however the virus can be spread from warts in areas not covered by the condom.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http://www.guideline.gov/** by using the keyword "cervical cancer" (or synonyms). The following was recently posted:

- **Cervical cancer screening**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1994 September (revised 2002 Jun); 24 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3405&nbr=2631&string=cervical+AND+cancer

- **Cervical cancer screening for women who attend STD clinics or have a history of STDs. Sexually transmitted diseases treatment guidelines 2002**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1993 (revised 2002 May 10); 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3241&nbr=2467&string=cervical+AND+cancer

- **Primary treatment for locally advanced cervical cancer: concurrent platinum-based chemotherapy and radiation**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 2002 August 26 (updated online 2002 Dec); 27 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3533&nbr=2759&string=cervical+AND+cancer

- **Screening for cervical cancer: recommendations and rationale**

  Source: United States Preventive Services Task Force - Independent Expert Panel; 1996 (revised 2003 January 22); 21 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3532&nbr=2758&string=cervical+AND+cancer

Healthfinder™

Healthfinder™ is sponsored by the U.S. Department of Health and Human Services and offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **Breast and Cervical Cancer Prevention and Treatment**

  Summary: This site is intended to provide materials of interest to various audiences regarding the prevention and treatment of breast and cervical cancer.

  Source: Centers for Medicare and Medicaid Services (CMS), formerly the Health Care Financing Administration

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6795

- **Breast and Cervical Cancers Publications**

  Summary: A list of publications on breast and cervical cancers, available from the Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for

  Source: Division of Cancer Prevention and Control, Centers for Disease Control and Prevention

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=1246

- **Cancer Prevention and Control Page - Centers for Disease Control and Prevention**

  Summary: Prevention control resources that focus on the National Breast and Cervical Cancer Early Detection Program, the National Program of Cancer Registries, the National Skin Cancer Prevention Education

  Source: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=252

- **Cervical Cancer**

  Source: California Department of Health Services

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7428

- **Cervical Cancer (PDQ®): Screening**

  Summary: This up-to-date information from the National Cancer Institute's PDQ® database is intended for use by patients.

  Source: National Cancer Institute, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2437

- **Cervical Cancer and Pap Test Information**

  Summary: This page briefly describes cervical cancer and the benefits of Pap smears and links users to other resources, such as information about how to obtain free or low-cost Pap smears or mammograms.

  Source: National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7173

- **Cervical Cancer Home Page**

  Summary: This page provides information about the prevention, causes, genetics, screening, testing and treatment of cervical cancer. Also includes information on clinical trials and statistics.

  Source: National Cancer Institute, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=3744

- **Cervical Cancer Screening: What Vietnamese Women Should Know**

  Summary: This booklet, in the Vietnamese language, provides information about the importance of Pap tests to detect cervical cancer.

  Source: Educational Institution--Follow the Resource URL for More Information

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7182

- **Information to Live By: Human Papillomavirus (HPV)**

  Summary: Answers to basic questions about HPV viruses, types of which can cause warts on the hands and feet, genital warts, and have been linked to cervical cancer.

  Source: American Social Health Association

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=4625

- **National Breast and Cervical Cancer Early Detection Program**

  Summary: This site contains information and resources for health professionals, researchers and the general public.

  Source: Division of Cancer Prevention and Control, Centers for Disease Control and Prevention

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=4698

- **Natural History of Cervical Cancer: Even Infrequent Screening of Older Women Saves Lives**

  Summary: This fact sheet gives an overview of the natural history of cervical cancer and discusses human papillomavirus and screening.

  Source: Program for Appropriate Technology in Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6617

- **Prevention of Cervical Cancer**

  Source: Federation of Chinese American and Chinese Canadian Medical Societies

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7273

- **Screening for Cervical Cancer: Recommendations and Rationale**

  Summary: This statement summarizes the current U.S.

  Source: Agency for Healthcare Research and Quality

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7226

- **The National Breast and Cervical Cancer Early Detection Program AT-A-GLANCE**

  Summary: A summary of the program's efforts and services including screening, quality assurance, health professions and consumer education and outreach, partnership development and surveillance, tracking and

  Source: Division of Cancer Prevention and Control, Centers for Disease Control and Prevention

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=4705

- **Vietnamese Community Health Promotion Project Archives**

  Summary: These booklets in Vietnamese provide information on cervical cancer, hepatitis B, breast cancer, smoking, and nutrition.

  Source: Vietnamese Community Health Promotion Project

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7416

- **What You Need To Know About™ Cancer of the Cervix**

  Summary: Patient information about cervical cancer, including detection/screening, staging, treatment options, treatment side effects and research.

  Source: National Cancer Institute, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=4192

The NIH Search Utility

The NIH search utility allows you to search for documents on over 100 selected Web sites that comprise the NIH-WEB-SPACE. Each of these servers is "crawled" and indexed on an ongoing basis. Your search will produce a list of various documents, all of which will relate in some way to cervical cancer. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and patients. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

Additional Web Sources

A number of Web sites are available to the public that often link to government sites. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**
- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Associations and Cervical Cancer

The following is a list of associations that provide information on and resources relating to cervical cancer:

- **National Cervical Cancer Coalition**

  Telephone: (818) 909-3849 Toll-free: (800) 685-5531

  Fax: (818) 780-8199

  Email: ncccak@nccc-online.org

  Web Site: http://www.nccc-online.org

  Background: The National **Cervical Cancer** Coalition (NCCC) is a voluntary not-for-profit organization dedicated to educating the public and health care professionals about issues related to **cervical cancer.** Cancer of the cervix is one of the most common forms of cancer affecting females. (The cervix is the neck of the uterus or the lower portion of the uterus that extends into the vagina.) Prior to the development of cancer, abnormal changes occur within cells on the surface of the cervix (cervical dysplasia) that may be detected by a cervical smear test known as a 'Pap smear.' Abnormal cervical smears indicate the need for further investigation and possible treatment. The NCCC serves as an independent coalition of women's groups, affected individuals and family members, health care providers and other medical professionals, and technological and research companies and associations. Established in 1997 and currently consisting of approximately 800 members, the Coalition is dedicated to enhancing awareness of the traditional Pap smear and new technologies, treatments for cervical dysplasia and cancer, and reimbursement issues concerning **cervical cancer** screening. The NCCC is also committed to serving as a clearinghouse of information on **cervical cancer** for affected women and their families; reviewing national and international **cervical cancer** screening and treatment programs; and developing a grass roots effort explaining the difficulties that current below cost reimbursement rates cause for the traditional Pap smear and potential new technology. In addition, the Coalition communicates the continued importance and success of such cancer screening to lower **cervical cancer** rates, emphasizing access to quality testing for all women, including those most in need of receiving Pap smears. The NCCC offers a variety of educational materials and has a web site on the Internet that discusses the Coalition's mission, provides a listing of its

Medical Advisory Panel, and offers information on family planning, managed care, and current research.

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to cervical cancer. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with cervical cancer.

The National Health Information Center (NHIC)

The National Health Information Center (NHIC) offers a free referral service to help people find organizations that provide information about cervical cancer. For more information, see the NHIC's Web site at **http://www.health.gov/NHIC/** or contact an information specialist by calling 1-800-336-4797.

Directory of Health Organizations

The Directory of Health Organizations, provided by the National Library of Medicine Specialized Information Services, is a comprehensive source of information on associations. The Directory of Health Organizations database can be accessed via the Internet at **http://www.sis.nlm.nih.gov/Dir/DirMain.html**. It is composed of two parts: DIRLINE and Health Hotlines.

The DIRLINE database comprises some 10,000 records of organizations, research centers, and government institutes and associations that primarily focus on health and biomedicine. To access DIRLINE directly, go to the following Web site: **http://dirline.nlm.nih.gov/**. Simply type in "cervical cancer" (or a synonym), and you will receive information on all relevant organizations listed in the database.

Health Hotlines directs you to toll-free numbers to over 300 organizations. You can access this database directly at **http://www.sis.nlm.nih.gov/hotlines/**. On this page, you are given the option to search by keyword or by browsing the subject list. When you have received your search results, click on the name of the organization for its description and contact information.

The Combined Health Information Database

Another comprehensive source of information on healthcare associations is the Combined Health Information Database. Using the "Detailed Search" option, you will need to limit your search to "Organizations" and "cervical cancer". Type the following hyperlink into your Web browser: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Then, select your preferred language and the format option "Organization Resource Sheet." Type "cervical cancer" (or synonyms) into the "For

these words:" box. You should check back periodically with this database since it is updated every three months.

The National Organization for Rare Disorders, Inc.

The National Organization for Rare Disorders, Inc. has prepared a Web site that provides, at no charge, lists of associations organized by health topic. You can access this database at the following Web site: **http://www.rarediseases.org/search/orgsearch.html**. Type "cervical cancer" (or a synonym) into the search box, and click "Submit Query."

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Your local public library and medical libraries have interlibrary loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[26]

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries in the U.S. and Canada

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries with reference facilities that are open to the public. The following is the NLM's list and includes hyperlinks to each library's Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of

[26] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located)[27]:

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute)
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System, Humboldt), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos, **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**
- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** Los Gatos PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation, Sacramento), **http://suttermedicalcenter.org/library/**
- **California:** Health Sciences Libraries (University of California, Davis), **http://www.lib.ucdavis.edu/healthsci/**
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System, Pleasanton), **http://gaelnet.stmarys-ca.edu/other.libs/gbal/east/vchl.html**
- **California:** Washington Community Health Resource Library (Fremont), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.saintjosephdenver.org/yourhealth/libraries/**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**

[27] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), **http://hml.org/CHIS/**
- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Chicago), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center, Peoria), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), **http://www.centralbap.com/education/community/library.cfm**
- **Kentucky:** University of Kentucky - Health Information Library (Chandler Medical Center, Lexington), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center, Portland), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital (Brunswick), **http://www.parkviewhospital.org/**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), **http://www.wmhcc.org/Library/**

- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), **http://www.deerlodge.mb.ca/crane_library/about.asp**
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School, Worchester), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information (Detroit), **http://www.henryford.com/body.cfm?id=39330**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**

- **Nevada:** Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital, Rahway), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York, Syracuse), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), **http://www.sfh-tulsa.com/services/healthinfo.asp**
- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), **http://www.hsls.pitt.edu/guides/chi/hopwood/index_html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System, Williamsport), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://www.mghlib.mcgill.ca/**

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), **http://www.rcrh.org/Services/Library/Default.asp**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), **http://www.swmedicalcenter.com/body.cfm?id=72**

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://cancerweb.ncl.ac.uk/omd/**
- Rare Diseases Terms (Office of Rare Diseases): **http://ord.aspensys.com/asp/diseases/diseases.asp**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a**). The NIH suggests the following Web sites in the ADAM Medical Encyclopedia when searching for information on cervical cancer:

- **Basic Guidelines for Cervical Cancer**

  Cancer
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001289.htm

  Cervical cancer
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000893.htm

  HIV Infection
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000602.htm

- **Signs & Symptoms for Cervical Cancer**

  Edema
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003103.htm

  Vaginal discharge
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003158.htm

- **Diagnostics and Tests for Cervical Cancer**

  Biopsy
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003416.htm

  Carcinoembryonic antigen
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003574.htm

  CBC
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003642.htm

  Chest X-ray
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003804.htm

  CT
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003330.htm

  IVP
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003782.htm

  MRI
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003335.htm

  Sigmoidoscopy
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003885.htm

  X-ray
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003337.htm

- **Surgery and Procedures for Cervical Cancer**

  Hysterectomy
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002915.htm

  Removal of the uterus
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002915.htm

- **Background Topics for Cervical Cancer**

  Condoms
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/004001.htm

  Physical examination
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002274.htm

  Smoking
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002032.htm

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

CERVICAL CANCER DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

9-cis retinoic acid: A drug being studied for cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Aberrant: Wandering or deviating from the usual or normal course. [EU]

Abscess: Accumulation of purulent material in tissues, organs, or circumscribed spaces, usually associated with signs of infection. [NIH]

Absolute risk: The observed or calculated probability of an event in a population under study, as contrasted with the relative risk. [NIH]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

Accommodation: Adjustment, especially that of the eye for various distances. [EU]

Acculturation: Process of cultural change in which one group or members of a group assimilates various cultural patterns from another. [NIH]

Acetyltransferases: Enzymes catalyzing the transfer of an acetyl group, usually from acetyl coenzyme A, to another compound. EC 2.3.1. [NIH]

Acid Phosphatase: An enzyme that catalyzes the conversion of an orthophosphoric monoester and water to an alcohol and orthophosphate. EC 3.1.3.2. [NIH]

Acne: A disorder of the skin marked by inflammation of oil glands and hair glands. [NIH]

Acne Vulgaris: A chronic disorder of the pilosebaceous apparatus associated with an increase in sebum secretion. It is characterized by open comedones (blackheads), closed comedones (whiteheads), and pustular nodules. The cause is unknown, but heredity and age are predisposing factors. [NIH]

Actin: Essential component of the cell skeleton. [NIH]

Acute lymphoblastic leukemia: ALL. A quickly progressing disease in which too many immature white blood cells called lymphoblasts are found in the blood and bone marrow. Also called acute lymphocytic leukemia. [NIH]

Acute lymphocytic leukemia: ALL. A quickly progressing disease in which too many immature white blood cells called lymphoblasts are found in the blood and bone marrow. Also called acute lymphoblastic leukemia. [NIH]

Adaptability: Ability to develop some form of tolerance to conditions extremely different from those under which a living organism evolved. [NIH]

Adaptation: 1. The adjustment of an organism to its environment, or the process by which it enhances such fitness. 2. The normal ability of the eye to adjust itself to variations in the intensity of light; the adjustment to such variations. 3. The decline in the frequency of firing of a neuron, particularly of a receptor, under conditions of constant stimulation. 4. In

dentistry, (a) the proper fitting of a denture, (b) the degree of proximity and interlocking of restorative material to a tooth preparation, (c) the exact adjustment of bands to teeth. 5. In microbiology, the adjustment of bacterial physiology to a new environment. [EU]

Adduct: Complex formed when a carcinogen combines with DNA or a protein. [NIH]

Adenocarcinoma: A malignant epithelial tumor with a glandular organization. [NIH]

Adenoma: A benign epithelial tumor with a glandular organization. [NIH]

Adenovirus: A group of viruses that cause respiratory tract and eye infections. Adenoviruses used in gene therapy are altered to carry a specific tumor-fighting gene. [NIH]

Adjuvant: A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

Adrenal Cortex: The outer layer of the adrenal gland. It secretes mineralocorticoids, androgens, and glucocorticoids. [NIH]

Adverse Effect: An unwanted side effect of treatment. [NIH]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

Agar: A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

Aggressiveness: The quality of being aggressive (= characterized by aggression; militant; enterprising; spreading with vigour; chemically active; variable and adaptable). [EU]

Agonist: In anatomy, a prime mover. In pharmacology, a drug that has affinity for and stimulates physiologic activity at cell receptors normally stimulated by naturally occurring substances. [EU]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [NIH]

Alkaline: Having the reactions of an alkali. [EU]

Alkaline Phosphatase: An enzyme that catalyzes the conversion of an orthophosphoric monoester and water to an alcohol and orthophosphate. EC 3.1.3.1. [NIH]

Alkaloid: A member of a large group of chemicals that are made by plants and have nitrogen in them. Some alkaloids have been shown to work against cancer. [NIH]

Alkylating Agents: Highly reactive chemicals that introduce alkyl radicals into biologically active molecules and thereby prevent their proper functioning. Many are used as antineoplastic agents, but most are very toxic, with carcinogenic, mutagenic, teratogenic, and immunosuppressant actions. They have also been used as components in poison gases. [NIH]

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on

homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Allelic Imbalance: A situation where one member (allele) of a gene pair is lost (loss of heterozygosity) or amplified. [NIH]

Allogeneic: Taken from different individuals of the same species. [NIH]

Alpha Particles: Positively charged particles composed of two protons and two neutrons, i.e., helium nuclei, emitted during disintegration of very heavy isotopes; a beam of alpha particles or an alpha ray has very strong ionizing power, but weak penetrability. [NIH]

Alpha-helix: One of the secondary element of protein. [NIH]

Alternative medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used instead of standard treatments. Alternative medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Amenorrhea: Absence of menstruation. [NIH]

Amifostine: A phosphorothioate proposed as a radiation-protective agent. It causes splenic vasodilation and may block autonomic ganglia. [NIH]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amplification: The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

Anaerobic: 1. Lacking molecular oxygen. 2. Growing, living, or occurring in the absence of molecular oxygen; pertaining to an anaerobe. [EU]

Anaesthesia: Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

Anal: Having to do with the anus, which is the posterior opening of the large bowel. [NIH]

Analog: In chemistry, a substance that is similar, but not identical, to another. [NIH]

Analogous: Resembling or similar in some respects, as in function or appearance, but not in origin or development;. [EU]

Anaphylatoxins: The family of peptides C3a, C4a, C5a, and C5a des-arginine produced in the serum during complement activation. They produce smooth muscle contraction, mast cell histamine release, affect platelet aggregation, and act as mediators of the local inflammatory process. The order of anaphylatoxin activity from strongest to weakest is C5a, C3a, C4a, and C5a des-arginine. The latter is the so-called "classical" anaphylatoxin but shows no spasmogenic activity though it contains some chemotactic ability. [NIH]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Anesthesia: A state characterized by loss of feeling or sensation. This depression of nerve function is usually the result of pharmacologic action and is induced to allow performance of surgery or other painful procedures. [NIH]

Angiogenesis: Blood vessel formation. Tumor angiogenesis is the growth of blood vessels from surrounding tissue to a solid tumor. This is caused by the release of chemicals by the tumor. [NIH]

Animal Husbandry: The science of breeding, feeding, and care of domestic animals; includes housing and nutrition. [NIH]

Animal model: An animal with a disease either the same as or like a disease in humans. Animal models are used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Annealing: The spontaneous alignment of two single DNA strands to form a double helix. [NIH]

Anogenital: Pertaining to the anus and external genitals. [EU]

Anomalies: Birth defects; abnormalities. [NIH]

Anovulation: Suspension or cessation of ovulation in animals and humans. [NIH]

Antagonism: Interference with, or inhibition of, the growth of a living organism by another living organism, due either to creation of unfavorable conditions (e. g. exhaustion of food supplies) or to production of a specific antibiotic substance (e. g. penicillin). [NIH]

Anthracycline: A member of a family of anticancer drugs that are also antibiotics. [NIH]

Antibacterial: A substance that destroys bacteria or suppresses their growth or reproduction. [EU]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Antibodies: Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

Anticoagulant: A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antigen-Antibody Complex: The complex formed by the binding of antigen and antibody molecules. The deposition of large antigen-antibody complexes leading to tissue damage causes immune complex diseases. [NIH]

Antigen-presenting cell: APC. A cell that shows antigen on its surface to other cells of the immune system. This is an important part of an immune response. [NIH]

Anti-infective: An agent that so acts. [EU]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

Anti-Inflammatory Agents: Substances that reduce or suppress inflammation. [NIH]

Antimetabolite: A chemical that is very similar to one required in a normal biochemical reaction in cells. Antimetabolites can stop or slow down the reaction. [NIH]

Antimitotic: Inhibiting or preventing mitosis. [EU]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Antineoplastic Agents: Substances that inhibit or prevent the proliferation of neoplasms. [NIH]

Antioxidant: A substance that prevents damage caused by free radicals. Free radicals are highly reactive chemicals that often contain oxygen. They are produced when molecules are split to give products that have unpaired electrons. This process is called oxidation. [NIH]

Antitumour: Counteracting tumour formation. [EU]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anus: The opening of the rectum to the outside of the body. [NIH]

Apoptosis: One of the two mechanisms by which cell death occurs (the other being the pathological process of necrosis). Apoptosis is the mechanism responsible for the physiological deletion of cells and appears to be intrinsically programmed. It is characterized by distinctive morphologic changes in the nucleus and cytoplasm, chromatin cleavage at regularly spaced sites, and the endonucleolytic cleavage of genomic DNA (DNA fragmentation) at internucleosomal sites. This mode of cell death serves as a balance to mitosis in regulating the size of animal tissues and in mediating pathologic processes associated with tumor growth. [NIH]

