Herpes Virus

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 herpes virus 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 herpes virus, 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 herpes virus, 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 herpes virus. 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 herpes virus, 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 herpes virus.

The Editors

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

CHAPTER 1. STUDIES ON HERPES VIRUS

Overview

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

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and herpes virus, 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 "herpes virus" (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:

- **Skin Manifestations Related to HIV**

  Source: STEP Perspective; Vol. 4, No. 2.

  Contact: Seattle Treatment Education Project, 1123 E John St, Seattle, WA, 98102, (206) 329-4857, http://www.thebody.com/step/steppage.html.

  Summary: Afflictions of the skin are a serious concern for HIV-infected people. This article discusses the most commonly seen skin conditions and ways to treat them. These include seborrheic dermatitis, a dandruff-like skin condition affecting the scalp, face, chest, back, groin, and armpits. Individuals who have recurrent episodes of seborrheic dermatitis may benefit from using dandruff shampoo as a body wash. Psoriasis often occurs after HIV infection. The initial lesions often begin like seborrheic dermatitis but spread to the armpits, groin, elbows, knees, and lower back. Significant improvement is

often seen after using AZT at higher doses and from phototherapy. Herpes simplex virus is a common infection among people with HIV. Because the **herpes virus** contributes to immune suppression, many physicians prescribe oral acyclovir as a prophylaxis. Herpes zoster, or shingles, is common in people with HIV. Acyclovir is used in an intravenous form to treat the shingles, as are topical creams. Molluscum contagiosum is a viral infection producing lesions that can appear anywhere on the body. Treatment includes topical ointments, AZT, and retinoic acid. Human Papillomavirus (HPV) causes warts that are treated with cryotherapy, electrocautery, excision, or injections of alpha interferon. Xeroderma is a dry skin condition treated with oil and lotions. Folliculitis can be found around hair follicles and responds well to ketoconazole treatment. Bacillary angiomatosis appears as papules or nodules and often resembles Kaposi's sarcoma. Treatment includes a 3- to 4-week regimen of antibiotic. A review of photodermatitis, insect bite reactions, drug reactions, nail disorders, and hair changes conclude the article.

- **Fulminant Herpes Hepatitis in a Healthy Adult: A Treatable Disorder?**

  Source: Journal of Clinical Gastroenterology. 28(4): 386-389. June 1999.

  Contact: Available from Lippincott-Raven Publishers. P.O. Box 1550, Hagerstown, MD 21741. (800) 638-3030 or (301) 714-2300.

  Summary: Hepatitis arising from herpes simplex virus (HSV) is a potentially fatal disorder that is often not considered in the differential diagnosis of acute hepatitis. This disease occurs most often in patients with impaired immunity and is very uncommon in healthy people. HSV hepatitis presents with a wide clinical spectrum, and the clinical diagnosis is difficult. This article describes a case of disseminated **herpes virus** infection with fulminant hepatitis mimicking an acute human immunodeficiency virus (HIV) infection in a 33 year old healthy man. Preliminary studies suggest that early treatment of HSV hepatitis with acyclovir may be beneficial in these patients. A high index of suspicion and the availability of early diagnostic tools, such as HSV DNA detection, may dramatically improve the clinical outcome of severe HSV hepatitis, which is potentially treatable. Indeed, among five patients treated with acyclovir, four survived, compared with an 80 percent mortality rate among untreated cases. Although these data are uncontrolled and retrospective, they strongly suggest that acyclovir treatment may be life saving, provided an early diagnosis is made. 3 figures. 24 references. (AA-M).

- **Transmission of Human Herpesvirus 8 Infection from Renal-Transplant Donors to Recipients**

  Source: New England Journal of Medicine. 339(19): 1358-1363. November 5, 1998.