Appendicitis: Acute inflammation of the vermiform appendix. [NIH]

Applicability: A list of the commodities to which the candidate method can be applied as presented or with minor modifications. [NIH]

Aqueous: Having to do with water. [NIH]

Arachidonic Acid: An unsaturated, essential fatty acid. It is found in animal and human fat as well as in the liver, brain, and glandular organs, and is a constituent of animal phosphatides. It is formed by the synthesis from dietary linoleic acid and is a precursor in the biosynthesis of prostaglandins, thromboxanes, and leukotrienes. [NIH]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Aromatic: Having a spicy odour. [EU]

Arsenic trioxide: An anticancer drug that induces programmed cell death (apoptosis) in certain cancer cells. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Arteriovenous: Both arterial and venous; pertaining to or affecting an artery and a vein. [EU]

Articular: Of or pertaining to a joint. [EU]

Asbestos: Fibrous incombustible mineral composed of magnesium and calcium silicates with or without other elements. It is relatively inert chemically and used in thermal

insulation and fireproofing. Inhalation of dust causes asbestosis and later lung and gastrointestinal neoplasms. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Ataxia: Impairment of the ability to perform smoothly coordinated voluntary movements. This condition may affect the limbs, trunk, eyes, pharnyx, larnyx, and other structures. Ataxia may result from impaired sensory or motor function. Sensory ataxia may result from posterior column injury or peripheral nerve diseases. Motor ataxia may be associated with cerebellar diseases; cerebral cortex diseases; thalamic diseases; basal ganglia diseases; injury to the red nucleus; and other conditions. [NIH]

ATP: ATP an abbreviation for adenosine triphosphate, a compound which serves as a carrier of energy for cells. [NIH]

Atrophy: Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Atypical: Irregular; not conformable to the type; in microbiology, applied specifically to strains of unusual type. [EU]

Autologous: Taken from an individual's own tissues, cells, or DNA. [NIH]

Autonomic: Self-controlling; functionally independent. [EU]

Autonomic Nervous System: The enteric, parasympathetic, and sympathetic nervous systems taken together. Generally speaking, the autonomic nervous system regulates the internal environment during both peaceful activity and physical or emotional stress. Autonomic activity is controlled and integrated by the central nervous system, especially the hypothalamus and the solitary nucleus, which receive information relayed from visceral afferents; these and related central and sensory structures are sometimes (but not here) considered to be part of the autonomic nervous system itself. [NIH]

Bacteremia: The presence of viable bacteria circulating in the blood. Fever, chills, tachycardia, and tachypnea are common acute manifestations of bacteremia. The majority of cases are seen in already hospitalized patients, most of whom have underlying diseases or procedures which render their bloodstreams susceptible to invasion. [NIH]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccal, rodlike or bacillary, and spiral or spirochetal. [NIH]

Bacteriophage: A virus whose host is a bacterial cell; A virus that exclusively infects bacteria. It generally has a protein coat surrounding the genome (DNA or RNA). One of the coliphages most extensively studied is the lambda phage, which is also one of the most important. [NIH]

Bacterium: Microscopic organism which may have a spherical, rod-like, or spiral unicellular or non-cellular body. Bacteria usually reproduce through asexual processes. [NIH]

Basal cell carcinoma: A type of skin cancer that arises from the basal cells, small round cells found in the lower part (or base) of the epidermis, the outer layer of the skin. [NIH]

Basal cells: Small, round cells found in the lower part (or base) of the epidermis, the outer layer of the skin. [NIH]

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

Basal Ganglia Diseases: Diseases of the basal ganglia including the putamen; globus pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [NIH]

Base: In chemistry, the nonacid part of a salt; a substance that combines with acids to form salts; a substance that dissociates to give hydroxide ions in aqueous solutions; a substance whose molecule or ion can combine with a proton (hydrogen ion); a substance capable of donating a pair of electrons (to an acid) for the formation of a coordinate covalent bond. [EU]

Basement Membrane: Ubiquitous supportive tissue adjacent to epithelium and around smooth and striated muscle cells. This tissue contains intrinsic macromolecular components such as collagen, laminin, and sulfated proteoglycans. As seen by light microscopy one of its subdivisions is the basal (basement) lamina. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Bereavement: Refers to the whole process of grieving and mourning and is associated with a deep sense of loss and sadness. [NIH]

Bevacizumab: A monoclonal antibody that may prevent the growth of blood vessels from surrounding tissue to a solid tumor. [NIH]

Bewilderment: Impairment or loss of will power. [NIH]

Bilateral: Affecting both the right and left side of body. [NIH]

Bile: An emulsifying agent produced in the liver and secreted into the duodenum. Its composition includes bile acids and salts, cholesterol, and electrolytes. It aids digestion of fats in the duodenum. [NIH]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Biological response modifier: BRM. A substance that stimulates the body's response to infection and disease. [NIH]

Biological therapy: Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

Biological Transport: The movement of materials (including biochemical substances and drugs) across cell membranes and epithelial layers, usually by passive diffusion. [NIH]

Biomarkers: Substances sometimes found in an increased amount in the blood, other body fluids, or tissues and that may suggest the presence of some types of cancer. Biomarkers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and GI tract cancers), and PSA (prostate cancer). Also called tumor markers. [NIH]

Biomedical Engineering: Application of principles and practices of engineering science to biomedical research and health care. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

Biotechnology: Body of knowledge related to the use of organisms, cells or cell-derived constituents for the purpose of developing products which are technically, scientifically and clinically useful. Alteration of biologic function at the molecular level (i.e., genetic engineering) is a central focus; laboratory methods used include transfection and cloning technologies, sequence and structure analysis algorithms, computer databases, and gene and

protein structure function analysis and prediction. [NIH]

Biotransformation: The chemical alteration of an exogenous substance by or in a biological system. The alteration may inactivate the compound or it may result in the production of an active metabolite of an inactive parent compound. The alteration may be either non-synthetic (oxidation-reduction, hydrolysis) or synthetic (glucuronide formation, sulfate conjugation, acetylation, methylation). This also includes metabolic detoxication and clearance. [NIH]

Bladder: The organ that stores urine. [NIH]

Bleomycin: A complex of related glycopeptide antibiotics from Streptomyces verticillus consisting of bleomycin A2 and B2. It inhibits DNA metabolism and is used as an antineoplastic, especially for solid tumors. [NIH]

Blood Glucose: Glucose in blood. [NIH]

Blood pressure: The pressure of blood against the walls of a blood vessel or heart chamber. Unless there is reference to another location, such as the pulmonary artery or one of the heart chambers, it refers to the pressure in the systemic arteries, as measured, for example, in the forearm. [NIH]

Blood vessel: A tube in the body through which blood circulates. Blood vessels include a network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Blot: To transfer DNA, RNA, or proteins to an immobilizing matrix such as nitrocellulose. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Bone Marrow: The soft tissue filling the cavities of bones. Bone marrow exists in two types, yellow and red. Yellow marrow is found in the large cavities of large bones and consists mostly of fat cells and a few primitive blood cells. Red marrow is a hematopoietic tissue and is the site of production of erythrocytes and granular leukocytes. Bone marrow is made up of a framework of connective tissue containing branching fibers with the frame being filled with marrow cells. [NIH]

Bowel: The long tube-shaped organ in the abdomen that completes the process of digestion. There is both a small and a large bowel. Also called the intestine. [NIH]

Bowel Movement: Body wastes passed through the rectum and anus. [NIH]

Brachytherapy: A collective term for interstitial, intracavity, and surface radiotherapy. It uses small sealed or partly-sealed sources that may be placed on or near the body surface or within a natural body cavity or implanted directly into the tissues. [NIH]

Branch: Most commonly used for branches of nerves, but applied also to other structures. [NIH]

Breeding: The science or art of changing the constitution of a population of plants or animals through sexual reproduction. [NIH]

Bronchi: The larger air passages of the lungs arising from the terminal bifurcation of the trachea. [NIH]

Bronchitis: Inflammation (swelling and reddening) of the bronchi. [NIH]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Calcium: A basic element found in nearly all organized tissues. It is a member of the alkaline earth family of metals with the atomic symbol Ca, atomic number 20, and atomic weight 40. Calcium is the most abundant mineral in the body and combines with phosphorus to form calcium phosphate in the bones and teeth. It is essential for the normal

functioning of nerves and muscles and plays a role in blood coagulation (as factor IV) and in many enzymatic processes. [NIH]

Camptothecin: An alkaloid isolated from the stem wood of the Chinese tree, Camptotheca acuminata. This compound selectively inhibits the nuclear enzyme DNA topoisomerase. Several semisynthetic analogs of camptothecin have demonstrated antitumor activity. [NIH]

Cancer vaccine: A vaccine designed to prevent or treat cancer. [NIH]

Candidiasis: Infection with a fungus of the genus Candida. It is usually a superficial infection of the moist cutaneous areas of the body, and is generally caused by C. albicans; it most commonly involves the skin (dermatocandidiasis), oral mucous membranes (thrush, def. 1), respiratory tract (bronchocandidiasis), and vagina (vaginitis). Rarely there is a systemic infection or endocarditis. Called also moniliasis, candidosis, oidiomycosis, and formerly blastodendriosis. [EU]

Candidosis: An infection caused by an opportunistic yeasts that tends to proliferate and become pathologic when the environment is favorable and the host resistance is weakened. [NIH]

Capecitabine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Capsid: The outer protein protective shell of a virus, which protects the viral nucleic acid. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carbon Dioxide: A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carboplatin: An organoplatinum compound that possesses antineoplastic activity. [NIH]

Carcinogen: Any substance that causes cancer. [NIH]

Carcinogenesis: The process by which normal cells are transformed into cancer cells. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Carcinoid: A type of tumor usually found in the gastrointestinal system (most often in the appendix), and sometimes in the lungs or other sites. Carcinoid tumors are usually benign. [NIH]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

Carcinoma in Situ: A malignant tumor that has not yet invaded the basement membrane of the epithelial cell of origin and has not spread to other tissues. [NIH]

Cardiotoxicity: Toxicity that affects the heart. [NIH]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

Carotene: The general name for a group of pigments found in green, yellow, and leafy vegetables, and yellow fruits. The pigments are fat-soluble, unsaturated aliphatic hydrocarbons functioning as provitamins and are converted to vitamin A through enzymatic processes in the intestinal wall. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Case series: A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. [NIH]

Case-Control Studies: Studies which start with the identification of persons with a disease of interest and a control (comparison, referent) group without the disease. The relationship of an attribute to the disease is examined by comparing diseased and non-diseased persons with regard to the frequency or levels of the attribute in each group. [NIH]

Caspase: Enzyme released by the cell at a crucial stage in apoptosis in order to shred all cellular proteins. [NIH]

Cathode: An electrode, usually an incandescent filament of tungsten, which emits electrons in an X-ray tube. [NIH]

Caudal: Denoting a position more toward the cauda, or tail, than some specified point of reference; same as inferior, in human anatomy. [EU]

Causal: Pertaining to a cause; directed against a cause. [EU]

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Caustic: An escharotic or corrosive agent. Called also cauterant. [EU]

Cauterization: The destruction of tissue with a hot instrument, an electrical current, or a caustic substance. [NIH]

Celecoxib: A drug that reduces pain. Celecoxib belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is being studied for cancer prevention. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Adhesion: Adherence of cells to surfaces or to other cells. [NIH]

Cell Count: A count of the number of cells of a specific kind, usually measured per unit volume of sample. [NIH]

Cell Cycle: The complex series of phenomena, occurring between the end of one cell division and the end of the next, by which cellular material is divided between daughter cells. [NIH]

Cell Death: The termination of the cell's ability to carry out vital functions such as metabolism, growth, reproduction, responsiveness, and adaptability. [NIH]

Cell Differentiation: Progressive restriction of the developmental potential and increasing specialization of function which takes place during the development of the embryo and leads to the formation of specialized cells, tissues, and organs. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell Fusion: Fusion of somatic cells in vitro or in vivo, which results in somatic cell hybridization. [NIH]

Cell membrane: Cell membrane = plasma membrane. The structure enveloping a cell, enclosing the cytoplasm, and forming a selective permeability barrier; it consists of lipids, proteins, and some carbohydrates, the lipids thought to form a bilayer in which integral proteins are embedded to varying degrees. [EU]

Cell proliferation: An increase in the number of cells as a result of cell growth and cell division. [NIH]

Cell Size: The physical dimensions of a cell. It refers mainly to changes in dimensions correlated with physiological or pathological changes in cells. [NIH]

Cell Survival: The span of viability of a cell characterized by the capacity to perform certain functions such as metabolism, growth, reproduction, some form of responsiveness, and adaptability. [NIH]

Cell Transplantation: Transference of cells within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Cellobiose: A disaccharide consisting of two glucose units in beta (1-4) glycosidic linkage. Obtained from the partial hydrolysis of cellulose. [NIH]

Cellulose: A polysaccharide with glucose units linked as in cellobiose. It is the chief constituent of plant fibers, cotton being the purest natural form of the substance. As a raw material, it forms the basis for many derivatives used in chromatography, ion exchange materials, explosives manufacturing, and pharmaceutical preparations. [NIH]

Central Nervous System: The main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

Cervical: Relating to the neck, or to the neck of any organ or structure. Cervical lymph nodes are located in the neck; cervical cancer refers to cancer of the uterine cervix, which is the lower, narrow end (the "neck") of the uterus. [NIH]

Cervical intraepithelial neoplasia: CIN. A general term for the growth of abnormal cells on the surface of the cervix. Numbers from 1 to 3 may be used to describe how much of the cervix contains abnormal cells. [NIH]

Cervix: The lower, narrow end of the uterus that forms a canal between the uterus and vagina. [NIH]

Chemoprevention: The use of drugs, vitamins, or other agents to try to reduce the risk of, or delay the development or recurrence of, cancer. [NIH]

Chemotactic Factors: Chemical substances that attract or repel cells or organisms. The concept denotes especially those factors released as a result of tissue injury, invasion, or immunologic activity, that attract leukocytes, macrophages, or other cells to the site of infection or insult. [NIH]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Chlamydia: A genus of the family Chlamydiaceae whose species cause a variety of diseases in vertebrates including humans, mice, and swine. Chlamydia species are gram-negative and produce glycogen. The type species is Chlamydia trachomatis. [NIH]

Chlorambucil: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Chloride Channels: Cell membrane glycoproteins selective for chloride ions. [NIH]

Cholecystitis: Inflammation of the gallbladder. [NIH]

Cholinergic: Resembling acetylcholine in pharmacological action; stimulated by or releasing acetylcholine or a related compound. [EU]

Choriocarcinoma: A malignant tumor of trophoblastic epithelium characterized by secretion of large amounts of chorionic gonadotropin. It usually originates from chorionic products of conception (i.e., hydatidiform mole, normal pregnancy, or following abortion), but can originate in a teratoma of the testis, mediastinum, or pineal gland. [NIH]

Chromatin: The material of chromosomes. It is a complex of DNA, histones, and nonhistone proteins (chromosomal proteins, non-histone) found within the nucleus of a cell. [NIH]

Chromium: A trace element that plays a role in glucose metabolism. It has the atomic symbol Cr, atomic number 24, and atomic weight 52. According to the Fourth Annual Report on Carcinogens (NTP85-002,1985), chromium and some of its compounds have been listed as known carcinogens. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

Chronic Disease: Disease or ailment of long duration. [NIH]

Chronic renal: Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

CIS: Cancer Information Service. The CIS is the National Cancer Institute's link to the public, interpreting and explaining research findings in a clear and understandable manner, and providing personalized responses to specific questions about cancer. Access the CIS by calling 1-800-4-CANCER, or by using the Web site at http://cis.nci.nih.gov. [NIH]

Cisplatin: An inorganic and water-soluble platinum complex. After undergoing hydrolysis, it reacts with DNA to produce both intra and interstrand crosslinks. These crosslinks appear to impair replication and transcription of DNA. The cytotoxicity of cisplatin correlates with cellular arrest in the G2 phase of the cell cycle. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [NIH]

Clinical study: A research study in which patients receive treatment in a clinic or other medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

Clinical trial: A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

Clone: The term "clone" has acquired a new meaning. It is applied specifically to the bits of inserted foreign DNA in the hybrid molecules of the population. Each inserted segment originally resided in the DNA of a complex genome amid millions of other DNA segment. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Codon: A set of three nucleotides in a protein coding sequence that specifies individual amino acids or a termination signal (codon, terminator). Most codons are universal, but some organisms do not produce the transfer RNAs (RNA, transfer) complementary to all codons. These codons are referred to as unassigned codons (codons, nonsense). [NIH]

Coenzyme: An organic nonprotein molecule, frequently a phosphorylated derivative of a water-soluble vitamin, that binds with the protein molecule (apoenzyme) to form the active enzyme (holoenzyme). [EU]

Cofactor: A substance, microorganism or environmental factor that activates or enhances the action of another entity such as a disease-causing agent. [NIH]

Cognition: Intellectual or mental process whereby an organism becomes aware of or obtains knowledge. [NIH]

Cohort Effect: Variation in health status arising from different causal factors to which each birth cohort in a population is exposed as environment and society change. [NIH]

Cohort Studies: Studies in which subsets of a defined population are identified. These groups may or may not be exposed to factors hypothesized to influence the probability of the occurrence of a particular disease or other outcome. Cohorts are defined populations which, as a whole, are followed in an attempt to determine distinguishing subgroup characteristics. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in mammalian organisms. It is the main constituent of skin, connective tissue, and the organic substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

Colorectal: Having to do with the colon or the rectum. [NIH]

Colorectal Cancer: Cancer that occurs in the colon (large intestine) or the rectum (the end of the large intestine). A number of digestive diseases may increase a person's risk of colorectal cancer, including polyposis and Zollinger-Ellison Syndrome. [NIH]

Colposcope: A lighted magnifying instrument used for examination of the vagina and cervix. [NIH]

Colposcopy: The examination, therapy or surgery of the cervix and vagina by means of a specially designed endoscope introduced vaginally. [NIH]

Combination chemotherapy: Treatment using more than one anticancer drug. [NIH]

Communicable disease: A disease that can be transmitted by contact between persons. [NIH]

Competency: The capacity of the bacterium to take up DNA from its surroundings. [NIH]

Complement: A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin system) and complement regulatory proteins are known by semisystematic or trivial names. Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative

pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complementary medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complete remission: The disappearance of all signs of cancer. Also called a complete response. [NIH]

Computational Biology: A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

Computed tomography: CT scan. A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized tomography and computerized axial tomography (CAT) scan. [NIH]

Computerized axial tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called CAT scan, computed tomography (CT scan), or computerized tomography. [NIH]

Computerized tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized axial tomography (CAT) scan and computed tomography (CT scan). [NIH]

Conception: The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

Concomitant: Accompanying; accessory; joined with another. [EU]

Condoms: A sheath that is worn over the penis during sexual behavior in order to prevent pregnancy or spread of sexually transmitted disease. [NIH]

Cone: One of the special retinal receptor elements which are presumed to be primarily concerned with perception of light and color stimuli when the eye is adapted to light. [NIH]

Cone biopsy: Surgery to remove a cone-shaped piece of tissue from the cervix and cervical canal. Cone biopsy may be used to diagnose or treat a cervical condition. Also called conization. [NIH]

Confidence Intervals: A range of values for a variable of interest, e.g., a rate, constructed so

that this range has a specified probability of including the true value of the variable. [NIH]

Confusion: A mental state characterized by bewilderment, emotional disturbance, lack of clear thinking, and perceptual disorientation. [NIH]

Conization: The excision of a cone of tissue, especially of the cervix uteri. [NIH]