  Summary: Human **herpes virus** 8 (HHV 8) has been detected in all forms of Kaposi's sarcoma, including transplantation associated Kaposi's sarcoma. This article reports on a study undertaken to investigate the possibility of transmission of HHV 8 through allografts, in which the authors measured the seroprevalence of HHV 8 before and after renal transplantation. The authors analyzed serum samples from 220 renal transplant recipients for the presence of antibodies to HHV 8 on the day of transplantation and 1 year later. Positive results were confirmed by an indirect immunofluorescence assay that detects antibodies to latent antigen and by Western blotting. Followup lasted at least 4 years. The seroprevalence of HHV 8 in graft recipients increased from 6.4 percent on the day of transplantation to 17.7 percent 1 year after transplantation. Seroconversion occurred within the first year after transplantation in 25 patients, and Kaposi's sarcoma developed in 2 of them within 26 months after transplantation. Sequential serum

samples were obtained from 10 of the patients with seroconversion, and in 8 of these patients, IgM antibodies to HHV 8 appeared within 3 months after transplantation. In the case of six patients who seroconverted, serum samples from the donors were available, and five (83 percent) tested positive for HHV 8. In a control group of eight patients who were seronegative at the time of transplantation and who received allografts from HHV 8 negative donors, none seroconverted within the year after transplantation. The authors conclude that HHV 8 is transmitted through renal allografts and is a risk factor for transplantation associated Kaposi's sarcoma. 2 figures. 2 tables. 24 references. (AA-M).

- **Classic Kaposi's Sarcoma of the Tongue: Case Report with Emphasis on the Differential Diagnosis**

  Source: Journal of Oral and Maxillofacial Surgery. 60(8): 951-954. August 2002.

  Contact: Available from W.B. Saunders Company. Periodicals Department, P.O. Box 629239, Orlando, FL 32862-8239. (800) 654-2452. Website: www.harcourthealth.com.

  Summary: Kaposi's sarcoma (KS) is a well-known malignant vascular tumor that shows a high prevalence in immunocompromised patients, mainly in those with AIDS. Currently, there is strong evidence that KS is caused by the human **herpes virus** VIII (HHV-8). KS is usually classified as classic or Mediterranean, endemic or African, posttransplant, and epidemic or AIDS-associated KS. In all of the clinical forms, the histopathological and immunohistochemical features are similar. This article reports a recently diagnosed, unusual case of classic KS affecting the tongue of a nonimmunocompromised European white elderly woman. The authors emphasize the main clinical and pathologic differential diagnosis. Oral KS in immunocompetent patients is rare and is often clinically misdiagnosed as pyogenic granuloma or another benign vascular lesion. 3 figures. 14 references.

- **Strategies for Management of Commonly Encountered Oral Mucosal Disorders**

  Source: CDA Journal. Journal of the California Dental Association. 27(3): 210-212, 215, 218-219, 221-227. March 1999.

  Contact: Available from California Dental Association (CDA). 1201 K Street, Sacramento, CA 95814. (916) 443-0505.

  Summary: Oral mucosal disorders are frequently encountered by the practicing dentist. These lesions may represent oral manifestations of dermatologic or systemic disease, reactive lesions, or occult neoplasms. The diagnosis of these conditions is usually based on case specific historical findings, clinical appearance, and the results of diagnostic procedures. This article discusses the diagnosis and management of commonly occurring oral mucosal conditions such as candidosis, recurrent aphthous ulceration, **herpes virus** infection, and lichen planus. The article represents a synthesis of the literature and the management approach utilized by the author. The author stresses that management of painful oral mucosal conditions may be either topical or systemic. Oral therapy should address patient nutrition and hydration, oral discomfort, oral hygiene, and management of secondary infection, as well as local control of the disease process. Depending on the extent, severity, and location of oral lesions, consideration should be given to obtaining a consultation from a dentist who specializes in oral medicine, oral pathology, oral surgery, or periodontics. 8 figures. 6 tables. 35 references.

- **Complicating Mucosal Reactions in Patients Receiving Radiation Therapy for Head and Neck Cancer**

  Source: SCD. Special Care in Dentistry. 17(8): 88-93. May-June 1997.

  Summary: The oral sequelae resulting from head and neck radiotherapy may include mucositis, hyposalivation, taste loss, radiation caries, osteonecrosis, and trismus. Radiation mucositis is characterized by erythema, pseudomembranes, and ulceration of mucosa in the irradiated field. In this article, the authors present two cases of oral mucosal changes in patients treated with radiotherapy in the head and neck region, which included mucosal erythema and ulceration outside of the radiated fields. One case was confirmed as **herpes virus** infection, and the other was diagnosed as Sweet's syndrome. The authors discuss both case histories as well as the possible contribution of Herpes simplex virus (HSV) infection in oral mucositis associated with radiation treatment. The authors stress that, when mucositis extends beyond the radiation fields, the clinician should consider other causes of mucosal inflammation and erythema in order to begin appropriate management. 8 figures. 19 references. (AA-M).

- **Oral Adverse Effects of Medical Management in Patients with HIV Infection**

  Source: AIDS Patient Care. 7(6): 304-311. December 1993.

  Summary: This article explores the oral adverse effects of medical management in patients with HIV infection. The authors discuss the medical management of HIV, the common infections and neoplasms, and the basis of action of the common medications currently used, and their importance in oral care. Specific topics covered include antiretroviral agents, including zidovudine (Retrovir), dideoxyinosine (ddI), dideoxycytidine (ddC); the treatment of penumocystic carinii pneumonia (PCP); mucosal candidiasis; systemic mycoses; **herpes virus** infections; tuberculosis; syphilis; and malignant disease in AIDS, including Kaposi's sarcoma. The authors stress that the alert clinician should be aware of the diagnoses of the patient, the current medical therapy, and implications for oral care, and should alert the patient if untoward symptoms suggesting toxicity are developing. 1 table. 72 references.

- **Cold Sore Comfort**

  Source: POZ. 38-41. April 2001.

  Contact: Available from POZ Publishing, LLC. 349 West 12th Street, New York, NY 10014. (815) 734-4151. E-mail: subscription@poz.com.

  Summary: This article offers information about herpes simplex virus (HSV) and its implications for patients who are living with human immunodeficiency virus (HIV). Transmitted through contact with mucous membranes or small breaks in the skin, herpes (type 1 or 2) is usually marked by red, painful sores on the lips, genitals or anal area, swollen lymph nodes, or flu-like symptoms. After the initial outbreak, HSV takes refuge in the ganglia, the mass of nerve tissue at the base of the vertebrae, waiting to reemerge at a moment of immune stress. For people with HIV, even a dormant virus can be damaging. However, drugs to prevent herpes activity are nontoxic and may also help prevent HIV related lymphoma, a potentially fatal cancer showing up in more and more healthy people with HIV. Herpes' most serious medical consequence for people with HIV may be sustained increases in HIV viral load, though this matter is still subject to some debate. The article discusses the three available antivirals (acyclovir, valacyclovir, and famciclovir) that can help make sores go away faster, prevent outbreaks by suppressing HSV, and suppress Epstein Barr virus (EBV). One sidebar reviews the

family of herpes viruses, to help readers differentiate them; another covers treatment strategies to try in addition to the antiviral drugs when coping with HSV outbreaks. The article concludes with a hotline number from the American Social Health Association (919-361-8488, or www.ashastd.org).

- **Periodontal and Soft-Tissue Abnormalities**

  Source: Dental Clinics of North America. 39(4): 837-850. October 1995.

  Summary: This article reviews periodontal and soft-tissue abnormalities as they may be found in young children. Topics include normal gingival tissues and gingivitis in young children; periodontitis and tooth loss in young children, including that caused by neutropenia, Papillon-Lefevre syndrome, metabolic disorders, histiocytosis X, and hypophosphatasia; congenital lesions; developmental lesions including geographic tongue, fissured tongue, retrocuspid papillae, and gingival fibromatosis; benign tumors, including hemangioma, lymphangioma, mucocele, and fibroma; odontogenic cysts, including parulis, eruption cyst and hematoma; infectious diseases, such as **herpes virus** infection, Coxsackie virus, hand-foot-and-mouth disease, recurrent aphthous ulceration, candidiasis, impetigo, and HIV infection; hematologic diseases, notably leukemias; and factitial injuries. The author recommends periodic review of soft-tissue lesions to help the dental team recognize both common and rare abnormalities affecting young children. 5 figures. 14 references.

- **Viral Infections in the Immunocompetent Patient**

  Source: Dermatologic Clinics. 14(2): 225-241. April 1996.