Conjunctiva: The mucous membrane that lines the inner surface of the eyelids and the anterior part of the sclera. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connexins: A group of homologous proteins which form the intermembrane channels of gap junctions. The connexins are the products of an identified gene family which has both highly conserved and highly divergent regions. The variety contributes to the wide range of functional properties of gap junctions. [NIH]

Consciousness: Sense of awareness of self and of the environment. [NIH]

Consultation: A deliberation between two or more physicians concerning the diagnosis and the proper method of treatment in a case. [NIH]

Consumption: Pulmonary tuberculosis. [NIH]

Contamination: The soiling or pollution by inferior material, as by the introduction of organisms into a wound, or sewage into a stream. [EU]

Contraception: Use of agents, devices, methods, or procedures which diminish the likelihood of or prevent conception. [NIH]

Contraceptive: An agent that diminishes the likelihood of or prevents conception. [EU]

Contraindications: Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

Control group: In a clinical trial, the group that does not receive the new treatment being studied. This group is compared to the group that receives the new treatment, to see if the new treatment works. [NIH]

Controlled study: An experiment or clinical trial that includes a comparison (control) group. [NIH]

Conventional therapy: A currently accepted and widely used treatment for a certain type of disease, based on the results of past research. Also called conventional treatment. [NIH]

Conventional treatment: A currently accepted and widely used treatment for a certain type of disease, based on the results of past research. Also called conventional therapy. [NIH]

Cornea: The transparent part of the eye that covers the iris and the pupil and allows light to enter the inside. [NIH]

Corneum: The superficial layer of the epidermis containing keratinized cells. [NIH]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

Coronary Thrombosis: Presence of a thrombus in a coronary artery, often causing a myocardial infarction. [NIH]

Coronavirus: A genus of the family Coronaviridae which causes respiratory or gastrointestinal disease in a variety of vertebrates. [NIH]

Corpus: The body of the uterus. [NIH]

Corpus Luteum: The yellow glandular mass formed in the ovary by an ovarian follicle that has ruptured and discharged its ovum. [NIH]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Cost Savings: Reductions in all or any portion of the costs of providing goods or services. Savings may be incurred by the provider or the consumer. [NIH]

Cowpox: A mild, eruptive skin disease of milk cows caused by cowpox virus, with lesions occurring principally on the udder and teats. Human infection may occur while milking an infected animal. [NIH]

Cowpox Virus: A species of orthopoxvirus that is the etiologic agent of cowpox. It is closely related to but antigenically different from vaccina virus. [NIH]

Criterion: A standard by which something may be judged. [EU]

Crossing-over: The exchange of corresponding segments between chromatids of homologous chromosomes during meiosia, forming a chiasma. [NIH]

Cross-Sectional Studies: Studies in which the presence or absence of disease or other health-related variables are determined in each member of the study population or in a representative sample at one particular time. This contrasts with longitudinal studies which are followed over a period of time. [NIH]

Cruciferous vegetables: A family of vegetables that includes kale, collard greens, broccoli, cauliflower, cabbage, brussels sprouts, and turnip. These vegetables contain substances that may protect against cancer. [NIH]

Cryosurgery: The use of freezing as a special surgical technique to destroy or excise tissue. [NIH]

Cryotherapy: Any method that uses cold temperature to treat disease. [NIH]

Cryptococcosis: Infection with a fungus of the species Cryptococcus neoformans. [NIH]

Cryptosporidiosis: Parasitic intestinal infection with severe diarrhea caused by a protozoan, Cryptosporidium. It occurs in both animals and humans. [NIH]

Culture Media: Any liquid or solid preparation made specifically for the growth, storage, or transport of microorganisms or other types of cells. The variety of media that exist allow for the culturing of specific microorganisms and cell types, such as differential media, selective media, test media, and defined media. Solid media consist of liquid media that have been solidified with an agent such as agar or gelatin. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Curettage: Removal of tissue with a curette, a spoon-shaped instrument with a sharp edge. [NIH]

Curette: A spoon-shaped instrument with a sharp edge. [NIH]

Cutaneous: Having to do with the skin. [NIH]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cyclin: Molecule that regulates the cell cycle. [NIH]

Cyclophosphamide: Precursor of an alkylating nitrogen mustard antineoplastic and immunosuppressive agent that must be activated in the liver to form the active aldophosphamide. It is used in the treatment of lymphomas, leukemias, etc. Its side effect, alopecia, has been made use of in defleecing sheep. Cyclophosphamide may also cause sterility, birth defects, mutations, and cancer. [NIH]

Cyclosporine: A drug used to help reduce the risk of rejection of organ and bone marrow transplants by the body. It is also used in clinical trials to make cancer cells more sensitive to anticancer drugs. [NIH]

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

Cystine: A covalently linked dimeric nonessential amino acid formed by the oxidation of cysteine. Two molecules of cysteine are joined together by a disulfide bridge to form cystine. [NIH]

Cytokine: Small but highly potent protein that modulates the activity of many cell types, including T and B cells. [NIH]

Cytomegalovirus: A genus of the family Herpesviridae, subfamily Betaherpesvirinae, infecting the salivary glands, liver, spleen, lungs, eyes, and other organs, in which they produce characteristically enlarged cells with intranuclear inclusions. Infection with Cytomegalovirus is also seen as an opportunistic infection in AIDS. [NIH]

Cytoplasm: The protoplasm of a cell exclusive of that of the nucleus; it consists of a continuous aqueous solution (cytosol) and the organelles and inclusions suspended in it (phaneroplasm), and is the site of most of the chemical activities of the cell. [EU]

Cytosine: A pyrimidine base that is a fundamental unit of nucleic acids. [NIH]

Cytoskeleton: The network of filaments, tubules, and interconnecting filamentous bridges which give shape, structure, and organization to the cytoplasm. [NIH]

Cytostatic: An agent that suppresses cell growth and multiplication. [EU]

Cytotoxic: Cell-killing. [NIH]

Cytotoxic chemotherapy: Anticancer drugs that kill cells, especially cancer cells. [NIH]

Cytotoxicity: Quality of being capable of producing a specific toxic action upon cells of special organs. [NIH]

Data Collection: Systematic gathering of data for a particular purpose from various sources, including questionnaires, interviews, observation, existing records, and electronic devices. The process is usually preliminary to statistical analysis of the data. [NIH]

Databases, Bibliographic: Extensive collections, reputedly complete, of references and citations to books, articles, publications, etc., generally on a single subject or specialized subject area. Databases can operate through automated files, libraries, or computer disks. The concept should be differentiated from factual databases which is used for collections of data and facts apart from bibliographic references to them. [NIH]

Daunorubicin: Very toxic anthracycline aminoglycoside antibiotic isolated from Streptomyces peucetius and others, used in treatment of leukemias and other neoplasms. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Deletion: A genetic rearrangement through loss of segments of DNA (chromosomes), bringing sequences, which are normally separated, into close proximity. [NIH]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is

multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [NIH]

Denaturation: Rupture of the hydrogen bonds by heating a DNA solution and then cooling it rapidly causes the two complementary strands to separate. [NIH]

Dendrites: Extensions of the nerve cell body. They are short and branched and receive stimuli from other neurons. [NIH]

Dendritic: 1. Branched like a tree. 2. Pertaining to or possessing dendrites. [EU]

Dendritic cell: A special type of antigen-presenting cell (APC) that activates T lymphocytes. [NIH]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Deoxycytidine: A drug that protects healthy tissues from the toxic effects of anticancer drugs. [NIH]

Deoxyglucose: 2-Deoxy-D-arabino-hexose. An antimetabolite of glucose with antiviral activity. [NIH]

Depolarization: The process or act of neutralizing polarity. In neurophysiology, the reversal of the resting potential in excitable cell membranes when stimulated, i.e., the tendency of the cell membrane potential to become positive with respect to the potential outside the cell. [EU]

Detergents: Purifying or cleansing agents, usually salts of long-chain aliphatic bases or acids, that exert cleansing (oil-dissolving) and antimicrobial effects through a surface action that depends on possessing both hydrophilic and hydrophobic properties. [NIH]

Detoxification: Treatment designed to free an addict from his drug habit. [EU]

Developed Countries: Countries that have reached a level of economic achievement through an increase of production, per capita income and consumption, and utilization of natural and human resources. [NIH]

Developing Countries: Countries in the process of change directed toward economic growth, that is, an increase in production, per capita consumption, and income. The process of economic growth involves better utilization of natural and human resources, which results in a change in the social, political, and economic structures. [NIH]

Dextran Sulfate: Long-chain polymer of glucose containing 17-20% sulfur. It has been used as an anticoagulant and also has been shown to inhibit the binding of HIV-1 to CD4+ T-lymphocytes. It is commonly used as both an experimental and clinical laboratory reagent and has been investigated for use as an antiviral agent, in the treatment of hypolipidemia, and for the prevention of free radical damage, among other applications. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diagnostic Imaging: Any visual display of structural or functional patterns of organs or tissues for diagnostic evaluation. It includes measuring physiologic and metabolic responses to physical and chemical stimuli, as well as ultramicroscopy. [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diencephalon: The paired caudal parts of the prosencephalon from which the thalamus, hypothalamus, epithalamus, and subthalamus are derived. [NIH]

Diffusion: The tendency of a gas or solute to pass from a point of higher pressure or concentration to a point of lower pressure or concentration and to distribute itself throughout the available space; a major mechanism of biological transport. [NIH]

Difluoromethylornithine: DFMO. An anticancer drug that has been shown to reduce the risk of cancer in animals. [NIH]

Digestion: The process of breakdown of food for metabolism and use by the body. [NIH]

Digestive system: The organs that take in food and turn it into products that the body can use to stay healthy. Waste products the body cannot use leave the body through bowel movements. The digestive system includes the salivary glands, mouth, esophagus, stomach, liver, pancreas, gallbladder, small and large intestines, and rectum. [NIH]

Digestive tract: The organs through which food passes when food is eaten. These organs are the mouth, esophagus, stomach, small and large intestines, and rectum. [NIH]

Digital photography: A type of photography in which images can be viewed on a computer screen. [NIH]

Dihydrotestosterone: Anabolic agent. [NIH]

Dilatation: The act of dilating. [NIH]

Diploid: Having two sets of chromosomes. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Discrimination: The act of qualitative and/or quantitative differentiation between two or more stimuli. [NIH]

Disease Progression: The worsening of a disease over time. This concept is most often used for chronic and incurable diseases where the stage of the disease is an important determinant of therapy and prognosis. [NIH]

Disease-Free Survival: Period after successful treatment in which there is no appearance of the symptoms or effects of the disease. [NIH]

Disorientation: The loss of proper bearings, or a state of mental confusion as to time, place, or identity. [EU]

Dissection: Cutting up of an organism for study. [NIH]

Dissociation: 1. The act of separating or state of being separated. 2. The separation of a molecule into two or more fragments (atoms, molecules, ions, or free radicals) produced by the absorption of light or thermal energy or by solvation. 3. In psychology, a defense mechanism in which a group of mental processes are segregated from the rest of a person's mental activity in order to avoid emotional distress, as in the dissociative disorders (q.v.), or in which an idea or object is segregated from its emotional significance; in the first sense it is roughly equivalent to splitting, in the second, to isolation. 4. A defect of mental integration in which one or more groups of mental processes become separated off from normal consciousness and, thus separated, function as a unitary whole. [EU]

Distal: Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

DNA Topoisomerase: An enzyme catalyzing ATP-independent breakage of single-stranded DNA, followed by passage and rejoining of another single-stranded DNA. This enzyme class brings about the conversion of one topological isomer of DNA into another, e.g., the relaxation of superhelical turns in DNA, the interconversion of simple and knotted rings of single-stranded DNA, and the intertwisting of single-stranded rings of complementary sequences. (From Enzyme Nomenclature, 1992) EC 5.99.1.2. [NIH]

Docetaxel: An anticancer drug that belongs to the family of drugs called mitotic inhibitors. [NIH]

Domestic Violence: Deliberate, often repetitive, physical abuse by one family member

against another: marital partners, parents, children, siblings, or any other member of a household. [NIH]

Dose-rate: The strength of a treatment given over a period of time. [NIH]

Doxorubicin: Antineoplastic antibiotic obtained from Streptomyces peucetics. It is a hydroxy derivative of daunorubicin and is used in treatment of both leukemia and solid tumors. [NIH]

Drug Design: The molecular designing of drugs for specific purposes (such as DNA-binding, enzyme inhibition, anti-cancer efficacy, etc.) based on knowledge of molecular properties such as activity of functional groups, molecular geometry, and electronic structure, and also on information cataloged on analogous molecules. Drug design is generally computer-assisted molecular modeling and does not include pharmacokinetics, dosage analysis, or drug administration analysis. [NIH]

Drug Interactions: The action of a drug that may affect the activity, metabolism, or toxicity of another drug. [NIH]

Drug Resistance: Diminished or failed response of an organism, disease or tissue to the intended effectiveness of a chemical or drug. It should be differentiated from drug tolerance which is the progressive diminution of the susceptibility of a human or animal to the effects of a drug, as a result of continued administration. [NIH]

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

Duodenum: The first part of the small intestine. [NIH]

Dyes: Chemical substances that are used to stain and color other materials. The coloring may or may not be permanent. Dyes can also be used as therapeutic agents and test reagents in medicine and scientific research. [NIH]

Dyspareunia: Painful sexual intercourse. [NIH]

Dysplasia: Cells that look abnormal under a microscope but are not cancer. [NIH]

Dystrophy: Any disorder arising from defective or faulty nutrition, especially the muscular dystrophies. [EU]

Ectopic: Pertaining to or characterized by ectopia. [EU]

Ectopic Pregnancy: The pregnancy occurring elsewhere than in the cavity of the uterus. [NIH]

Education, Professional: Formal education and training in preparation for the practice of a profession. [NIH]

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

Effector cell: A cell that performs a specific function in response to a stimulus; usually used to describe cells in the immune system. [NIH]

Efficacy: The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

Elective: Subject to the choice or decision of the patient or physician; applied to procedures that are advantageous to the patient but not urgent. [EU]

Electrolyte: A substance that dissociates into ions when fused or in solution, and thus

becomes capable of conducting electricity; an ionic solute. [EU]

Electrons: Stable elementary particles having the smallest known negative charge, present in all elements; also called negatrons. Positively charged electrons are called positrons. The numbers, energies and arrangement of electrons around atomic nuclei determine the chemical identities of elements. Beams of electrons are called cathode rays or beta rays, the latter being a high-energy biproduct of nuclear decay. [NIH]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Empirical: A treatment based on an assumed diagnosis, prior to receiving confirmatory laboratory test results. [NIH]

Emulsion: A preparation of one liquid distributed in small globules throughout the body of a second liquid. The dispersed liquid is the discontinuous phase, and the dispersion medium is the continuous phase. When oil is the dispersed liquid and an aqueous solution is the continuous phase, it is known as an oil-in-water emulsion, whereas when water or aqueous solution is the dispersed phase and oil or oleaginous substance is the continuous phase, it is known as a water-in-oil emulsion. Pharmaceutical emulsions for which official standards have been promulgated include cod liver oil emulsion, cod liver oil emulsion with malt, liquid petrolatum emulsion, and phenolphthalein in liquid petrolatum emulsion. [EU]

Enamel: A very hard whitish substance which covers the dentine of the anatomical crown of a tooth. [NIH]

Encapsulated: Confined to a specific, localized area and surrounded by a thin layer of tissue. [NIH]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

Endocarditis: Exudative and proliferative inflammatory alterations of the endocardium, characterized by the presence of vegetations on the surface of the endocardium or in the endocardium itself, and most commonly involving a heart valve, but sometimes affecting the inner lining of the cardiac chambers or the endocardium elsewhere. It may occur as a primary disorder or as a complication of or in association with another disease. [EU]

Endocervical curettage: The scraping of the mucous membrane of the cervical canal using a spoon-shaped instrument called a curette. [NIH]

Endocrinology: A subspecialty of internal medicine concerned with the metabolism, physiology, and disorders of the endocrine system. [NIH]

Endometrial: Having to do with the endometrium (the layer of tissue that lines the uterus). [NIH]

Endometriosis: A condition in which tissue more or less perfectly resembling the uterine mucous membrane (the endometrium) and containing typical endometrial granular and stromal elements occurs aberrantly in various locations in the pelvic cavity. [NIH]

Endometrium: The layer of tissue that lines the uterus. [NIH]

Endoscope: A thin, lighted tube used to look at tissues inside the body. [NIH]

Endothelial cell: The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart. [NIH]

Endotoxins: Toxins closely associated with the living cytoplasm or cell wall of certain microorganisms, which do not readily diffuse into the culture medium, but are released upon lysis of the cells. [NIH]

End-stage renal: Total chronic kidney failure. When the kidneys fail, the body retains fluid and harmful wastes build up. A person with ESRD needs treatment to replace the work of

the failed kidneys. [NIH]

Enhancer: Transcriptional element in the virus genome. [NIH]

Environmental Exposure: The exposure to potentially harmful chemical, physical, or biological agents in the environment or to environmental factors that may include ionizing radiation, pathogenic organisms, or toxic chemicals. [NIH]

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

Epidemic: Occurring suddenly in numbers clearly in excess of normal expectancy; said especially of infectious diseases but applied also to any disease, injury, or other health-related event occurring in such outbreaks. [EU]

Epidemiologic Studies: Studies designed to examine associations, commonly, hypothesized causal relations. They are usually concerned with identifying or measuring the effects of risk factors or exposures. The common types of analytic study are case-control studies, cohort studies, and cross-sectional studies. [NIH]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epidermal: Pertaining to or resembling epidermis. Called also epidermic or epidermoid. [EU]

Epidermal Growth Factor: A 6 kD polypeptide growth factor initially discovered in mouse submaxillary glands. Human epidermal growth factor was originally isolated from urine based on its ability to inhibit gastric secretion and called urogastrone. epidermal growth factor exerts a wide variety of biological effects including the promotion of proliferation and differentiation of mesenchymal and epithelial cells. [NIH]

Epidermis: Nonvascular layer of the skin. It is made up, from within outward, of five layers: 1) basal layer (stratum basale epidermidis); 2) spinous layer (stratum spinosum epidermidis); 3) granular layer (stratum granulosum epidermidis); 4) clear layer (stratum lucidum epidermidis); and 5) horny layer (stratum corneum epidermidis). [NIH]

Epidermodysplasia Verruciformis: An autosomal recessive trait with impaired cell-mediated immunity. About 15 human papillomaviruses are implicated in associated infection, four of which lead to skin neoplasms. The disease begins in childhood with red papules and later spreads over the body as gray or yellow scales. [NIH]

Epidermoid carcinoma: A type of cancer in which the cells are flat and look like fish scales. Also called squamous cell carcinoma. [NIH]

Epinephrine: The active sympathomimetic hormone from the adrenal medulla in most species. It stimulates both the alpha- and beta- adrenergic systems, causes systemic vasoconstriction and gastrointestinal relaxation, stimulates the heart, and dilates bronchi and cerebral vessels. It is used in asthma and cardiac failure and to delay absorption of local anesthetics. [NIH]

Epirubicin: An anthracycline antibiotic which is the 4'-epi-isomer of doxorubicin. The compound exerts its antitumor effects by interference with the synthesis and function of DNA. Clinical studies indicate activity in breast cancer, non-Hodgkin's lymphomas, ovarian cancer, soft-tissue sarcomas, pancreatic cancer, gastric cancer, small-cell lung cancer and acute leukemia. It is equal in activity to doxorubicin but exhibits less acute toxicities and less cardiotoxicity. [NIH]

Episiotomy: An incision of the posterior vaginal wall and a portion of the pudenda which enlarges the vaginal introitus to facilitate delivery and prevent lacerations. [NIH]

Epithelial: Refers to the cells that line the internal and external surfaces of the body. [NIH]

Epithelial carcinoma: Cancer that begins in the cells that line an organ. [NIH]

Epithelial Cells: Cells that line the inner and outer surfaces of the body. [NIH]

Epithelium: One or more layers of epithelial cells, supported by the basal lamina, which covers the inner or outer surfaces of the body. [NIH]