  Summary: This article, from a series on disorders affecting the oral cavity, provides an update of viral infections that affect children and adults who have normal immunosurveillance. The author focuses on new advances and knowledge regarding the herpes viruses and the human papillomaviruses. Topics include the shedding of herpes simplex virus, recurrent herpes simplex virus Type 1 infections (herpes labialis and recurrent oral herpes), treatment of primary infection, treatment of recurrent infection, erythema multiforme, oral cancer, varicella zoster virus (chickenpox), herpes zoster (shingles), cytomegalovirus (CMV), intrauterine infection with CMV, Epstein-Barr virus (EBV), infectious mononucleosis, chronic fatigue syndrome, lymphoproliferative diseases, Sjogren's syndrome, human herpesvirus 6, human herpesvirus 7, herpes B virus infection, human papillomaviruses, squamous papilloma, verruca vulgaris, condyloma acuminatum, and other human papillomavirus-induced lesions. For each condition, the author describes the clinical presentation, risk factors, and recommended treatment options. The author concludes that, although much is known about human herpes viruses and HPVs, disease eradication will remain challenging for years to come, because latent virus serves as a continual source of reactivated virus that is involved in the development of many oral lesions. 10 figures. 206 references. (AA-M).

- **Viruses in the Etiopathogenesis of Sjogren's Syndrome**

  Source: Journal of Rheumatology. 24(Supp. 50):3-5; September 1997.

  Summary: This journal article for health professionals examines the role of herpes viruses and retroviruses in the etiopathogenesis of Sjogren's syndrome (SS). It reviews studies that have investigated the herpes viruses and retroviruses as etiological agents in SS. Although evidence from these studies is conflicting, herpes viruses could have a role in a subset of the disease. Studies of retroviruses in animals provide support for

their role in SS. However, the strongest evidence linking retroviruses to SS is the similarity between the pathology of SS and that which occurs in human immunodeficiency virus 1 and human T cell lymphotropic virus 1 infection. Studies investigating this association are highlighted. 28 references.

- **Foscarnet - Induced Hypocalcemia and Effect of Foscarnet on Calcium Metabolism**

  Source: Journal of Clinical Endocrinology and Metabolism; Vol. 72, No. 5, May 1991. p. 1130-1135.

  Contact: University of California Positive Health Program, San Francisco General Hospital, AIDS Program, Clinical Research Section, PO Box 0881, San Francisco, CA, 94110-0881, (415) 514-0550.

  Summary: Toscarnet (trisodium phosphonoformate), an investigational pyrophosphate analog increasingly used to treat refractory cytomegalovirus retinitis and mucocutaneous herpes simplex virus infections in immunocompromised patients, has been reported to cause abnormalities in serum calcium and phosphate, including cases of fatal hypocalcemia. To further elucidate the magnitude and mechanism of these abnormalities in humans treated with foscarnet for opportunistic **herpes virus** infections, we analyzed anaerobic serum specimens and 24-h urine samples before and after single and multiple doses of iv foscarnet and performed a series of in vitro experiments with normal human serum and plasma. Plasma ionized calcium concentrations acutely decreased by a mean 0.17 mmol/L in the 6 individuals who received a 90 mg/kg dose of foscarnet and by a mean 0.28 mmol/L in the 11 individuals who received a 120 mg/kg dose (P = 0.016, 90 vs. 120 mg/kg dose). Results of in vitro experiments showed a highly significant inverse linear relationship between foscarnet and ionized calcium concentrations, but no correlation between foscarnet and total calcium or phosphate concentration. Dialysis experiments suggested that the complexing of foscarnet with ionized calcium could be a cause of this ionized hypocalcemia. Physicians must be aware of this phenomenon and should measure serum ionized calcium during foscarnet therapy (preferably at the end of a foscarnet infusion) whenever neurological or cardiological abnormalities occur.

- **Viral Infections After Renal Transplantation**

  Source: American Journal of Kidney Diseases. 37(4): 659-676. April 2001.

  Contact: Available from W.B. Saunders Company. Periodicals Department, 6277 Sea Harbor Drive, Orlando, FL 32887-4800. (800) 654-2452 or (407) 345-4000.

  Summary: Viral infections are a leading cause of morbidity (illness) and mortality (death) in patients who receive renal (kidney) transplants. This article reviews a number of recent developments that have altered the understanding and management of these disorders. The pathogenetic (causative) roles of several viruses, including human herpes viruses 6 and 8, have been newly established. Molecular based diagnostic tests now make more rapid diagnosis possible. The licensing of new potent antiviral agents offers a wider choice of drugs for viral prevention and treatment. The authors caution that the use of more potent immunosuppressive agents (drugs used to prevent the recipient's body from rejecting the transplanted organ) is responsible in part for the increasing incidence of some viral infections, but this varies among drugs, and individual viruses differ in their sensitivity to immunosuppressive agents. The authors summarize the natural history, diagnosis, prevention, and treatment of many common viral infections after renal transplantation. Viral infections discussed include herpes viruses (including varicella zoster virus and Epstein Barr virus), cytomegalovirus, respiratory viruses

(including influenza and adenoviruses), polyomaviruses (small DNA viruses), and parvovirus. The authors also consider the effect of immunosuppressive regimens on the reactivation of viral infections and the role of vaccinations and screening. 3 tables. 103 references.

Federally Funded Research on Herpes Virus

The U.S. Government supports a variety of research studies relating to herpes virus. 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 herpes virus.

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 herpes virus. The following is typical of the type of information found when searching the CRISP database for herpes virus:

- **Project Title: ADULT THERAPEUTIC CLINICAL TRIALS PROGRAM FOR AIDS**

  Principal Investigator & Institution: Eron, Joseph J.; Associate Professor; Medicine; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 30-SEP-1987; Project End 31-DEC-2004

  Summary: (adapted from the application's abstract): The applicants propose to continue their multidisciplinary multi-year research program, that will integrate institutional expertise in infectious diseases, neurology, ophthalmology, gynecology, pharmacology, immunology, retrovirology, herpes viruses, and numerous clinical resources in North Carolina. The main focus is the evaluation of novel therapies for HIV-infected persons. Clinical investigators at the UNC and two satellite units, Greensboro, and Charlotte will study new compounds active against HIV and associated infections, malignancies, and neurologic disorders in new patients and follow previously enrolled patients. This proposes to continue a high rate of accrual among minorities, women, and intravenous (I.V.) drug users. The trials will be of all Phases (I, II, and III) and types. Patients will be followed for in vivo evidence of study drug effects on HIV, Mycobacterium avium intracellular complex (MAC), cytomegalovirus (CMV), herpes simplex virus (HSV), and other opportunistic infections using the ACTG-certified retrovirology and immunology virus laboratory, as well as UNC hospital laboratories. Pharmacokinetics (PK) will be monitored in the General Clinical Research Center (GCRC) and Microbiology and Pharmacology Laboratories. Concepts for new protocols will originate by participation in the Executive, Neurology, and Complications of HIV, HIV Pharmacology and Immunology ACTG committees. The established scientific advisory board (SAB) also

[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).

will be involved in concept development. The UNC group application has new proposals for many trials including the eradication of HIV, simplification of regimens, novel therapies, improving adherence and immune restoration. Outreach to the community may be accomplished through the community advisory boards (CAB) at each site, the website and through a statewide newsletter. Finally, low protocol costs may be maintained by cost sharing with NIH grants (GCRC, Pediatric ACTU, Center for AIDS Research (CFAR), as well as with UNC Hospitals, and the Departments of Medicine, Neurology, Ophthalmology, Microbiology and School of Pharmacy.

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

- **Project Title: ALPHA HERPESVIRUS INFECTIONS OF THE NERVOUS SYSTEM**

  Principal Investigator & Institution: Enquist, Lynn W.; Professor; Princeton University 4 New South Building Princeton, Nj 085440036

  Timing: Fiscal Year 2002

  Summary: The objective of the proposed research is a systematic analysis of host and viral gene expression after alpha-herpesvirus infection of the mammalian nervous system. The Specific Aims are (i) using gene array technology, I will compare cellular gene expression in primary cultures of sympathetic and sensory ganglionic neurons after infection by Herpes simplex virus type 1 (HSV-1) or pseudorabies virus (PRV). HSV-1 and PRV are two related alpha-herpesviruses able to invade and spread in the nervous system of the rat, a common host. These experiments will test the hypothesis that these diverse herpes viruses influence expression of a common set of cellular genes during acute infection. In addition, I will search for common response after infection of the functionally distinct neurons of sympathetic or sensory ganglia. (ii) I will analyze host and viral gene expression after infection of primary neuronal cultures by selected attenuated PRV and HSV-1 strains in an attempt to define the cellular responses involved in the mechanisms that attenuate these mutant viruses. (iii) I will analyze host and viral gene expression after direct infection of the CNS by PRV and HSV-1. The goal is to determine if discernible patterns of gene expression can be deduced from the many highly interconnected CNS cell types that are infected and infected. By comparing the results obtained from infection of pure neuronal cultures to results obtained from the complicated milieu of infected tissue, I seek to define key pathways of viral and host gene expression that characterize an acute CNS infection. Such information is essential to understand the interplay the infected neurons and uninfected supporting glial cells in limiting CNS pathology in a living animal. The information obtained in this study will be used to compare and contrast the host and viral response to infection by other herpesviruses.