Epitope: A molecule or portion of a molecule capable of binding to the combining site of an antibody. For every given antigenic determinant, the body can construct a variety of antibody-combining sites, some of which fit almost perfectly, and others which barely fit. [NIH]

Erectile: The inability to get or maintain an erection for satisfactory sexual intercourse. Also called impotence. [NIH]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [NIH]

Erythroleukemia: Cancer of the blood-forming tissues in which large numbers of immature, abnormal red blood cells are found in the blood and bone marrow. [NIH]

Esophageal: Having to do with the esophagus, the muscular tube through which food passes from the throat to the stomach. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Essential Tremor: A rhythmic, involuntary, purposeless, oscillating movement resulting from the alternate contraction and relaxation of opposing groups of muscles. [NIH]

Estradiol: The most potent mammalian estrogenic hormone. It is produced in the ovary, placenta, testis, and possibly the adrenal cortex. [NIH]

Estrogen: One of the two female sex hormones. [NIH]

Estrogen receptor: ER. Protein found on some cancer cells to which estrogen will attach. [NIH]

Ethnic Groups: A group of people with a common cultural heritage that sets them apart from others in a variety of social relationships. [NIH]

Etoposide: A semisynthetic derivative of podophyllotoxin that exhibits antitumor activity. Etoposide inhibits DNA synthesis by forming a complex with topoisomerase II and DNA. This complex induces breaks in double stranded DNA and prevents repair by topoisomerase II binding. Accumulated breaks in DNA prevent entry into the mitotic phase of cell division, and lead to cell death. Etoposide acts primarily in the G2 and S phases of the cell cycle. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Europium: An element of the rare earth family of metals. It has the atomic symbol Eu, atomic number 63, and atomic weight 152. Europium is used in the form of its salts as coatings for cathode ray tubes and in the form of its organic derivatives as shift reagents in NMR spectroscopy. [NIH]

Evoke: The electric response recorded from the cerebral cortex after stimulation of a peripheral sense organ. [NIH]

Excisional: The surgical procedure of removing a tumor by cutting it out. The biopsy is then examined under a microscope. [NIH]

Excitation: An act of irritation or stimulation or of responding to a stimulus; the addition of energy, as the excitation of a molecule by absorption of photons. [EU]

Excitatory: When cortical neurons are excited, their output increases and each new input they receive while they are still excited raises their output markedly. [NIH]

Exhaustion: The feeling of weariness of mind and body. [NIH]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Exon: The part of the DNA that encodes the information for the actual amino acid sequence of the protein. In many eucaryotic genes, the coding sequences consist of a series of exons alternating with intron sequences. [NIH]

Extensor: A muscle whose contraction tends to straighten a limb; the antagonist of a flexor. [NIH]

External radiation: Radiation therapy that uses a machine to aim high-energy rays at the cancer. Also called external-beam radiation. [NIH]

External-beam radiation: Radiation therapy that uses a machine to aim high-energy rays at the cancer. Also called external radiation. [NIH]

Extracellular: Outside a cell or cells. [EU]

Extracellular Matrix: A meshwork-like substance found within the extracellular space and in association with the basement membrane of the cell surface. It promotes cellular proliferation and provides a supporting structure to which cells or cell lysates in culture dishes adhere. [NIH]

Extracellular Matrix Proteins: Macromolecular organic compounds that contain carbon, hydrogen, oxygen, nitrogen, and usually, sulfur. These macromolecules (proteins) form an intricate meshwork in which cells are embedded to construct tissues. Variations in the relative types of macromolecules and their organization determine the type of extracellular matrix, each adapted to the functional requirements of the tissue. The two main classes of macromolecules that form the extracellular matrix are: glycosaminoglycans, usually linked to proteins (proteoglycans), and fibrous proteins (e.g., collagen, elastin, fibronectins and laminin). [NIH]

Extraction: The process or act of pulling or drawing out. [EU]

Eye Infections: Infection, moderate to severe, caused by bacteria, fungi, or viruses, which occurs either on the external surface of the eye or intraocularly with probable inflammation, visual impairment, or blindness. [NIH]

Fallopian Tubes: Two long muscular tubes that transport ova from the ovaries to the uterus. They extend from the horn of the uterus to the ovaries and consist of an ampulla, an infundibulum, an isthmus, two ostia, and a pars uterina. The walls of the tubes are composed of three layers: mucosal, muscular, and serosal. [NIH]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fat: Total lipids including phospholipids. [NIH]

Fatal Outcome: Death resulting from the presence of a disease in an individual, as shown by a single case report or a limited number of patients. This should be differentiated from death, the physiological cessation of life and from mortality, an epidemiological or statistical concept. [NIH]

Fatigue: The state of weariness following a period of exertion, mental or physical, characterized by a decreased capacity for work and reduced efficiency to respond to stimuli. [NIH]

Fatty acids: A major component of fats that are used by the body for energy and tissue development. [NIH]

Fermentation: An enzyme-induced chemical change in organic compounds that takes place in the absence of oxygen. The change usually results in the production of ethanol or lactic acid, and the production of energy. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibroblast Growth Factor: Peptide isolated from the pituitary gland and from the brain. It is a potent mitogen which stimulates growth of a variety of mesodermal cells including chondrocytes, granulosa, and endothelial cells. The peptide may be active in wound healing and animal limb regeneration. [NIH]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Fine-needle aspiration: The removal of tissue or fluid with a needle for examination under a microscope. Also called needle biopsy. [NIH]

Fistulas: An abnormal passage from one hollow structure of the body to another, or from a hollow structure to the surface, formed by an abscess, disease process, incomplete closure of a wound, or by a congenital anomaly. [NIH]

Fixation: 1. The act or operation of holding, suturing, or fastening in a fixed position. 2. The condition of being held in a fixed position. 3. In psychiatry, a term with two related but distinct meanings : (1) arrest of development at a particular stage, which like regression (return to an earlier stage), if temporary is a normal reaction to setbacks and difficulties but if protracted or frequent is a cause of developmental failures and emotional problems, and (2) a close and suffocating attachment to another person, especially a childhood figure, such as one's mother or father. Both meanings are derived from psychoanalytic theory and refer to 'fixation' of libidinal energy either in a specific erogenous zone, hence fixation at the oral, anal, or phallic stage, or in a specific object, hence mother or father fixation. 4. The use of a fixative (q.v.) to preserve histological or cytological specimens. 5. In chemistry, the process whereby a substance is removed from the gaseous or solution phase and localized, as in carbon dioxide fixation or nitrogen fixation. 6. In ophthalmology, direction of the gaze so that the visual image of the object falls on the fovea centralis. 7. In film processing, the chemical removal of all undeveloped salts of the film emulsion, leaving only the developed silver to form a permanent image. [EU]

Flow Cytometry: Technique using an instrument system for making, processing, and displaying one or more measurements on individual cells obtained from a cell suspension. Cells are usually stained with one or more fluorescent dyes specific to cell components of interest, e.g., DNA, and fluorescence of each cell is measured as it rapidly transverses the excitation beam (laser or mercury arc lamp). Fluorescence provides a quantitative measure of various biochemical and biophysical properties of the cell, as well as a basis for cell sorting. Other measurable optical parameters include light absorption and light scattering, the latter being applicable to the measurement of cell size, shape, density, granularity, and stain uptake. [NIH]

Fludarabine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Fluorescence: The property of emitting radiation while being irradiated. The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Fluorescent Dyes: Dyes that emit light when exposed to light. The wave length of the emitted light is usually longer than that of the incident light. Fluorochromes are substances that cause fluorescence in other substances, i.e., dyes used to mark or label other compounds with fluorescent tags. They are used as markers in biochemistry and immunology. [NIH]

Fluorouracil: A pyrimidine analog that acts as an antineoplastic antimetabolite and also has immunosuppressant. It interferes with DNA synthesis by blocking the thymidylate synthetase conversion of deoxyuridylic acid to thymidylic acid. [NIH]

Focus Groups: A method of data collection and a qualitative research tool in which a small group of individuals are brought together and allowed to interact in a discussion of their opinions about topics, issues, or questions. [NIH]

Folate: A B-complex vitamin that is being studied as a cancer prevention agent. Also called folic acid. [NIH]

Fold: A plication or doubling of various parts of the body. [NIH]

Folic Acid: N-(4-(((2-Amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid. A member of the vitamin B family that stimulates the hematopoietic system. It is present in the liver and kidney and is found in mushrooms, spinach, yeast, green leaves, and grasses. Folic acid is used in the treatment and prevention of folate deficiencies and megaloblastic anemia. [NIH]

Fornix: A bundle of nerves connected to the hippocampus. [NIH]

Fovea: The central part of the macula that provides the sharpest vision. [NIH]

Fractionation: Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days. [NIH]

Fungus: A general term used to denote a group of eukaryotic protists, including mushrooms, yeasts, rusts, moulds, smuts, etc., which are characterized by the absence of chlorophyll and by the presence of a rigid cell wall composed of chitin, mannans, and sometimes cellulose. They are usually of simple morphological form or show some reversible cellular specialization, such as the formation of pseudoparenchymatous tissue in the fruiting body of a mushroom. The dimorphic fungi grow, according to environmental conditions, as moulds or yeasts. [EU]

Gallbladder: The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

Gamma Rays: Very powerful and penetrating, high-energy electromagnetic radiation of shorter wavelength than that of x-rays. They are emitted by a decaying nucleus, usually between 0.01 and 10 MeV. They are also called nuclear x-rays. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Gap Junctions: Connections between cells which allow passage of small molecules and electric current. Gap junctions were first described anatomically as regions of close apposition between cells with a narrow (1-2 nm) gap between cell membranes. The variety in the properties of gap junctions is reflected in the number of connexins, the family of proteins which form the junctions. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastritis: Inflammation of the stomach. [EU]

Gastroenteritis: An acute inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhoea, abdominal pain, and weakness, which has various causes, including food poisoning due to infection with such organisms as

Escherichia coli, Staphylococcus aureus, and Salmonella species; consumption of irritating food or drink; or psychological factors such as anger, stress, and fear. Called also enterogastritis. [EU]

Gastroenterologist: A doctor who specializes in diagnosing and treating disorders of the digestive system. [NIH]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

Gels: Colloids with a solid continuous phase and liquid as the dispersed phase; gels may be unstable when, due to temperature or other cause, the solid phase liquifies; the resulting colloid is called a sol. [NIH]

Gemcitabine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

Gene Amplification: A selective increase in the number of copies of a gene coding for a specific protein without a proportional increase in other genes. It occurs naturally via the excision of a copy of the repeating sequence from the chromosome and its extrachromosomal replication in a plasmid, or via the production of an RNA transcript of the entire repeating sequence of ribosomal RNA followed by the reverse transcription of the molecule to produce an additional copy of the original DNA sequence. Laboratory techniques have been introduced for inducing disproportional replication by unequal crossing over, uptake of DNA from lysed cells, or generation of extrachromosomal sequences from rolling circle replication. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

General practitioner: A medical practitioner who does not specialize in a particular branch of medicine or limit his practice to a specific class of diseases. [NIH]

Genetic Code: The specifications for how information, stored in nucleic acid sequence (base sequence), is translated into protein sequence (amino acid sequence). The start, stop, and order of amino acids of a protein is specified by consecutive triplets of nucleotides called codons (codon). [NIH]

Genetic Engineering: Directed modification of the gene complement of a living organism by such techniques as altering the DNA, substituting genetic material by means of a virus, transplanting whole nuclei, transplanting cell hybrids, etc. [NIH]

Genetic Markers: A phenotypically recognizable genetic trait which can be used to identify a genetic locus, a linkage group, or a recombination event. [NIH]

Genetic testing: Analyzing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder. [NIH]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genistein: An isoflavonoid derived from soy products. It inhibits protein-tyrosine kinase and topoisomerase-ii (dna topoisomerase (atp-hydrolysing)) activity and is used as an antineoplastic and antitumor agent. Experimentally, it has been shown to induce G2 phase arrest in human and murine cell lines. [NIH]

Genital: Pertaining to the genitalia. [EU]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Germ Cells: The reproductive cells in multicellular organisms. [NIH]

Gestation: The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

Gland: An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others produce hormones or participate in blood production. [NIH]

Glare: Scatter from bright light that decreases vision. [NIH]

Glioma: A cancer of the brain that comes from glial, or supportive, cells. [NIH]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glucuronic Acid: Derivatives of uronic acid found throughout the plant and animal kingdoms. They detoxify drugs and toxins by conjugating with them to form glucuronides in the liver which are more water-soluble metabolites that can be easily eliminated from the body. [NIH]

Glutamate: Excitatory neurotransmitter of the brain. [NIH]

Glutamic Acid: A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

Glutathione Peroxidase: An enzyme catalyzing the oxidation of 2 moles of glutathione in the presence of hydrogen peroxide to yield oxidized glutathione and water. EC 1.11.1.9. [NIH]

Glycogen: A sugar stored in the liver and muscles. It releases glucose into the blood when cells need it for energy. Glycogen is the chief source of stored fuel in the body. [NIH]

Gonadotropin: The water-soluble follicle stimulating substance, by some believed to originate in chorionic tissue, obtained from the serum of pregnant mares. It is used to supplement the action of estrogens. [NIH]

Gonorrhea: Acute infectious disease characterized by primary invasion of the urogenital tract. The etiologic agent, Neisseria gonorrhoeae, was isolated by Neisser in 1879. [NIH]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Grading: A system for classifying cancer cells in terms of how abnormal they appear when examined under a microscope. The objective of a grading system is to provide information about the probable growth rate of the tumor and its tendency to spread. The systems used to grade tumors vary with each type of cancer. Grading plays a role in treatment decisions. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

Graft Rejection: An immune response with both cellular and humoral components, directed against an allogeneic transplant, whose tissue antigens are not compatible with those of the recipient. [NIH]

Gram-negative: Losing the stain or decolorized by alcohol in Gram's method of staining, a primary characteristic of bacteria having a cell wall composed of a thin layer of

peptidoglycan covered by an outer membrane of lipoprotein and lipopolysaccharide. [EU]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Gravidity: Pregnancy; the condition of being pregnant, without regard to the outcome. [EU]

Groin: The external junctural region between the lower part of the abdomen and the thigh. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [NIH]

Growth factors: Substances made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy. [NIH]

Gynecologic cancer: Cancer of the female reproductive tract, including the cervix, endometrium, fallopian tubes, ovaries, uterus, and vagina. [NIH]

Gynecology: A medical-surgical specialty concerned with the physiology and disorders primarily of the female genital tract, as well as female endocrinology and reproductive physiology. [NIH]

Haploid: An organism with one basic chromosome set, symbolized by n; the normal condition of gametes in diploids. [NIH]

Haplotypes: The genetic constitution of individuals with respect to one member of a pair of allelic genes, or sets of genes that are closely linked and tend to be inherited together such as those of the major histocompatibility complex. [NIH]

Happiness: Highly pleasant emotion characterized by outward manifestations of gratification; joy. [NIH]

Haptens: Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody response. [NIH]

Headache: Pain in the cranial region that may occur as an isolated and benign symptom or as a manifestation of a wide variety of conditions including subarachnoid hemorrhage; craniocerebral trauma; central nervous system infections; intracranial hypertension; and other disorders. In general, recurrent headaches that are not associated with a primary disease process are referred to as headache disorders (e.g., migraine). [NIH]

Health Education: Education that increases the awareness and favorably influences the attitudes and knowledge relating to the improvement of health on a personal or community basis. [NIH]

Health Promotion: Encouraging consumer behaviors most likely to optimize health potentials (physical and psychosocial) through health information, preventive programs, and access to medical care. [NIH]

Health Services: Services for the diagnosis and treatment of disease and the maintenance of health. [NIH]

Health Status: The level of health of the individual, group, or population as subjectively assessed by the individual or by more objective measures. [NIH]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma

glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level may be 3 to 4 times the normal conentration. Generally, complications are substantially lower among patients with Hb levels of 7 percent or less than in patients with HbA1c levels of 9 percent or more. [NIH]

Hemoglobin C: A commonly occurring abnormal hemoglobin in which lysine replaces a glutamic acid residue at the sixth position of the beta chains. It results in reduced plasticity of erythrocytes. [NIH]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Heparin: Heparinic acid. A highly acidic mucopolysaccharide formed of equal parts of sulfated D-glucosamine and D-glucuronic acid with sulfaminic bridges. The molecular weight ranges from six to twenty thousand. Heparin occurs in and is obtained from liver, lung, mast cells, etc., of vertebrates. Its function is unknown, but it is used to prevent blood clotting in vivo and vitro, in the form of many different salts. [NIH]

Hepatic: Refers to the liver. [NIH]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatitis A: Hepatitis caused by hepatovirus. It can be transmitted through fecal contamination of food or water. [NIH]

Hepatocytes: The main structural component of the liver. They are specialized epithelial cells that are organized into interconnected plates called lobules. [NIH]

Hepatoma: A liver tumor. [NIH]

Hepatovirus: A genus of Picornaviridae causing infectious hepatitis naturally in humans and experimentally in other primates. It is transmitted through fecal contamination of food or water. [NIH]

Hereditary: Of, relating to, or denoting factors that can be transmitted genetically from one generation to another. [NIH]

Heredity: 1. The genetic transmission of a particular quality or trait from parent to offspring. 2. The genetic constitution of an individual. [EU]

Heritability: The proportion of observed variation in a particular trait that can be attributed to inherited genetic factors in contrast to environmental ones. [NIH]

Hernia: Protrusion of a loop or knuckle of an organ or tissue through an abnormal opening. [NIH]

Herpes: Any inflammatory skin disease caused by a herpesvirus and characterized by the formation of clusters of small vesicles. When used alone, the term may refer to herpes simplex or to herpes zoster. [EU]

Herpes virus: A member of the herpes family of viruses. [NIH]

Herpes Zoster: Acute vesicular inflammation. [NIH]

Heterogeneity: The property of one or more samples or populations which implies that they are not identical in respect of some or all of their parameters, e. g. heterogeneity of variance. [NIH]

Hippocampus: A curved elevation of gray matter extending the entire length of the floor of the temporal horn of the lateral ventricle (Dorland, 28th ed). The hippocampus, subiculum, and dentate gyrus constitute the hippocampal formation. Sometimes authors include the entorhinal cortex in the hippocampal formation. [NIH]

Histamine: 1H-Imidazole-4-ethanamine. A depressor amine derived by enzymatic decarboxylation of histidine. It is a powerful stimulant of gastric secretion, a constrictor of bronchial smooth muscle, a vasodilator, and also a centrally acting neurotransmitter. [NIH]

Histidine: An essential amino acid important in a number of metabolic processes. It is required for the production of histamine. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

Histone Deacetylase: Hydrolyzes N-acetyl groups on histones. [NIH]

Homologous: Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Hormone Replacement Therapy: Therapeutic use of hormones to alleviate the effects of hormone deficiency. [NIH]

Horny layer: The superficial layer of the epidermis containing keratinized cells. [NIH]

Host: Any animal that receives a transplanted graft. [NIH]

Human papillomavirus: HPV. A virus that causes abnormal tissue growth (warts) and is often associated with some types of cancer. [NIH]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used of endocrine factors as opposed to neural or somatic. [EU]

Humour: 1. A normal functioning fluid or semifluid of the body (as the blood, lymph or bile) especially of vertebrates. 2. A secretion that is itself an excitant of activity (as certain hormones). [EU]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

Hybridization: The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

Hydatidiform Mole: A trophoblastic disease characterized by hydrops of the mesenchymal portion of the villus. Its karyotype is paternal and usually homozygotic. The tumor is indistinguishable from chorioadenoma destruens or invasive mole (= hydatidiform mole, invasive) except by karyotype. There is no apparent relation by karyotype to choriocarcinoma. Hydatidiform refers to the presence of the hydropic state of some or all of the villi (Greek hydatis, a drop of water). [NIH]