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

- **Project Title: AMYGDALAR NEUROPEPTIDES AND ANXIETY**

  Principal Investigator & Institution: Wilson, Marlene A.; Professor; Pharmacology, Physiology and Neuroscience; University of South Carolina at Columbia Byrnes Bldg., Room 501 Columbia, Sc 29208

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-AUG-2007

  Summary: (provided by applicant): The amygdala is a brain structure that plays a crucial role in fear and anxiety, and the actions of anxiety-reducing compounds. The opioid peptide has also been shown to modulate anxiety-related responses within the amygdala. Using herpes virus-mediated gene transfer, we have demonstrated that overexpression of enkephalin in the amygdala enhances the anxiety-reducing influences

of the benzodiazepine diazepam (Valium) in rats. These initial results demonstrate that herpes virus-mediated gene transfer can transiently alter expression of neuropeptides in confined brain sites of adult rats, and that these changes can modify behavioral responses. The present studies continue to utilize this powerful technique to examine the role of amygdalar enkephalin in regulating anxiety-related behaviors and the actions of anxiolytic drugs. Both decreases and cell-targeted increases in peptide expression will be examined in several animal models of anxiety. Aim 1 will verify the ability of virus-mediated gene transfer to decrease and cell-specifically increase expression of enkephalin in select areas of amygdala. Anatomical and quantitative methods will assess changes in mRNA expression, while peptide changes will be assessed with immunohistochemistry and radioimmunoassay. AIM 2 examines if altered enkephalin expression in central amygdala modifies anxiety-related behaviors in additional animal tests of anxiety behaviors and/or the effectiveness of other anxiolytics in these tests. These studies 1) compare decreases with cell-specific increases in enkephalin expression, 2) test the activity of other anxiolytics (alcohol, the serotonergic compound buspirone), and 3) tests effects in several models of anxiety. AIM 3 assesses the effects of pharmacological modulation of enkephalin activity in amygdala. Using more traditional techniques selective opioid receptor (mu, delta) agonists and antagonists will be locally applied in amygdala, and the effect of these compounds on responses to anxiolytic drugs will be tested. These studies will lead to a better understanding of the role of amygdala and enkephalin in anxiety and anxiolytic responses, as well as elucidate the differences between animal models of anxiety. This understanding may also suggest novel, avenues for development of treatments for anxiety or affective disorders.

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- **Project Title: ANTIVIRAL MEDIATED APOPTOSIS OF NON HODGKIN'S LYMPHOMA**

  Principal Investigator & Institution: Harrington, William J.; Professor; Medicine; University of Miami-Medical Box 248293 Coral Gables, Fl 33124