Hydrogen: The first chemical element in the periodic table. It has the atomic symbol H, atomic number 1, and atomic weight 1. It exists, under normal conditions, as a colorless, odorless, tasteless, diatomic gas. Hydrogen ions are protons. Besides the common H1 isotope, hydrogen exists as the stable isotope deuterium and the unstable, radioactive isotope tritium. [NIH]

Hydrolysis: The process of cleaving a chemical compound by the addition of a molecule of water. [NIH]

Hydronephrosis: Abnormal enlargement of a kidney, which may be caused by blockage of the ureter (such as by a kidney stone) or chronic kidney disease that prevents urine from draining into the bladder. [NIH]

Hypersensitivity: Altered reactivity to an antigen, which can result in pathologic reactions

upon subsequent exposure to that particular antigen. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

Hyperthermia: A type of treatment in which body tissue is exposed to high temperatures to damage and kill cancer cells or to make cancer cells more sensitive to the effects of radiation and certain anticancer drugs. [NIH]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hypothalamic: Of or involving the hypothalamus. [EU]

Hypothalamic Hormones: Hormones isolated from the hypothalamus which exercise control over other organs, primarily the pituitary gland. Well-known members include certain pituitary hormone-releasing hormones and pituitary hormone release inhibiting hormones. Vasopressin and oxytocin which are found in the posterior pituitary may also be secreted by the hypothalamus but are not grouped here (pituitary hormones, posterior). [NIH]

Hypothalamus: Ventral part of the diencephalon extending from the region of the optic chiasm to the caudal border of the mammillary bodies and forming the inferior and lateral walls of the third ventricle. [NIH]

Hypoxia: Reduction of oxygen supply to tissue below physiological levels despite adequate perfusion of the tissue by blood. [EU]

Hysterectomy: Excision of the uterus. [NIH]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Ifosfamide: Positional isomer of cyclophosphamide which is active as an alkylating agent and an immunosuppressive agent. [NIH]

Imaging procedures: Methods of producing pictures of areas inside the body. [NIH]

Immune function: Production and action of cells that fight disease or infection. [NIH]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune Sera: Serum that contains antibodies. It is obtained from an animal that has been immunized either by antigen injection or infection with microorganisms containing the antigen. [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

Immunity: Nonsusceptibility to the invasive or pathogenic effects of foreign microorganisms or to the toxic effect of antigenic substances. [NIH]

Immunization: Deliberate stimulation of the host's immune response. Active immunization involves administration of antigens or immunologic adjuvants. Passive immunization involves administration of immune sera or lymphocytes or their extracts (e.g., transfer factor, immune RNA) or transplantation of immunocompetent cell producing tissue (thymus or bone marrow). [NIH]

Immunocompetence: The ability of lymphoid cells to mount a humoral or cellular immune response when challenged by antigen. [NIH]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [NIH]

Immunodeficiency syndrome: The inability of the body to produce an immune response. [NIH]

Immunodiffusion: Technique involving the diffusion of antigen or antibody through a semisolid medium, usually agar or agarose gel, with the result being a precipitin reaction. [NIH]

Immunodominant Epitopes: Subunits of the antigenic determinant that are most easily recognized by the immune system and thus most influence the specificity of the induced antibody. [NIH]

Immunoelectrophoresis: A technique that combines protein electrophoresis and double immunodiffusion. In this procedure proteins are first separated by gel electrophoresis (usually agarose), then made visible by immunodiffusion of specific antibodies. A distinct elliptical precipitin arc results for each protein detectable by the antisera. [NIH]

Immunogenic: Producing immunity; evoking an immune response. [EU]

Immunoglobulin: A protein that acts as an antibody. [NIH]

Immunologic: The ability of the antibody-forming system to recall a previous experience with an antigen and to respond to a second exposure with the prompt production of large amounts of antibody. [NIH]

Immunology: The study of the body's immune system. [NIH]

Immunosuppressant: An agent capable of suppressing immune responses. [EU]

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Immunosuppressive therapy: Therapy used to decrease the body's immune response, such as drugs given to prevent transplant rejection. [NIH]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

Implant radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called [NIH]

In situ: In the natural or normal place; confined to the site of origin without invasion of neighbouring tissues. [EU]

In Situ Hybridization: A technique that localizes specific nucleic acid sequences within intact chromosomes, eukaryotic cells, or bacterial cells through the use of specific nucleic acid-labeled probes. [NIH]

In vitro: In the laboratory (outside the body). The opposite of in vivo (in the body). [NIH]

In vivo: In the body. The opposite of in vitro (outside the body or in the laboratory). [NIH]

Incision: A cut made in the body during surgery. [NIH]

Incontinence: Inability to control the flow of urine from the bladder (urinary incontinence) or the escape of stool from the rectum (fecal incontinence). [NIH]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Indole-3-carbinol: A substance that is being studied as a cancer prevention drug. It is found in cruciferous vegetables. [NIH]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Infarction: A pathological process consisting of a sudden insufficient blood supply to an

area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

Infection: 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

Infertility: The diminished or absent ability to conceive or produce an offspring while sterility is the complete inability to conceive or produce an offspring. [NIH]

Infiltration: The diffusion or accumulation in a tissue or cells of substances not normal to it or in amounts of the normal. Also, the material so accumulated. [EU]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Influenza: An acute viral infection involving the respiratory tract. It is marked by inflammation of the nasal mucosa, the pharynx, and conjunctiva, and by headache and severe, often generalized, myalgia. [NIH]

Information Science: The field of knowledge, theory, and technology dealing with the collection of facts and figures, and the processes and methods involved in their manipulation, storage, dissemination, publication, and retrieval. It includes the fields of communication, publishing, library science and informatics. [NIH]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Inorganic: Pertaining to substances not of organic origin. [EU]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insomnia: Difficulty in going to sleep or getting enough sleep. [NIH]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Insulin-dependent diabetes mellitus: A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune, genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Insulin-like: Muscular growth factor. [NIH]

Interferon: A biological response modifier (a substance that can improve the body's natural response to disease). Interferons interfere with the division of cancer cells and can slow tumor growth. There are several types of interferons, including interferon-alpha, -beta, and -gamma. These substances are normally produced by the body. They are also made in the laboratory for use in treating cancer and other diseases. [NIH]

Interferon-alpha: One of the type I interferons produced by peripheral blood leukocytes or lymphoblastoid cells when exposed to live or inactivated virus, double-stranded RNA, or

bacterial products. It is the major interferon produced by virus-induced leukocyte cultures and, in addition to its pronounced antiviral activity, it causes activation of NK cells. [NIH]

Interleukin-2: Chemical mediator produced by activated T lymphocytes and which regulates the proliferation of T cells, as well as playing a role in the regulation of NK cell activity. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Internal radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called brachytherapy, implant radiation, or interstitial radiation therapy. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

Intestinal: Having to do with the intestines. [NIH]

Intestine: A long, tube-shaped organ in the abdomen that completes the process of digestion. There is both a large intestine and a small intestine. Also called the bowel. [NIH]

Intracellular: Inside a cell. [NIH]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intraepithelial: Within the layer of cells that form the surface or lining of an organ. [NIH]

Intravenous: IV. Into a vein. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Invasive: 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Invasive cervical cancer: Cancer that has spread from the surface of the cervix to tissue deeper in the cervix or to other parts of the body. [NIH]

Involuntary: Reaction occurring without intention or volition. [NIH]

Iodine: A nonmetallic element of the halogen group that is represented by the atomic symbol I, atomic number 53, and atomic weight of 126.90. It is a nutritionally essential element, especially important in thyroid hormone synthesis. In solution, it has anti-infective properties and is used topically. [NIH]

Ionization: 1. Any process by which a neutral atom gains or loses electrons, thus acquiring a net charge, as the dissociation of a substance in solution into ions or ion production by the passage of radioactive particles. 2. Iontophoresis. [EU]

Ionizing: Radiation comprising charged particles, e. g. electrons, protons, alpha-particles, etc., having sufficient kinetic energy to produce ionization by collision. [NIH]

Ions: An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

Irinotecan: An anticancer drug that belongs to a family of anticancer drugs called topoisomerase inhibitors. It is a camptothecin analogue. Also called CPT 11. [NIH]

Irradiation: The use of high-energy radiation from x-rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body.

Irradiation is also called radiation therapy, radiotherapy, and x-ray therapy. [NIH]

Ischemia: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kb: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA fragments are up to 50 kilobases long. [NIH]

Keratin: A class of fibrous proteins or scleroproteins important both as structural proteins and as keys to the study of protein conformation. The family represents the principal constituent of epidermis, hair, nails, horny tissues, and the organic matrix of tooth enamel. Two major conformational groups have been characterized, alpha-keratin, whose peptide backbone forms an alpha-helix, and beta-keratin, whose backbone forms a zigzag or pleated sheet structure. [NIH]

Keratinocytes: Epidermal cells which synthesize keratin and undergo characteristic changes as they move upward from the basal layers of the epidermis to the cornified (horny) layer of the skin. Successive stages of differentiation of the keratinocytes forming the epidermal layers are basal cell, spinous or prickle cell, and the granular cell. [NIH]

Kidney Disease: Any one of several chronic conditions that are caused by damage to the cells of the kidney. People who have had diabetes for a long time may have kidney damage. Also called nephropathy. [NIH]

Kidney stone: A stone that develops from crystals that form in urine and build up on the inner surfaces of the kidney, in the renal pelvis, or in the ureters. [NIH]

Killer Cells: Lymphocyte-like effector cells which mediate antibody-dependent cell cytotoxicity. They kill antibody-coated target cells which they bind with their Fc receptors. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Labile: 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

Lacerations: Torn, ragged, mangled wounds. [NIH]

Laparoscopy: Examination, therapy or surgery of the abdomen's interior by means of a laparoscope. [NIH]

Large Intestine: The part of the intestine that goes from the cecum to the rectum. The large intestine absorbs water from stool and changes it from a liquid to a solid form. The large intestine is 5 feet long and includes the appendix, cecum, colon, and rectum. Also called colon. [NIH]

Larynx: An irregularly shaped, musculocartilaginous tubular structure, lined with mucous membrane, located at the top of the trachea and below the root of the tongue and the hyoid bone. It is the essential sphincter guarding the entrance into the trachea and functioning secondarily as the organ of voice. [NIH]

Latent: Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

Lavage: A cleaning of the stomach and colon. Uses a special drink and enemas. [NIH]

Laxative: An agent that acts to promote evacuation of the bowel; a cathartic or purgative. [EU]

Lectin: A complex molecule that has both protein and sugars. Lectins are able to bind to the outside of a cell and cause biochemical changes in it. Lectins are made by both animals and

plants. [NIH]

Leprosy: A chronic granulomatous infection caused by Mycobacterium leprae. The granulomatous lesions are manifested in the skin, the mucous membranes, and the peripheral nerves. Two polar or principal types are lepromatous and tuberculoid. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Lethal: Deadly, fatal. [EU]

Leucine: An essential branched-chain amino acid important for hemoglobin formation. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Leukoencephalopathy: A condition with spongy holes in the brain's white matter. [NIH]

Leukoplakia: A white patch that may develop on mucous membranes such as the cheek, gums, or tongue and may become cancerous. [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Life cycle: The successive stages through which an organism passes from fertilized ovum or spore to the fertilized ovum or spore of the next generation. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Lipid: Fat. [NIH]

Lipoprotein: Any of the lipid-protein complexes in which lipids are transported in the blood; lipoprotein particles consist of a spherical hydrophobic core of triglycerides or cholesterol esters surrounded by an amphipathic monolayer of phospholipids, cholesterol, and apolipoproteins; the four principal classes are high-density, low-density, and very-low-density lipoproteins and chylomicrons. [EU]

Liposomal: A drug preparation that contains the active drug in very tiny fat particles. This fat-encapsulated drug is absorbed better, and its distribution to the tumor site is improved. [NIH]

Liposome: A spherical particle in an aqueous medium, formed by a lipid bilayer enclosing an aqueous compartment. [EU]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Liver cancer: A disease in which malignant (cancer) cells are found in the tissues of the liver. [NIH]

Lobe: A portion of an organ such as the liver, lung, breast, or brain. [NIH]

Localization: The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

Locally advanced cancer: Cancer that has spread only to nearby tissues or lymph nodes. [NIH]

Locomotion: Movement or the ability to move from one place or another. It can refer to

humans, vertebrate or invertebrate animals, and microorganisms. [NIH]

Longitudinal Studies: Studies in which variables relating to an individual or group of individuals are assessed over a period of time. [NIH]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Long-Term Care: Care over an extended period, usually for a chronic condition or disability, requiring periodic, intermittent, or continuous care. [NIH]

Loop: A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

Loss of Heterozygosity: The loss of one allele at a specific locus, caused by a deletion mutation; or loss of a chromosome from a chromosome pair. It is detected when heterozygous markers for a locus appear monomorphic because one of the alleles was deleted. When this occurs at a tumor suppressor gene locus where one of the alleles is already abnormal, it can result in neoplastic transformation. [NIH]

Lutetium: Lutetium. An element of the rare earth family of metals. It has the atomic symbol Lu, atomic number 71, and atomic weight 175. [NIH]

Lutetium texaphyrin: A substance that is being studied in photodynamic therapy. It belongs to the family of drugs called metallotexaphyrins. [NIH]

Lymph: The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

Lymph node: A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

Lymph node mapping: The use of dyes and radioactive substances to identify lymph nodes that contain tumor cells. [NIH]

Lymphadenectomy: A surgical procedure in which the lymph nodes are removed and examined to see whether they contain cancer. Also called lymph node dissection. [NIH]

Lymphangiography: An x-ray study of the lymphatic system. A dye is injected into a lymphatic vessel and travels throughout the lymphatic system. The dye outlines the lymphatic vessels and organs on the x-ray. [NIH]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphoblastic: One of the most aggressive types of non-Hodgkin lymphoma. [NIH]

Lymphoblasts: Interferon produced predominantly by leucocyte cells. [NIH]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and

diseases. [NIH]

Lymphocyte Subsets: A classification of lymphocytes based on structurally or functionally different populations of cells. [NIH]

Lymphocytic: Referring to lymphocytes, a type of white blood cell. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphoma: A general term for various neoplastic diseases of the lymphoid tissue. [NIH]

Lysine: An essential amino acid. It is often added to animal feed. [NIH]

Lytic: 1. Pertaining to lysis or to a lysin. 2. Producing lysis. [EU]

Magnetic Resonance Imaging: Non-invasive method of demonstrating internal anatomy based on the principle that atomic nuclei in a strong magnetic field absorb pulses of radiofrequency energy and emit them as radiowaves which can be reconstructed into computerized images. The concept includes proton spin tomographic techniques. [NIH]

Major Histocompatibility Complex: The genetic region which contains the loci of genes which determine the structure of the serologically defined (SD) and lymphocyte-defined (LD) transplantation antigens, genes which control the structure of the immune response-associated (Ia) antigens, the immune response (Ir) genes which control the ability of an animal to respond immunologically to antigenic stimuli, and genes which determine the structure and/or level of the first four components of complement. [NIH]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malignancy: A cancerous tumor that can invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant mesothelioma: A rare type of cancer in which malignant cells are found in the sac lining the chest or abdomen. Exposure to airborne asbestos particles increases one's risk of developing malignant mesothelioma. [NIH]

Malignant tumor: A tumor capable of metastasizing. [NIH]

Malnutrition: A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mammary: Pertaining to the mamma, or breast. [EU]

Mammogram: An x-ray of the breast. [NIH]

Mammography: Radiographic examination of the breast. [NIH]

Mandatory Testing: Testing or screening required by federal, state, or local law or other agencies for the diagnosis of specified conditions. It is usually limited to specific populations such as categories of health care providers, members of the military, and prisoners or to specific situations such as premarital examinations or donor screening. [NIH]

Mass Screening: Organized periodic procedures performed on large groups of people for the purpose of detecting disease. [NIH]

Matrix metalloproteinase: A member of a group of enzymes that can break down proteins, such as collagen, that are normally found in the spaces between cells in tissues (i.e., extracellular matrix proteins). Because these enzymes need zinc or calcium atoms to work properly, they are called metalloproteinases. Matrix metalloproteinases are involved in wound healing, angiogenesis, and tumor cell metastasis. [NIH]

Measles Virus: The type species of morbillivirus and the cause of the highly infectious

human disease measles, which affects mostly children. [NIH]

Meat: The edible portions of any animal used for food including domestic mammals (the major ones being cattle, swine, and sheep) along with poultry, fish, shellfish, and game. [NIH]

Mediastinum: The area between the lungs. The organs in this area include the heart and its large blood vessels, the trachea, the esophagus, the bronchi, and lymph nodes. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Medical Informatics: The field of information science concerned with the analysis and dissemination of medical data through the application of computers to various aspects of health care and medicine. [NIH]

Medical Records: Recording of pertinent information concerning patient's illness or illnesses. [NIH]

Medicament: A medicinal substance or agent. [EU]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Melanin: The substance that gives the skin its color. [NIH]

Melanocytes: Epidermal dendritic pigment cells which control long-term morphological color changes by alteration in their number or in the amount of pigment they produce and store in the pigment containing organelles called melanosomes. Melanophores are larger cells which do not exist in mammals. [NIH]

Melanoma: A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Melanosomes: Melanin-containing organelles found in melanocytes and melanophores. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Membrane Glycoproteins: Glycoproteins found on the membrane or surface of cells. [NIH]

Membrane Proteins: Proteins which are found in membranes including cellular and intracellular membranes. They consist of two types, peripheral and integral proteins. They include most membrane-associated enzymes, antigenic proteins, transport proteins, and drug, hormone, and lectin receptors. [NIH]

Memory: Complex mental function having four distinct phases: (1) memorizing or learning, (2) retention, (3) recall, and (4) recognition. Clinically, it is usually subdivided into immediate, recent, and remote memory. [NIH]

Menstrual Cycle: The period of the regularly recurring physiologic changes in the endometrium occurring during the reproductive period in human females and some primates and culminating in partial sloughing of the endometrium (menstruation). [NIH]

Menstruation: The normal physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus. [NIH]

Mental Disorders: Psychiatric illness or diseases manifested by breakdowns in the adaptational process expressed primarily as abnormalities of thought, feeling, and behavior producing either distress or impairment of function. [NIH]

Mental Health: The state wherein the person is well adjusted. [NIH]

Mentors: Senior professionals who provide guidance, direction and support to those persons desirous of improvement in academic positions, administrative positions or other career development situations. [NIH]

Mercury: A silver metallic element that exists as a liquid at room temperature. It has the atomic symbol Hg (from hydrargyrum, liquid silver), atomic number 80, and atomic weight 200.59. Mercury is used in many industrial applications and its salts have been employed therapeutically as purgatives, antisyphilitics, disinfectants, and astringents. It can be absorbed through the skin and mucous membranes which leads to mercury poisoning. Because of its toxicity, the clinical use of mercury and mercurials is diminishing. [NIH]

Mesenchymal: Refers to cells that develop into connective tissue, blood vessels, and lymphatic tissue. [NIH]

Mesothelial: It lines the peritonealla and pleural cavities. [NIH]

Mesothelioma: A benign (noncancerous) or malignant (cancerous) tumor affecting the lining of the chest or abdomen. Exposure to asbestos particles in the air increases the risk of developing malignant mesothelioma. [NIH]

Meta-Analysis: A quantitative method of combining the results of independent studies (usually drawn from the published literature) and synthesizing summaries and conclusions which may be used to evaluate therapeutic effectiveness, plan new studies, etc., with application chiefly in the areas of research and medicine. [NIH]

Metastasis: The spread of cancer from one part of the body to another. Tumors formed from cells that have spread are called "secondary tumors" and contain cells that are like those in the original (primary) tumor. The plural is metastases. [NIH]

Metastatic: Having to do with metastasis, which is the spread of cancer from one part of the body to another. [NIH]

Metastatic cancer: Cancer that has spread from the place in which it started to other parts of the body. [NIH]

MI: Myocardial infarction. Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Microcirculation: The vascular network lying between the arterioles and venules; includes capillaries, metarterioles and arteriovenous anastomoses. Also, the flow of blood through this network. [NIH]

Micronutrients: Essential dietary elements or organic compounds that are required in only small quantities for normal physiologic processes to occur. [NIH]

Microorganism: An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

Microscopy: The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

Microtubules: Slender, cylindrical filaments found in the cytoskeleton of plant and animal cells. They are composed of the protein tubulin. [NIH]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Mitochondrial Swelling: Increase in volume of mitochondria due to an influx of fluid; it occurs in hypotonic solutions due to osmotic pressure and in isotonic solutions as a result of altered permeability of the membranes of respiring mitochondria. [NIH]

Mitomycin: An antineoplastic antibiotic produced by Streptomyces caespitosus. It acts as a bi- or trifunctional alkylating agent causing cross-linking of DNA and inhibition of DNA synthesis. [NIH]

Mitosis: A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

Mitotic: Cell resulting from mitosis. [NIH]

Mitotic inhibitors: Drugs that kill cancer cells by interfering with cell division (mitostis). [NIH]

Mobilization: The process of making a fixed part or stored substance mobile, as by separating a part from surrounding structures to make it accessible for an operative procedure or by causing release into the circulation for body use of a substance stored in the body. [EU]

Modeling: A treatment procedure whereby the therapist presents the target behavior which the learner is to imitate and make part of his repertoire. [NIH]

Modification: A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Molecule: A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

Monitor: An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

Monoclonal: An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

Monoclonal antibodies: Laboratory-produced substances that can locate and bind to cancer cells wherever they are in the body. Many monoclonal antibodies are used in cancer detection or therapy; each one recognizes a different protein on certain cancer cells. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to a tumor. [NIH]

Monogenic: A human disease caused by a mutation in a single gene. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Morbillivirus: A genus of the family Paramyxoviridae (subfamily Paramyxovirinae) where all the virions have hemagglutinin but not neuraminidase activity. All members produce both cytoplasmic and intranuclear inclusion bodies. MEASLES VIRUS is the type species. [NIH]

Morphogenesis: The development of the form of an organ, part of the body, or organism. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Morphology: The science of the form and structure of organisms (plants, animals, and other forms of life). [NIH]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Mucositis: A complication of some cancer therapies in which the lining of the digestive system becomes inflamed. Often seen as sores in the mouth. [NIH]

Mucus: The viscous secretion of mucous membranes. It contains mucin, white blood cells, water, inorganic salts, and exfoliated cells. [NIH]

Multimodality treatment: Therapy that combines more than one method of treatment. [NIH]

Multiple Myeloma: A malignant tumor of plasma cells usually arising in the bone marrow; characterized by diffuse involvement of the skeletal system, hyperglobulinemia, Bence-Jones proteinuria, and anemia. [NIH]

Muscle Fibers: Large single cells, either cylindrical or prismatic in shape, that form the basic unit of muscle tissue. They consist of a soft contractile substance enclosed in a tubular sheath. [NIH]

Muscular Atrophy: Derangement in size and number of muscle fibers occurring with aging, reduction in blood supply, or following immobilization, prolonged weightlessness, malnutrition, and particularly in denervation. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Mustard Gas: Severe irritant and vesicant of skin, eyes, and lungs. It may cause blindness and lethal lung edema and was formerly used as a war gas. The substance has been proposed as a cytostatic and for treatment of psoriasis. It has been listed as a known carcinogen in the Fourth Annual Report on Carcinogens (NTP-85-002, 1985) (Merck, 11th ed). [NIH]

Mutagen: Any agent, such as X-rays, gamma rays, mustard gas, TCDD, that can cause abnormal mutation in living cells; having the power to cause mutations. [NIH]

Mutagenic: Inducing genetic mutation. [EU]

Myalgia: Pain in a muscle or muscles. [EU]

Myeloma: Cancer that arises in plasma cells, a type of white blood cell. [NIH]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myotonic Dystrophy: A condition presenting muscle weakness and wasting which may be progressive. [NIH]

Nasal Mucosa: The mucous membrane lining the nasal cavity. [NIH]

Natural killer cells: NK cells. A type of white blood cell that contains granules with enzymes that can kill tumor cells or microbial cells. Also called large granular lymphocytes (LGL). [NIH]

Nausea: An unpleasant sensation in the stomach usually accompanied by the urge to vomit. Common causes are early pregnancy, sea and motion sickness, emotional stress, intense pain, food poisoning, and various enteroviruses. [NIH]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at http://cancer.gov. [NIH]

Necrosis: A pathological process caused by the progressive degradative action of enzymes that is generally associated with severe cellular trauma. It is characterized by mitochondrial swelling, nuclear flocculation, uncontrolled cell lysis, and ultimately cell death. [NIH]

Need: A state of tension or dissatisfaction felt by an individual that impels him to action toward a goal he believes will satisfy the impulse. [NIH]

Needle biopsy: The removal of tissue or fluid with a needle for examination under a microscope. Also called fine-needle aspiration. [NIH]

Needs Assessment: Systematic identification of a population's needs or the assessment of individuals to determine the proper level of services needed. [NIH]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

Neoplasm: A new growth of benign or malignant tissue. [NIH]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephropathy: Disease of the kidneys. [EU]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [NIH]

Networks: Pertaining to a nerve or to the nerves, a meshlike structure of interlocking fibers or strands. [NIH]

Neural: 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

Neurons: The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

Neutrons: Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier nuclei during their decay. [NIH]

Nicotine: Nicotine is highly toxic alkaloid. It is the prototypical agonist at nicotinic cholinergic receptors where it dramatically stimulates neurons and ultimately blocks synaptic transmission. Nicotine is also important medically because of its presence in tobacco smoke. [NIH]

Nitrogen: An element with the atomic symbol N, atomic number 7, and atomic weight 14. Nitrogen exists as a diatomic gas and makes up about 78% of the earth's atmosphere by volume. It is a constituent of proteins and nucleic acids and found in all living cells. [NIH]

Node-negative: Cancer that has not spread to the lymph nodes. [NIH]

Nonoxynol: Nonionic surfactant mixtures varying in the number of repeating ethoxy (oxy-1,2-ethanediyl) groups. They are used as detergents, emulsifiers, wetting agents, defoaming agents, etc. Nonoxynol-9, the compound with 9 repeating ethoxy groups, is a spermatocide, formulated primarily as a component of vaginal foams and creams. [NIH]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the

chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleic Acid Hybridization: The process whereby two single-stranded polynucleotides form a double-stranded molecule, with hydrogen bonding between the complementary bases in the two strains. [NIH]

Nucleosomes: The repeating structural units of chromatin, each consisting of approximately 200 base pairs of DNA wound around a protein core. This core is composed of the histones H2A, H2B, H3, and H4. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Occult: Obscure; concealed from observation, difficult to understand. [EU]

Odds Ratio: The ratio of two odds. The exposure-odds ratio for case control data is the ratio of the odds in favor of exposure among cases to the odds in favor of exposure among noncases. The disease-odds ratio for a cohort or cross section is the ratio of the odds in favor of disease among the exposed to the odds in favor of disease among the unexposed. The prevalence-odds ratio refers to an odds ratio derived cross-sectionally from studies of prevalent cases. [NIH]

Odour: A volatile emanation that is perceived by the sense of smell. [EU]

Ointments: Semisolid preparations used topically for protective emollient effects or as a vehicle for local administration of medications. Ointment bases are various mixtures of fats, waxes, animal and plant oils and solid and liquid hydrocarbons. [NIH]

Oligomenorrhea: Abnormally infrequent menstruation. [NIH]

Oncogene: A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens. [NIH]

Oncogenic: Chemical, viral, radioactive or other agent that causes cancer; carcinogenic. [NIH]

Oncogenic Viruses: Viruses that produce tumors. [NIH]

Oncologist: A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment. For example, a radiation oncologist specializes in treating cancer with radiation. [NIH]

Oncology: The study of cancer. [NIH]

Oncolysis: The destruction of or disposal by absorption of any neoplastic cells. [NIH]

Oncolytic: Pertaining to, characterized by, or causing oncolysis (= the lysis or destruction of tumour cells). [EU]

Ophthalmology: A surgical specialty concerned with the structure and function of the eye and the medical and surgical treatment of its defects and diseases. [NIH]

Opportunistic Infections: An infection caused by an organism which becomes pathogenic under certain conditions, e.g., during immunosuppression. [NIH]

Optic Chiasm: The X-shaped structure formed by the meeting of the two optic nerves. At the optic chiasm the fibers from the medial part of each retina cross to project to the other side of the brain while the lateral retinal fibers continue on the same side. As a result each half of the brain receives information about the contralateral visual field from both eyes. [NIH]

Oral Health: The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

Orderly: A male hospital attendant. [NIH]

Organ Culture: The growth in aseptic culture of plant organs such as roots or shoots, beginning with organ primordia or segments and maintaining the characteristics of the organ. [NIH]

Organelles: Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysomomes; plastids; and vacuoles. [NIH]

Outpatient: A patient who is not an inmate of a hospital but receives diagnosis or treatment in a clinic or dispensary connected with the hospital. [NIH]

Ovarian epithelial cancer: Cancer that occurs in the cells lining the ovaries. [NIH]

Ovaries: The pair of female reproductive glands in which the ova, or eggs, are formed. The ovaries are located in the pelvis, one on each side of the uterus. [NIH]

Ovary: Either of the paired glands in the female that produce the female germ cells and secrete some of the female sex hormones. [NIH]

Ovulation: The discharge of a secondary oocyte from a ruptured graafian follicle. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [NIH]

Oxaliplatin: An anticancer drug that belongs to the family of drugs called platinum compounds. [NIH]

Oxidation: The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

Oxygenation: The process of supplying, treating, or mixing with oxygen. No:1245 - oxygenation the process of supplying, treating, or mixing with oxygen. [EU]

Oxytocin: A nonapeptide posterior pituitary hormone that causes uterine contractions and stimulates lactation. [NIH]

P53 gene: A tumor suppressor gene that normally inhibits the growth of tumors. This gene is altered in many types of cancer. [NIH]

Paclitaxel: Antineoplastic agent isolated from the bark of the Pacific yew tree, Taxus brevifolia. Paclitaxel stabilizes microtubules in their polymerized form and thus mimics the action of the proto-oncogene proteins c-mos. [NIH]

Palate: The structure that forms the roof of the mouth. It consists of the anterior hard palate and the posterior soft palate. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatic cancer: Cancer of the pancreas, a salivary gland of the abdomen. [NIH]

Pap test: The collection of cells from the cervix for examination under a microscope. It is

used to detect changes that may be cancer or may lead to cancer, and can show noncancerous conditions, such as infection or inflammation. Also called a Pap smear. [NIH]

Papilloma: A benign epithelial neoplasm which may arise from the skin, mucous membranes or glandular ducts. [NIH]

Papillomavirus: A genus of Papovaviridae causing proliferation of the epithelium, which may lead to malignancy. A wide range of animals are infected including humans, chimpanzees, cattle, rabbits, dogs, and horses. [NIH]

Paraffin: A mixture of solid hydrocarbons obtained from petroleum. It has a wide range of uses including as a stiffening agent in ointments, as a lubricant, and as a topical anti-inflammatory. It is also commonly used as an embedding material in histology. [NIH]

Parasite: An animal or a plant that lives on or in an organism of another species and gets at least some of its nutrition from that other organism. [NIH]

Parasitic: Having to do with or being a parasite. A parasite is an animal or a plant that lives on or in an organism of another species and gets at least some of its nutrients from it. [NIH]

Parity: The number of offspring a female has borne. It is contrasted with gravidity, which refers to the number of pregnancies, regardless of outcome. [NIH]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

Partial remission: The shrinking, but not complete disappearance, of a tumor in response to therapy. Also called partial response. [NIH]

Particle: A tiny mass of material. [EU]

Patch: A piece of material used to cover or protect a wound, an injured part, etc.: a patch over the eye. [NIH]

Pathogen: Any disease-producing microorganism. [EU]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Pathologies: The study of abnormality, especially the study of diseases. [NIH]

Patient Compliance: Voluntary cooperation of the patient in following a prescribed regimen. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

Patient Selection: Criteria and standards used for the determination of the appropriateness of the inclusion of patients with specific conditions in proposed treatment plans and the criteria used for the inclusion of subjects in various clinical trials and other research protocols. [NIH]

PDQ: Physician Data Query. PDQ is an online database developed and maintained by the National Cancer Institute. Designed to make the most current, credible, and accurate cancer information available to health professionals and the public, PDQ contains peer-reviewed summaries on cancer treatment, screening, prevention, genetics, and supportive care; a registry of cancer clinical trials from around the world; and directories of physicians, professionals who provide genetics services, and organizations that provide cancer care. Most of this information is available on the CancerNet Web site, and more specific

information about PDQ can be found at http://cancernet.nci.nih.gov/pdq.html. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Pelvic inflammatory disease: A bacteriological disease sometimes associated with intrauterine device (IUD) usage. [NIH]

Penicillin: An antibiotic drug used to treat infection. [NIH]

Penis: The external reproductive organ of males. It is composed of a mass of erectile tissue enclosed in three cylindrical fibrous compartments. Two of the three compartments, the corpus cavernosa, are placed side-by-side along the upper part of the organ. The third compartment below, the corpus spongiosum, houses the urethra. [NIH]

Peplomycin: An antineoplastic agent derived from bleomycin. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Peptide Mapping: Analysis of peptides generated from the digestion of a protein by a specific protease for the purpose of indentifing the protein or to look for polymorphisms. [NIH]

Perceived risk: Estimate or evaluation of risk as observed through personal experience or personal study, and personal evaluation of consequences. [NIH]

Perception: The ability quickly and accurately to recognize similarities and differences among presented objects, whether these be pairs of words, pairs of number series, or multiple sets of these or other symbols such as geometric figures. [NIH]

Perfusion: Bathing an organ or tissue with a fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread. [NIH]

Perinatal: Pertaining to or occurring in the period shortly before and after birth; variously defined as beginning with completion of the twentieth to twenty-eighth week of gestation and ending 7 to 28 days after birth. [EU]

Perineal: Pertaining to the perineum. [EU]

Perineum: The area between the anus and the sex organs. [NIH]

Perineural: Around a nerve or group of nerves. [NIH]

Peripheral blood: Blood circulating throughout the body. [NIH]

Peripheral Nerves: The nerves outside of the brain and spinal cord, including the autonomic, cranial, and spinal nerves. Peripheral nerves contain non-neuronal cells and connective tissue as well as axons. The connective tissue layers include, from the outside to the inside, the epineurium, the perineurium, and the endoneurium. [NIH]

Peripheral stem cell transplantation: A method of replacing blood-forming cells destroyed by cancer treatment. Immature blood cells (stem cells) in the circulating blood that are similar to those in the bone marrow are given after treatment to help the bone marrow recover and continue producing healthy blood cells. Transplantation may be autologous (an individual's own blood cells saved earlier), allogeneic (blood cells donated by someone else), or syngeneic (blood cells donated by an identical twin). Also called peripheral stem cell support. [NIH]

Peritoneal: Having to do with the peritoneum (the tissue that lines the abdominal wall and covers most of the organs in the abdomen). [NIH]

Peritoneum: Endothelial lining of the abdominal cavity, the parietal peritoneum covering the inside of the abdominal wall and the visceral peritoneum covering the bowel, the mesentery, and certain of the organs. The portion that covers the bowel becomes the serosal

layer of the bowel wall. [NIH]

Petroleum: Naturally occurring complex liquid hydrocarbons which, after distillation, yield combustible fuels, petrochemicals, and lubricants. [NIH]

Phallic: Pertaining to the phallus, or penis. [EU]

Pharmaceutical Preparations: Drugs intended for human or veterinary use, presented in their finished dosage form. Included here are materials used in the preparation and/or formulation of the finished dosage form. [NIH]

Pharmacogenetics: A branch of genetics which deals with the genetic components of variability in individual responses to and metabolism (biotransformation) of drugs. [NIH]

Pharmacokinetic: The mathematical analysis of the time courses of absorption, distribution, and elimination of drugs. [NIH]

Pharmacologic: Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

Pharynx: The hollow tube about 5 inches long that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach). [NIH]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

Phenylalanine: An aromatic amino acid that is essential in the animal diet. It is a precursor of melanin, dopamine, noradrenalin, and thyroxine. [NIH]

Phospholipases: A class of enzymes that catalyze the hydrolysis of phosphoglycerides or glycerophosphatidates. EC 3.1.-. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nevers, bones, and teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

Phosphorylation: The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

Photodynamic therapy: Treatment with drugs that become active when exposed to light. These drugs kill cancer cells. [NIH]

Physical Examination: Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

Pigment: A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair. [NIH]

Pilot Projects: Small-scale tests of methods and procedures to be used on a larger scale if the pilot study demonstrates that these methods and procedures can work. [NIH]

Pilot study: The initial study examining a new method or treatment. [NIH]

Pineal gland: A tiny organ located in the cerebrum that produces melatonin. Also called pineal body or pineal organ. [NIH]

Pituitary Gland: A small, unpaired gland situated in the sella turcica tissue. It is connected to the hypothalamus by a short stalk. [NIH]

Pituitary Hormone Release Inhibiting Hormones: Polypeptide hormones produced in the

hypothalamus which inhibit the release of pituitary hormones. Used for PHRIH in general or for which there is no specific heading. [NIH]

Pituitary Hormone-Releasing Hormones: Hormones released by one structure (e.g., the hypothalamus or the thyroid gland) that effect the secretion of hormones from the pituitary gland. [NIH]

Pituitary Hormones: Hormones secreted by the anterior and posterior lobes of the pituitary gland and the pars intermedia, an ill-defined region between the two. Their secretion is regulated by the hypothalamus. [NIH]

Placenta: A highly vascular fetal organ through which the fetus absorbs oxygen and other nutrients and excretes carbon dioxide and other wastes. It begins to form about the eighth day of gestation when the blastocyst adheres to the decidua. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plaque: A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

Plasmacytoma: Any discrete, presumably solitary, mass of neoplastic plasma cells either in bone marrow or various extramedullary sites. [NIH]

Plasmid: An autonomously replicating, extra-chromosomal DNA molecule found in many bacteria. Plasmids are widely used as carriers of cloned genes. [NIH]

Plasticity: In an individual or a population, the capacity for adaptation: a) through gene changes (genetic plasticity) or b) through internal physiological modifications in response to changes of environment (physiological plasticity). [NIH]

Platelet Activation: A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness, aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [NIH]

Platinum: Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

Platinum Compounds: Inorganic compounds which contain platinum as the central atom. [NIH]

Pleated: Particular three-dimensional pattern of amyloidoses. [NIH]

Pleural: A circumscribed area of hyaline whorled fibrous tissue which appears on the surface of the parietal pleura, on the fibrous part of the diaphragm or on the pleura in the interlobar fissures. [NIH]

Plexus: A network or tangle; a general term for a network of lymphatic vessels, nerves, or veins. [EU]

Ploidy: The number of sets of chromosomes in a cell or an organism. For example, haploid

means one set and diploid means two sets. [NIH]

Podophyllotoxin: The main active constituent of the resin from the roots of may apple or mandrake (Podophyllum peltatum and P. emodi). It is a potent spindle poison, toxic if taken internally, and has been used as a cathartic. It is very irritating to skin and mucous membranes, has keratolytic actions, has been used to treat warts and keratoses, and may have antineoplastic properties, as do some of its congeners and derivatives. [NIH]

Point Mutation: A mutation caused by the substitution of one nucleotide for another. This results in the DNA molecule having a change in a single base pair. [NIH]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Polycystic: An inherited disorder characterized by many grape-like clusters of fluid-filled cysts that make both kidneys larger over time. These cysts take over and destroy working kidney tissue. PKD may cause chronic renal failure and end-stage renal disease. [NIH]