  Timing: Fiscal Year 2002; Project Start 01-APR-2000; Project End 31-MAR-2003

  Summary: (Applicant's Abstract) The applicant has found that certain high grade **Herpes virus** associated lymphomas are sensitive to anti-viral mediated apoptosis in vitro and in vivo. Epstein-Barr Virus positive Burkitt's lymphoma and Human **Herpes Virus** Type 8 related Primary Effusion Lymphomas undergo apoptosis when cultured in the presence of Azidothymidine (AZT) or AZT and Interferon Alpha (IFN Alpha). He has investigated the mechanisms by which this therapy causes apoptosis in these lymphoma subtypes. He has found that incubation of Burkitt's lymphoma cells with AZT results in upregulation of CD95 and apoptosis. Primary Effusion Lymphoma requires Interferon Alpha to potentiate AZT mediated apoptosis. He has also found that Interferon Alpha induces the death receptor ligands, TRAIL and Fas Ligand in B cell lymphomas. In contrast to Burkitt's lymphoma and Primary Effusion Lymphoma, EBV positive large cell immunoblastic lymphomas and Epstein-Barr virus negative lymphomas were resistant to AZT and Interferon Alpha. These initial findings indicate that some lymphomas might be selectively sensitive to anti-viral therapy. In susceptible lymphomas, AZT and Interferon Alpha mediated apoptosis does not occur solely through Fas/Fas-Ligand interaction and likely involves activation of additional mechanisms of apoptosis. The applicant will investigate the role of viral and cellular pro- and anti-apoptotic proteins in blocking or facilitating AZT and Interferon Alpha induction of apoptosis in primary lymphoma specimens and cell lines developed from

these tumors. A mechanism of inducing apoptosis in aggressive lymphomas would benefit patients with these diseases.

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

- **Project Title: B CELL SIGNALING BY THE EBV TRANSFORMING PROTEIN, LMP1**

  Principal Investigator & Institution: Bishop, Gail A.; Professor; Microbiology; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2003; Project Start 07-MAR-2003; Project End 29-FEB-2008

  Summary: (provided by applicant): Greater than 90% of the world's population is infected with the human **herpes virus** Epstein-Barr virus (EBV), which establishes latency in B lymphocytes. In immunocompromised individuals, reactivation of latent EBV in the absence of normal immune control can result in the development or B cell lymphoma. Among the EBV-encoded proteins implicated in lymphomagenesis, considerable attention has focused upon latent membrane protein-1 (LMP1), the only EBV-produced protein that can directly transform cells in culture; LMP1- mutant viruses cannot transform B cells. Our lab studies CD40, a member of the tumor necrosis factor receptor (TNF-R) family expressed on B cells, macrophages, and dendritic cells that induces B cell proliferation, isotype switching, and upregulation of surface molecules involved in antigen presentation. We became very interested in LMP 1 upon learning that this viral protein interacts with certain cytoplasmic adapter proteins (TNF-R associated factors, or TRAFs), previously characterized as only binding to TNF-R family molecules, such as CD40. We found that LMP1 signals in B cells mimic CD40 to a striking extent. However, when we directly compare signaling to B cells by the two molecules, LMP 1 signals occur more rapidly, and are amplified and sustained compared to those delivered through CD40. These differences map to the cytoplasmic (CY) domains of the two molecules, and correlate with the ability of CD40 to induce TRAF degradation, an ability that LMP1 lacks. In the present proposal we wish to determine the molecular basis for differences between CD40 and LMP1 signaling, and how these affect B cell behavior. Our specific goals and the questions to be addressed are as follows: Aim 1. What is the molecular basis for differences in signaling between LMP 1 and its normal cellular counterpart, CD40? A. What is the role of the reduced binding affinity of TRAF2 for LMP1, compared to CD40, in the failure of LMP1 to induce TRAF2 and 3 degradation? B. Does association of TRAF6 with CD40, but not LMP 1, contribute to signaling differences between the two molecules? C. How do the signaling pathways of LMP 1 and CD40 show differential dependence upon distinct TRAFs? Aim 2. How do signaling differences between LMP1 and CD40 affect the function of B cells in the intact animal? A. What is the phenotype of antigen-presenting cells in mice expressing Wt CD40 versus CD40 with an LMP1 cytoplasmic domain? B. How does the humoral response to T-dependent (TD) and T-independent (TI) antigens compare in WtmCD40tg and mCD40LMP 1tg mice? C. What are the characteristics of TRAF association and regulation with CD40 and CD40-LMP1 in cells from transgenic mice expressing these receptors? D. How do differences in TRAF association between LMP1 and CD40 affect the B cell response? Aim 3. What is the effect of signaling via the LMP 1 cytoplasmic domain on autoimmune responses? A. What is the relationship between LMP 1 signals and autoantibody production? B. How does LMP1 expression affect the development and progression of autoimmune disease?