Polycystic Ovary Syndrome: Clinical symptom complex characterized by oligomenorrhea or amenorrhea, anovulation, and regularly associated with bilateral polycystic ovaries. [NIH]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymerase Chain Reaction: In vitro method for producing large amounts of specific DNA or RNA fragments of defined length and sequence from small amounts of short oligonucleotide flanking sequences (primers). The essential steps include thermal denaturation of the double-stranded target molecules, annealing of the primers to their complementary sequences, and extension of the annealed primers by enzymatic synthesis with DNA polymerase. The reaction is efficient, specific, and extremely sensitive. Uses for the reaction include disease diagnosis, detection of difficult-to-isolate pathogens, mutation analysis, genetic testing, DNA sequencing, and analyzing evolutionary relationships. [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polyposis: The development of numerous polyps (growths that protrude from a mucous membrane). [NIH]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Posterior: Situated in back of, or in the back part of, or affecting the back or dorsal surface of the body. In lower animals, it refers to the caudal end of the body. [EU]

Postoperative: After surgery. [NIH]

Postsynaptic: Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

Post-translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Potentiation: An overall effect of two drugs taken together which is greater than the sum of the effects of each drug taken alone. [NIH]

Practicability: A non-standard characteristic of an analytical procedure. It is dependent on the scope of the method and is determined by requirements such as sample throughout and

costs. [NIH]

Practice Guidelines: Directions or principles presenting current or future rules of policy for the health care practitioner to assist him in patient care decisions regarding diagnosis, therapy, or related clinical circumstances. The guidelines may be developed by government agencies at any level, institutions, professional societies, governing boards, or by the convening of expert panels. The guidelines form a basis for the evaluation of all aspects of health care and delivery. [NIH]

Precancerous: A term used to describe a condition that may (or is likely to) become cancer. Also called premalignant. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Predisposition: A latent susceptibility to disease which may be activated under certain conditions, as by stress. [EU]

Premalignant: A term used to describe a condition that may (or is likely to) become cancer. Also called precancerous. [NIH]

Premenstrual: Occurring before menstruation. [EU]

Premenstrual Syndrome: A syndrome occurring most often during the last week of the menstrual cycle and ending soon after the onset of menses. Some of the symptoms are emotional instability, insomnia, headache, nausea, vomiting, abdominal distension, and painful breasts. [NIH]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Prickle: Several layers of the epidermis where the individual cells are connected by cell bridges. [NIH]

Primary tumor: The original tumor. [NIH]

Primary vaccination: First or principal vaccination (= introduction of a vaccine into the body for the purpose of inducing immunity). [EU]

Probe: An instrument used in exploring cavities, or in the detection and dilatation of strictures, or in demonstrating the potency of channels; an elongated instrument for exploring or sounding body cavities. [NIH]

Progesterone: Pregn-4-ene-3,20-dione. The principal progestational hormone of the body, secreted by the corpus luteum, adrenal cortex, and placenta. Its chief function is to prepare the uterus for the reception and development of the fertilized ovum. It acts as an antiovulatory agent when administered on days 5-25 of the menstrual cycle. [NIH]

Prognostic factor: A situation or condition, or a characteristic of a patient, that can be used to estimate the chance of recovery from a disease, or the chance of the disease recurring (coming back). [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Proline: A non-essential amino acid that is synthesized from glutamic acid. It is an essential component of collagen and is important for proper functioning of joints and tendons. [NIH]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [NIH]

Prone: Having the front portion of the body downwards. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Proportional: Being in proportion : corresponding in size, degree, or intensity, having the same or a constant ratio; of, relating to, or used in determining proportions. [EU]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostaglandin: Any of a group of components derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway that are extremely potent mediators of a diverse group of physiologic processes. The abbreviation for prostaglandin is PG; specific compounds are designated by adding one of the letters A through I to indicate the type of substituents found on the hydrocarbon skeleton and a subscript (1, 2 or 3) to indicate the number of double bonds in the hydrocarbon skeleton e.g., PGE2. The predominant naturally occurring prostaglandins all have two double bonds and are synthesized from arachidonic acid (5,8,11,14-eicosatetraenoic acid) by the pathway shown in the illustration. The 1 series and 3 series are produced by the same pathway with fatty acids having one fewer double bond (8,11,14-eicosatrienoic acid or one more double bond (5,8,11,14,17-eicosapentaenoic acid) than arachidonic acid. The subscript a or ß indicates the configuration at C-9 (a denotes a substituent below the plane of the ring, ß, above the plane). The naturally occurring PGF's have the a configuration, e.g., PGF2a. All of the prostaglandins act by binding to specific cell-surface receptors causing an increase in the level of the intracellular second messenger cyclic AMP (and in some cases cyclic GMP also). The effect produced by the cyclic AMP increase depends on the specific cell type. In some cases there is also a positive feedback effect. Increased cyclic AMP increases prostaglandin synthesis leading to further increases in cyclic AMP. [EU]

Prostaglandins A: (13E,15S)-15-Hydroxy-9-oxoprosta-10,13-dien-1-oic acid (PGA(1)); (5Z,13E,15S)-15-hydroxy-9-oxoprosta-5,10,13-trien-1-oic acid (PGA(2)); (5Z,13E,15S,17Z)-15-hydroxy-9-oxoprosta-5,10,13,17-tetraen-1-oic acid (PGA(3)). A group of naturally occurring secondary prostaglandins derived from PGE. PGA(1) and PGA(2) as well as their 19-hydroxy derivatives are found in many organs and tissues. [NIH]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protein C: A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

Protein Conformation: The characteristic 3-dimensional shape of a protein, including the secondary, supersecondary (motifs), tertiary (domains) and quaternary structure of the peptide chain. Quaternary protein structure describes the conformation assumed by multimeric proteins (aggregates of more than one polypeptide chain). [NIH]

Protein S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino

acids determines the shape and function of the protein. [NIH]

Protein-Tyrosine Kinase: An enzyme that catalyzes the phosphorylation of tyrosine residues in proteins with ATP or other nucleotides as phosphate donors. EC 2.7.1.112. [NIH]

Proteinuria: The presence of protein in the urine, indicating that the kidneys are not working properly. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Protocol: The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

Protons: Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

Proto-Oncogene Proteins: Products of proto-oncogenes. Normally they do not have oncogenic or transforming properties, but are involved in the regulation or differentiation of cell growth. They often have protein kinase activity. [NIH]

Proto-Oncogene Proteins c-mos: Cellular proteins encoded by the c-mos genes. They function in the cell cycle to maintain maturation promoting factor in the active state and have protein-serine/threonine kinase activity. Oncogenic transformation can take place when c-mos proteins are expressed at the wrong time. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

Psoriasis: A common genetically determined, chronic, inflammatory skin disease characterized by rounded erythematous, dry, scaling patches. The lesions have a predilection for nails, scalp, genitalia, extensor surfaces, and the lumbosacral region. Accelerated epidermopoiesis is considered to be the fundamental pathologic feature in psoriasis. [NIH]

Psychiatry: The medical science that deals with the origin, diagnosis, prevention, and treatment of mental disorders. [NIH]

Puberty: The period during which the secondary sex characteristics begin to develop and the capability of sexual reproduction is attained. [EU]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

Public Policy: A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

Publishing: "The business or profession of the commercial production and issuance of literature" (Webster's 3d). It includes the publisher, publication processes, editing and editors. Production may be by conventional printing methods or by electronic publishing. [NIH]

Pulse: The rhythmical expansion and contraction of an artery produced by waves of pressure caused by the ejection of blood from the left ventricle of the heart as it contracts. [NIH]

Purulent: Consisting of or containing pus; associated with the formation of or caused by pus. [EU]

Pustular: Pertaining to or of the nature of a pustule; consisting of pustules (= a visible collection of pus within or beneath the epidermis). [EU]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

Rabies: A highly fatal viral infection of the nervous system which affects all warm-blooded animal species. It is one of the most important of the zoonoses because of the inevitably fatal outcome for the infected human. [NIH]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

Radiation oncologist: A doctor who specializes in using radiation to treat cancer. [NIH]

Radiation therapy: The use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy. [NIH]

Radioactive: Giving off radiation. [NIH]

Radioactivity: The quality of emitting or the emission of corpuscular or electromagnetic radiations consequent to nuclear disintegration, a natural property of all chemical elements of atomic number above 83, and possible of induction in all other known elements. [EU]

Radioimmunotherapy: Radiotherapy where cytotoxic radionuclides are linked to antibodies in order to deliver toxins directly to tumor targets. Therapy with targeted radiation rather than antibody-targeted toxins (immunotoxins) has the advantage that adjacent tumor cells, which lack the appropriate antigenic determinants, can be destroyed by radiation cross-fire. Radioimmunotherapy is sometimes called targeted radiotherapy, but this latter term can also refer to radionuclides linked to non-immune molecules (radiotherapy). [NIH]

Radioisotope: An unstable element that releases radiation as it breaks down. Radioisotopes can be used in imaging tests or as a treatment for cancer. [NIH]

Radiolabeled: Any compound that has been joined with a radioactive substance. [NIH]

Radiological: Pertaining to radiodiagnostic and radiotherapeutic procedures, and interventional radiology or other planning and guiding medical radiology. [NIH]

Radiologist: A doctor who specializes in creating and interpreting pictures of areas inside the body. The pictures are produced with x-rays, sound waves, or other types of energy. [NIH]

Radiology: A specialty concerned with the use of x-ray and other forms of radiant energy in the diagnosis and treatment of disease. [NIH]

Radiosensitization: The use of a drug that makes tumor cells more sensitive to radiation therapy. [NIH]

Radiotherapy: The use of ionizing radiation to treat malignant neoplasms and other benign conditions. The most common forms of ionizing radiation used as therapy are x-rays, gamma rays, and electrons. A special form of radiotherapy, targeted radiotherapy, links a cytotoxic radionuclide to a molecule that targets the tumor. When this molecule is an antibody or other immunologic molecule, the technique is called radioimmunotherapy. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects

are assigned by chance to separate groups that compare different treatments. [NIH]

Randomized clinical trial: A study in which the participants are assigned by chance to separate groups that compare different treatments; neither the researchers nor the participants can choose which group. Using chance to assign people to groups means that the groups will be similar and that the treatments they receive can be compared objectively. At the time of the trial, it is not known which treatment is best. It is the patient's choice to be in a randomized trial. [NIH]

Reactivation: The restoration of activity to something that has been inactivated. [EU]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Rebound effect: The characteristic of a drug to produce reverse effects when either the effect of the drug has passed, or when the patient no longer responds to the drug. [EU]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

Recombinant: A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Recombination: The formation of new combinations of genes as a result of segregation in crosses between genetically different parents; also the rearrangement of linked genes due to crossing-over. [NIH]

Rectal: By or having to do with the rectum. The rectum is the last 8 to 10 inches of the large intestine and ends at the anus. [NIH]

Rectovaginal Fistula: Abnormal communication between the rectum and the vagina. [NIH]

Rectum: The last 8 to 10 inches of the large intestine. [NIH]

Recurrence: The return of a sign, symptom, or disease after a remission. [NIH]

Recurrent cancer: Cancer that has returned, at the same site as the original (primary) tumor or in another location, after the tumor had disappeared. [NIH]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [NIH]

Red Nucleus: A pinkish-yellow portion of the midbrain situated in the rostral mesencephalic tegmentum. It receives a large projection from the contralateral half of the cerebellum via the superior cerebellar peduncle and a projection from the ipsilateral motor cortex. [NIH]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Reflective: Capable of throwing back light, images, sound waves : reflecting. [EU]

Reflex: An involuntary movement or exercise of function in a part, excited in response to a stimulus applied to the periphery and transmitted to the brain or spinal cord. [NIH]

Refraction: A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

Refractory: Not readily yielding to treatment. [EU]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Regional lymph node: In oncology, a lymph node that drains lymph from the region

around a tumor. [NIH]

Registries: The systems and processes involved in the establishment, support, management, and operation of registers, e.g., disease registers. [NIH]

Relapse: The return of signs and symptoms of cancer after a period of improvement. [NIH]

Relative risk: The ratio of the incidence rate of a disease among individuals exposed to a specific risk factor to the incidence rate among unexposed individuals; synonymous with risk ratio. Alternatively, the ratio of the cumulative incidence rate in the exposed to the cumulative incidence rate in the unexposed (cumulative incidence ratio). The term relative risk has also been used synonymously with odds ratio. This is because the odds ratio and relative risk approach each other if the disease is rare (5 percent of population) and the number of subjects is large. [NIH]

Relative survival rate: A specific measurement of survival. In cancer, the rate is calculated by adjusting the survival rate to remove all causes of death except cancer. The rate is determined at specific time intervals, such as 2 years and 5 years after diagnosis. [NIH]

Reliability: Used technically, in a statistical sense, of consistency of a test with itself, i. e. the extent to which we can assume that it will yield the same result if repeated a second time. [NIH]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [NIH]

Research Design: A plan for collecting and utilizing data so that desired information can be obtained with sufficient precision or so that an hypothesis can be tested properly. [NIH]

Resected: Surgical removal of part of an organ. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [NIH]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

Restoration: Broad term applied to any inlay, crown, bridge or complete denture which restores or replaces loss of teeth or oral tissues. [NIH]

Retinal: 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another, all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

Retinoids: Derivatives of vitamin A. Used clinically in the treatment of severe cystic acne, psoriasis, and other disorders of keratinization. Their possible use in the prophylaxis and treatment of cancer is being actively explored. [NIH]

Retroperitoneal: Having to do with the area outside or behind the peritoneum (the tissue that lines the abdominal wall and covers most of the organs in the abdomen). [NIH]

Retrospective: Looking back at events that have already taken place. [NIH]

Retrospective study: A study that looks backward in time, usually using medical records and interviews with patients who already have or had a disease. [NIH]

Retroviral vector: RNA from a virus that is used to insert genetic material into cells. [NIH]

Retrovirus: A member of a group of RNA viruses, the RNA of which is copied during viral replication into DNA by reverse transcriptase. The viral DNA is then able to be integrated into the host chromosomal DNA. [NIH]

Reversion: A return to the original condition, e. g. the reappearance of the normal or wild type in previously mutated cells, tissues, or organisms. [NIH]

Rhabdomyosarcoma: A malignant tumor of muscle tissue. [NIH]

Ribose: A pentose active in biological systems usually in its D-form. [NIH]

Ribosome: A granule of protein and RNA, synthesized in the nucleolus and found in the cytoplasm of cells. Ribosomes are the main sites of protein synthesis. Messenger RNA attaches to them and there receives molecules of transfer RNA bearing amino acids. [NIH]

Rigidity: Stiffness or inflexibility, chiefly that which is abnormal or morbid; rigor. [EU]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Risk patient: Patient who is at risk, because of his/her behaviour or because of the type of person he/she is. [EU]

Rod: A reception for vision, located in the retina. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Salmonella: A genus of gram-negative, facultatively anaerobic, rod-shaped bacteria that utilizes citrate as a sole carbon source. It is pathogenic for humans, causing enteric fevers, gastroenteritis, and bacteremia. Food poisoning is the most common clinical manifestation. Organisms within this genus are separated on the basis of antigenic characteristics, sugar fermentation patterns, and bacteriophage susceptibility. [NIH]

Sanitary: Relating or belonging to health and hygiene; conductive to the restoration or maintenance of health. [NIH]

Sarcoma: A connective tissue neoplasm formed by proliferation of mesodermal cells; it is usually highly malignant. [NIH]

Scleroproteins: Simple proteins characterized by their insolubility and fibrous structure. Within the body, they perform a supportive or protective function. [NIH]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Sebum: The oily substance secreted by sebaceous glands. It is composed of keratin, fat, and cellular debris. [NIH]

Secondary tumor: Cancer that has spread from the organ in which it first appeared to another organ. For example, breast cancer cells may spread (metastasize) to the lungs and cause the growth of a new tumor. When this happens, the disease is called metastatic breast cancer, and the tumor in the lungs is called a secondary tumor. Also called secondary cancer. [NIH]

Secretion: 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the

elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

Segregation: The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

Seizures: Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

Selenium: An element with the atomic symbol Se, atomic number 34, and atomic weight 78.96. It is an essential micronutrient for mammals and other animals but is toxic in large amounts. Selenium protects intracellular structures against oxidative damage. It is an essential component of glutathione peroxidase. [NIH]

Semen: The thick, yellowish-white, viscid fluid secretion of male reproductive organs discharged upon ejaculation. In addition to reproductive organ secretions, it contains spermatozoa and their nutrient plasma. [NIH]

Semisynthetic: Produced by chemical manipulation of naturally occurring substances. [EU]

Senescence: The bodily and mental state associated with advancing age. [NIH]

Sentinel lymph node: The first lymph node that cancer is likely to spread to from the primary tumor. Cancer cells may appear first in the sentinel node before spreading to other lymph nodes. [NIH]

Sequence Homology: The degree of similarity between sequences. Studies of amino acid and nucleotide sequences provide useful information about the genetic relatedness of certain species. [NIH]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Serologic: Analysis of a person's serum, especially specific immune or lytic serums. [NIH]

Serologic Tests: Diagnostic procedures involving immunoglobulin reactions. [NIH]

Serology: The study of serum, especially of antigen-antibody reactions in vitro. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Sex Characteristics: Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

Sex Determination: The biological characteristics which distinguish human beings as female or male. [NIH]

Sexual Abstinence: Refraining from sexual intercourse. [NIH]

Sexually Transmitted Diseases: Diseases due to or propagated by sexual contact. [NIH]

Shock: The general bodily disturbance following a severe injury; an emotional or moral upset occasioned by some disturbing or unexpected experience; disruption of the circulation, which can upset all body functions: sometimes referred to as circulatory shock. [NIH]

Side effect: A consequence other than the one(s) for which an agent or measure is used, as the adverse effects produced by a drug, especially on a tissue or organ system other than the one sought to be benefited by its administration. [EU]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an

activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

Sizofiran: A beta-D-glucan obtained from the Aphyllophoral fungus Schizophyllum commune. It is used as an immunoadjuvant in the treatment of neoplasms, especially tumors found in the stomach. [NIH]

Skeletal: Having to do with the skeleton (boney part of the body). [NIH]

Skeleton: The framework that supports the soft tissues of vertebrate animals and protects many of their internal organs. The skeletons of vertebrates are made of bone and/or cartilage. [NIH]

Skin Neoplasms: Tumors or cancer of the skin. [NIH]

Skull: The skeleton of the head including the bones of the face and the bones enclosing the brain. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Smallpox: A generalized virus infection with a vesicular rash. [NIH]

Social Class: A stratum of people with similar position and prestige; includes social stratification. Social class is measured by criteria such as education, occupation, and income. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Social Problems: Situations affecting a significant number of people, that are believed to be sources of difficulty or threaten the stability of the community, and that require programs of amelioration. [NIH]

Social Support: Support systems that provide assistance and encouragement to individuals with physical or emotional disabilities in order that they may better cope. Informal social support is usually provided by friends, relatives, or peers, while formal assistance is provided by churches, groups, etc. [NIH]

Sodium: An element that is a member of the alkali group of metals. It has the atomic symbol Na, atomic number 11, and atomic weight 23. With a valence of 1, it has a strong affinity for oxygen and other nonmetallic elements. Sodium provides the chief cation of the extracellular body fluids. Its salts are the most widely used in medicine. (From Dorland, 27th ed) Physiologically the sodium ion plays a major role in blood pressure regulation, maintenance of fluid volume, and electrolyte balance. [NIH]

Soft tissue: Refers to muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. [NIH]

Solid tumor: Cancer of body tissues other than blood, bone marrow, or the lymphatic

system. [NIH]

Soma: The body as distinct from the mind; all the body tissue except the germ cells; all the axial body. [NIH]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Somatic cells: All the body cells except the reproductive (germ) cells. [NIH]

Sound wave: An alteration of properties of an elastic medium, such as pressure, particle displacement, or density, that propagates through the medium, or a superposition of such alterations. [NIH]

Specialist: In medicine, one who concentrates on 1 special branch of medical science. [NIH]

Species: A taxonomic category subordinate to a genus (or subgenus) and superior to a subspecies or variety, composed of individuals possessing common characters distinguishing them from other categories of individuals of the same taxonomic level. In taxonomic nomenclature, species are designated by the genus name followed by a Latin or Latinized adjective or noun. [EU]

Specificity: Degree of selectivity shown by an antibody with respect to the number and types of antigens with which the antibody combines, as well as with respect to the rates and the extents of these reactions. [NIH]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Speculum: An instrument used to widen an opening of the body to make it easier to look inside. [NIH]

Sperm: The fecundating fluid of the male. [NIH]

Spermatozoa: Mature male germ cells that develop in the seminiferous tubules of the testes. Each consists of a head, a body, and a tail that provides propulsion. The head consists mainly of chromatin. [NIH]

Spermicide: An agent that is destructive to spermatozoa. [EU]

Sphincter: A ringlike band of muscle fibres that constricts a passage or closes a natural orifice; called also musculus sphincter. [EU]

Spinal cord: The main trunk or bundle of nerves running down the spine through holes in the spinal bone (the vertebrae) from the brain to the level of the lower back. [NIH]

Spinous: Like a spine or thorn in shape; having spines. [NIH]

Spirochete: Lyme disease. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Spotting: A slight discharge of blood via the vagina, especially as a side-effect of oral contraceptives. [EU]

Squamous: Scaly, or platelike. [EU]

Squamous cell carcinoma: Cancer that begins in squamous cells, which are thin, flat cells resembling fish scales. Squamous cells are found in the tissue that forms the surface of the

skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts. Also called epidermoid carcinoma. [NIH]

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Squamous cells: Flat cells that look like fish scales under a microscope. These cells cover internal and external surfaces of the body. [NIH]

Squamous Epithelium: Tissue in an organ such as the esophagus. Consists of layers of flat, scaly cells. [NIH]

Squamous intraepithelial lesion: SIL. A general term for the abnormal growth of squamous cells on the surface of the cervix. The changes in the cells are described as low grade or high grade, depending on how much of the cervix is affected and how abnormal the cells appear. [NIH]

Stabilization: The creation of a stable state. [EU]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Standardize: To compare with or conform to a standard; to establish standards. [EU]

Stem cell transplantation: A method of replacing immature blood-forming cells that were destroyed by cancer treatment. The stem cells are given to the person after treatment to help the bone marrow recover and continue producing healthy blood cells. [NIH]

Stem Cells: Relatively undifferentiated cells of the same lineage (family type) that retain the ability to divide and cycle throughout postnatal life to provide cells that can become specialized and take the place of those that die or are lost. [NIH]

Sterility: 1. The inability to produce offspring, i.e., the inability to conceive (female s.) or to induce conception (male s.). 2. The state of being aseptic, or free from microorganisms. [EU]

Stimulant: 1. Producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. An agent or remedy that produces stimulation. [EU]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stomatitis: Inflammation of the oral mucosa, due to local or systemic factors which may involve the buccal and labial mucosa, palate, tongue, floor of the mouth, and the gingivae. [EU]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Stroma: The middle, thickest layer of tissue in the cornea. [NIH]

Stromal: Large, veil-like cell in the bone marrow. [NIH]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subclinical: Without clinical manifestations; said of the early stage(s) of an infection or other disease or abnormality before symptoms and signs become apparent or detectable by clinical examination or laboratory tests, or of a very mild form of an infection or other disease or abnormality. [EU]

Submaxillary: Four to six lymph glands, located between the lower jaw and the submandibular salivary gland. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

Sulfates: Inorganic salts of sulfuric acid. [NIH]

Sulfur: An element that is a member of the chalcogen family. It has an atomic symbol S, atomic number 16, and atomic weight 32.066. It is found in the amino acids cysteine and methionine. [NIH]

Sulfuric acid: A strong acid that, when concentrated is extemely corrosive to the skin and mucous membranes. It is used in making fertilizers, dyes, electroplating, and industrial explosives. [NIH]

Supportive care: Treatment given to prevent, control, or relieve complications and side effects and to improve the comfort and quality of life of people who have cancer. [NIH]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Surfactant: A fat-containing protein in the respiratory passages which reduces the surface tension of pulmonary fluids and contributes to the elastic properties of pulmonary tissue. [NIH]

Survival Rate: The proportion of survivors in a group, e.g., of patients, studied and followed over a period, or the proportion of persons in a specified group alive at the beginning of a time interval who survive to the end of the interval. It is often studied using life table methods. [NIH]

Sympathetic Nervous System: The thoracolumbar division of the autonomic nervous system. Sympathetic preganglionic fibers originate in neurons of the intermediolateral column of the spinal cord and project to the paravertebral and prevertebral ganglia, which in turn project to target organs. The sympathetic nervous system mediates the body's response to stressful situations, i.e., the fight or flight reactions. It often acts reciprocally to the parasympathetic system. [NIH]

Symphysis: A secondary cartilaginous joint. [NIH]

Synaptic: Pertaining to or affecting a synapse (= site of functional apposition between neurons, at which an impulse is transmitted from one neuron to another by electrical or chemical means); pertaining to synapsis (= pairing off in point-for-point association of homologous chromosomes from the male and female pronuclei during the early prophase of meiosis). [EU]

Synaptic Transmission: The communication from a neuron to a target (neuron, muscle, or secretory cell) across a synapse. In chemical synaptic transmission, the presynaptic neuron

releases a neurotransmitter that diffuses across the synaptic cleft and binds to specific synaptic receptors. These activated receptors modulate ion channels and/or second-messenger systems to influence the postsynaptic cell. Electrical transmission is less common in the nervous system, and, as in other tissues, is mediated by gap junctions. [NIH]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Syphilis: A contagious venereal disease caused by the spirochete Treponema pallidum. [NIH]

Systemic: Affecting the entire body. [NIH]

Taxanes: Anticancer drugs that inhibit cancer cell growth by stopping cell division. Also called antimitotic or antimicrotubule agents or mitotic inhibitors. [NIH]

Technetium: The first artificially produced element and a radioactive fission product of uranium. The stablest isotope has a mass number 99 and is used diagnostically as a radioactive imaging agent. Technetium has the atomic symbol Tc, atomic number 43, and atomic weight 98.91. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Telomerase: Essential ribonucleoprotein reverse transcriptase that adds telomeric DNA to the ends of eukaryotic chromosomes. Telomerase appears to be repressed in normal human somatic tissues but reactivated in cancer, and thus may be necessary for malignant transformation. EC 2.7.7.-. [NIH]

Temporal: One of the two irregular bones forming part of the lateral surfaces and base of the skull, and containing the organs of hearing. [NIH]

Teratogenic: Tending to produce anomalies of formation, or teratism (= anomaly of formation or development : condition of a monster). [EU]

Teratoma: A type of germ cell tumor that may contain several different types of tissue, such as hair, muscle, and bone. Teratomas occur most often in the ovaries in women, the testicles in men, and the tailbone in children. Not all teratomas are malignant. [NIH]

Terminator: A DNA sequence sited at the end of a transcriptional unit that signals the end of transcription. [NIH]

Testicles: The two egg-shaped glands found inside the scrotum. They produce sperm and male hormones. Also called testes. [NIH]

Testis: Either of the paired male reproductive glands that produce the male germ cells and the male hormones. [NIH]

Testosterone: A hormone that promotes the development and maintenance of male sex characteristics. [NIH]

Thalamic: Cell that reaches the lateral nucleus of amygdala. [NIH]

Thalamic Diseases: Disorders of the centrally located thalamus, which integrates a wide range of cortical and subcortical information. Manifestations include sensory loss, movement disorders; ataxia, pain syndromes, visual disorders, a variety of neuropsychological conditions, and coma. Relatively common etiologies include cerebrovascular disorders; craniocerebral trauma; brain neoplasms; brain hypoxia; intracranial hemorrhages; and infectious processes. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermal: Pertaining to or characterized by heat. [EU]

Thigh: A leg; in anatomy, any elongated process or part of a structure more or less

comparable to a leg. [NIH]

Third Ventricle: A narrow cleft inferior to the corpus callosum, within the diencephalon, between the paired thalami. Its floor is formed by the hypothalamus, its anterior wall by the lamina terminalis, and its roof by ependyma. It communicates with the fourth ventricle by the cerebral aqueduct, and with the lateral ventricles by the interventricular foramina. [NIH]

Thorax: A part of the trunk between the neck and the abdomen; the chest. [NIH]

Threshold: For a specified sensory modality (e. g. light, sound, vibration), the lowest level (absolute threshold) or smallest difference (difference threshold, difference limen) or intensity of the stimulus discernible in prescribed conditions of stimulation. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thymidine: A chemical compound found in DNA. Also used as treatment for mucositis. [NIH]

Thymidine Kinase: An enzyme that catalyzes the conversion of ATP and thymidine to ADP and thymidine 5'-phosphate. Deoxyuridine can also act as an acceptor and dGTP as a donor. (From Enzyme Nomenclature, 1992) EC 2.7.1.21. [NIH]

Thymidine Phosphorylase: The enzyme catalyzing the transfer of 2-deoxy-D-ribose from thymidine to orthophosphate, thereby liberating thymidine. EC 2.4.2.4. [NIH]

Thymidylate Synthase: An enzyme of the transferase class that catalyzes the reaction 5,10-methylenetetrahydrofolate and dUMP to dihydrofolate and dTMP in the synthesis of thymidine triphosphate. (From Dorland, 27th ed) EC 2.1.1.45. [NIH]

Thymosin: A family of heat-stable, polypeptide hormones secreted by the thymus gland. Their biological activities include lymphocytopoiesis, restoration of immunological competence and enhancement of expression of T-cell characteristics and function. They have therapeutic potential in patients having primary or secondary immunodeficiency diseases, cancer or diseases related to aging. [NIH]

Thymus: An organ that is part of the lymphatic system, in which T lymphocytes grow and multiply. The thymus is in the chest behind the breastbone. [NIH]

Thymus Gland: A single, unpaired primary lymphoid organ situated in the mediastinum, extending superiorly into the neck to the lower edge of the thyroid gland and inferiorly to the fourth costal cartilage. It is necessary for normal development of immunologic function early in life. By puberty, it begins to involute and much of the tissue is replaced by fat. [NIH]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyroid Gland: A highly vascular endocrine gland consisting of two lobes, one on either side of the trachea, joined by a narrow isthmus; it produces the thyroid hormones which are concerned in regulating the metabolic rate of the body. [NIH]

Thyroid Hormones: Hormones secreted by the thyroid gland. [NIH]

Thyrotropin: A peptide hormone secreted by the anterior pituitary. It promotes the growth of the thyroid gland and stimulates the synthesis of thyroid hormones and the release of thyroxine by the thyroid gland. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [NIH]

Tin: A trace element that is required in bone formation. It has the atomic symbol Sn, atomic number 50, and atomic weight 118.71. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tissue Culture: Maintaining or growing of tissue, organ primordia, or the whole or part of an organ in vitro so as to preserve its architecture and/or function (Dorland, 28th ed). Tissue culture includes both organ culture and cell culture. [NIH]

Tomography: Imaging methods that result in sharp images of objects located on a chosen plane and blurred images located above or below the plane. [NIH]

Topical: On the surface of the body. [NIH]

Topoisomerase inhibitors: A family of anticancer drugs. The topoisomerase enzymes are responsible for the arrangement and rearrangement of DNA in the cell and for cell growth and replication. Inhibiting these enzymes may kill cancer cells or stop their growth. [NIH]

Topotecan: An antineoplastic agent used to treat ovarian cancer. It works by inhibiting DNA topoisomerase. [NIH]

Total-body irradiation: Radiation therapy to the entire body. Usually followed by bone marrow or peripheral stem cell transplantation. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxicology: The science concerned with the detection, chemical composition, and pharmacologic action of toxic substances or poisons and the treatment and prevention of toxic manifestations. [NIH]

Toxins: Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

Toxoplasmosis: The acquired form of infection by Toxoplasma gondii in animals and man. [NIH]

Trace element: Substance or element essential to plant or animal life, but present in extremely small amounts. [NIH]

Tracer: A substance (such as a radioisotope) used in imaging procedures. [NIH]

Trachea: The cartilaginous and membranous tube descending from the larynx and branching into the right and left main bronchi. [NIH]

Transcriptase: An enzyme which catalyses the synthesis of a complementary mRNA molecule from a DNA template in the presence of a mixture of the four ribonucleotides (ATP, UTP, GTP and CTP). [NIH]

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

Transfer Factor: Factor derived from leukocyte lysates of immune donors which can transfer both local and systemic cellular immunity to nonimmune recipients. [NIH]

Transgenes: Genes that are introduced into an organism using gene transfer techniques. [NIH]

Translation: The process whereby the genetic information present in the linear sequence of ribonucleotides in mRNA is converted into a corresponding sequence of amino acids in a

protein. It occurs on the ribosome and is unidirectional. [NIH]

Translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Translocate: The attachment of a fragment of one chromosome to a non-homologous chromosome. [NIH]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Trauma: Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

Treatment Failure: A measure of the quality of health care by assessment of unsuccessful results of management and procedures used in combating disease, in individual cases or series. [NIH]

Treatment Outcome: Evaluation undertaken to assess the results or consequences of management and procedures used in combating disease in order to determine the efficacy, effectiveness, safety, practicability, etc., of these interventions in individual cases or series. [NIH]

Triad: Trivalent. [NIH]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [NIH]

Tuberous Sclerosis: A rare congenital disease in which the essential pathology is the appearance of multiple tumors in the cerebrum and in other organs, such as the heart or kidneys. [NIH]

Tubulin: A microtubule subunit protein found in large quantities in mammalian brain. It has also been isolated from sperm flagella, cilia, and other sources. Structurally, the protein is a dimer with a molecular weight of approximately 120,000 and a sedimentation coefficient of 5.8S. It binds to colchicine, vincristine, and vinblastine. [NIH]

Tumor marker: A substance sometimes found in an increased amount in the blood, other body fluids, or tissues and which may mean that a certain type of cancer is in the body. Examples of tumor markers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). Also called biomarker. [NIH]

Tumor model: A type of animal model which can be used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Tumor suppressor gene: Genes in the body that can suppress or block the development of cancer. [NIH]

Tumorigenic: Chemical, viral, radioactive or other agent that causes cancer; carcinogenic. [NIH]

Tumour: 1. Swelling, one of the cardinal signs of inflammations; morbid enlargement. 2. A new growth of tissue in which the multiplication of cells is uncontrolled and progressive; called also neoplasm. [EU]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

Ubiquitin: A highly conserved 76 amino acid-protein found in all eukaryotic cells. [NIH]

Unconscious: Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

Universal Precautions: Prudent standard preventive measures to be taken by professional and other health personnel in contact with persons afflicted with a communicable disease, to avoid contracting the disease by contagion or infection. Precautions are especially applicable in the diagnosis and care of AIDS patients. [NIH]

Uranium: A radioactive element of the actinide series of metals. It has an atomic symbol U, atomic number 92, and atomic weight 238.03. U-235 is used as the fissionable fuel in nuclear weapons and as fuel in nuclear power reactors. [NIH]

Ureter: One of a pair of thick-walled tubes that transports urine from the kidney pelvis to the bladder. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Urinary: Having to do with urine or the organs of the body that produce and get rid of urine. [NIH]

Urinary tract: The organs of the body that produce and discharge urine. These include the kidneys, ureters, bladder, and urethra. [NIH]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Urogenital: Pertaining to the urinary and genital apparatus; genitourinary. [EU]

Uterus: The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb. [NIH]

Vaccination: Administration of vaccines to stimulate the host's immune response. This includes any preparation intended for active immunological prophylaxis. [NIH]

Vaccine: A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

Vaccinia: The cutaneous and occasional systemic reactions associated with vaccination using smallpox (variola) vaccine. [NIH]

Vaccinia Virus: The type species of Orthopoxvirus, related to cowpox virus, but whose true origin is unknown. It has been used as a live vaccine against smallpox. It is also used as a vector for inserting foreign DNA into animals. Rabbitpox virus is a subspecies of vaccinia virus. [NIH]

Vagina: The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

Vaginal: Of or having to do with the vagina, the birth canal. [NIH]

Vaginal Discharge: A common gynecologic disorder characterized by an abnormal, nonbloody discharge from the genital tract. [NIH]

Vaginitis: Inflammation of the vagina characterized by pain and a purulent discharge. [NIH]

Valine: A branched-chain essential amino acid that has stimulant activity. It promotes muscle growth and tissue repair. It is a precursor in the penicillin biosynthetic pathway. [NIH]

Variola: A generalized virus infection with a vesicular rash. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vascular endothelial growth factor: VEGF. A substance made by cells that stimulates new blood vessel formation. [NIH]

Vasodilation: Physiological dilation of the blood vessels without anatomic change. For dilation with anatomic change, dilatation, pathologic or aneurysm (or specific aneurysm) is

used. [NIH]

Vector: Plasmid or other self-replicating DNA molecule that transfers DNA between cells in nature or in recombinant DNA technology. [NIH]

Vein: Vessel-carrying blood from various parts of the body to the heart. [NIH]

Venereal: Pertaining or related to or transmitted by sexual contact. [EU]

Venous: Of or pertaining to the veins. [EU]

Ventricle: One of the two pumping chambers of the heart. The right ventricle receives oxygen-poor blood from the right atrium and pumps it to the lungs through the pulmonary artery. The left ventricle receives oxygen-rich blood from the left atrium and pumps it to the body through the aorta. [NIH]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Vesicular: 1. Composed of or relating to small, saclike bodies. 2. Pertaining to or made up of vesicles on the skin. [EU]

Vestibular: Pertaining to or toward a vestibule. In dental anatomy, used to refer to the tooth surface directed toward the vestibule of the mouth. [EU]

Vestibule: A small, oval, bony chamber of the labyrinth. The vestibule contains the utricle and saccule, organs which are part of the balancing apparatus of the ear. [NIH]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Vial: A small bottle. [EU]

Vinblastine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. It is a mitotic inhibitor. [NIH]

Vinca Alkaloids: A class of alkaloids from the genus of apocyanaceous woody herbs including periwinkles. They are some of the most useful antineoplastic agents. [NIH]

Vincristine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

Vinorelbine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viral Load: The quantity of measurable virus in the blood. Change in viral load, measured in plasma, is used as a surrogate marker in HIV disease progression. [NIH]

Viral vector: A type of virus used in cancer therapy. The virus is changed in the laboratory and cannot cause disease. Viral vectors produce tumor antigens (proteins found on a tumor cell) and can stimulate an antitumor immune response in the body. Viral vectors may also be used to carry genes that can change cancer cells back to normal cells. [NIH]

Virion: The infective system of a virus, composed of the viral genome, a protein core, and a protein coat called a capsid, which may be naked or enclosed in a lipoprotein envelope called the peplos. [NIH]

Virulence: The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the tissues of the host. [NIH]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

Viscera: Any of the large interior organs in any one of the three great cavities of the body, especially in the abdomen. [NIH]

Vitro: Descriptive of an event or enzyme reaction under experimental investigation occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

Vivo: Outside of or removed from the body of a living organism. [NIH]

Vulva: The external female genital organs, including the clitoris, vaginal lips, and the opening to the vagina. [NIH]

Wart: A raised growth on the surface of the skin or other organ. [NIH]

Wetting Agents: A surfactant that renders a surface wettable by water or enhances the spreading of water over the surface; used in foods and cosmetics; important in contrast media; also with contact lenses, dentures, and some prostheses. Synonyms: humectants; hydrating agents. [NIH]

White blood cell: A type of cell in the immune system that helps the body fight infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others. [NIH]

Womb: A hollow, thick-walled, muscular organ in which the impregnated ovum is developed into a child. [NIH]

Wound Healing: Restoration of integrity to traumatized tissue. [NIH]

Xenograft: The cells of one species transplanted to another species. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

X-ray therapy: The use of high-energy radiation from x-rays to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. X-ray therapy is also called radiation therapy, radiotherapy, and irradiation. [NIH]

Yeasts: A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

Zoonoses: Diseases of non-human animals that may be transmitted to man or may be transmitted from man to non-human animals. [NIH]

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