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

- **Project Title: CHARACTERIZATION SIGNAL TRANSDUCTION IN KAPOSIS SARCOMA**

  Principal Investigator & Institution: Ganju, Ramesh K.; Assistant Professor; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

  Timing: Fiscal Year 2002; Project Start 01-FEB-1998; Project End 30-NOV-2002

  Summary: (Adapted from applicant's abstract): Kaposi's sarcoma (KS) is the major neoplastic manifestation of AIDS. Prior data indicate that KS spindle cell growth and spread can be driven by cytokines like IL-6, oncostatin M, VEGF and bFGF as well as the HIV gene product TAT. HIV-1 TAT can bind to the FLK-1/KDR receptor for the vascular endothelial growth factor (VEGF), and contains a classical RGD sequence which may activate surface integrin receptors for fibronectin and vitronectin. Furthermore, the Kaposi's sarcoma **herpes virus** (KSHV)/human **herpes virus** type 8 (HHV-8) appears to be a "molecular pirate" whose open reading frames encode homologs of IL-6, the chemokine MIP1 and an activated IL-8 chemokine receptor. Despite extensive studies on modulation of KS cell growth by these soluble mediators, relatively little is known about their signal transduction pathways. To that end, we have begun to characterize cytokine, chemokine and TAT signaling pathways in a permanent KS spindle cell line with authentic properties of primary cells. We observed that the related adhesion focal tyrosine kinase (RAFTK), a newly discovered signaling molecule, prominently participates in all three pathways, and transmits signals to the transcriptional apparatus and the cytoskeleton. Our overall aim is to characterize signal transduction pathways in KS spindle cells that mediate their growth and spread using RAFTK as a primary focus of study. We are assisted in these studies by having specific reagents against RAFTK as well as dominant-negative RAFTK mutants. We will seek first to identify the signaling molecules that associate with cytokine, chemokine and TAT surface receptors, then study how these molecules connect to RAFTK, and proceed to characterize mediators downstream of RAFTK which lead to cytoskeletal and transcriptional activation. This structured approach to characterize cytokine, chemokine and TAT signaling pathways and their functional roles in KS spindle cells should provide insight into the mechanisms of KS growth and spread.

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

- **Project Title: CONTROL OF VESICULAR TRAFFICKING IN THE HEPATOCYTE**

  Principal Investigator & Institution: Wolkoff, Allan W.; Professor of Medicine; Yeshiva University 500 W 185Th St New York, Ny 10033

  Timing: Fiscal Year 2002; Project Start 15-MAY-1990; Project End 31-MAR-2007

  Summary: (provided by applicant): In previous studies, we provided evidence that the cytoskeleton provides an important organizational component of receptor-mediated endocytosis in hepatocytes. In particular, receptor-mediated endocytosis of asialoorosomucoid (ASOR) by hepatocytes results in formation of early endocytic vesicles that undergo fission, with one daughter vesicle that contains most of the receptor recycling back to the cell surface, while the other daughter vesicle that contains most of the ligand, trafficking to the lysosome where ligand is degraded. During the past funding period, we showed that endocytic vesicles bind to and move along microtubules. We (reconstituted this process as well as the process of early endocytic vesicle fission and segregation in vitro using a novel fluorescence microscopy system that we developed. These studies showed that kinesins, both plus and minus-end directed, provided the force for this process. We now propose to extend these studies to dissect mechanistically those cellular components that are required for vesicle

processing. This will include studies in which these events have been reconstituted from well-defined subcellular constituents. We will utilize similar technology to continue our mechanistic studies of **Herpes virus** egress. In the previous funding period we developed assays to monitor both the assembly of enveloped HSV particles and their traffic through the hepatocyte cytoplasm. We also established techniques to enable the isolation of HSV-containing cytoplasmic organelles from infected HuH-7 cells. These techniques should enable us to extend these studies to the Trfl and Trfl trafficking mutants. The Specific Aims of this application are: (1) to characterize endosome/microtubule interaction and motility at specific stages of the endocytic process and to determine and quantify direction of motility, motors, and accessory regulatory proteins; (2) to reconstitute endocytic vesicle motility and fission from defined components in vitro and to determine the regulatory role of phosphorylation in these processes; and (3) to examine the cellular components that are required for trafficking of Herpes simplex virus (HSV) from the nucleus to the cell surface.

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- **Project Title: CONTROL OF VIRAL RNA SYNTHESIS IN HERPES VIRUS INFECTION**

  Principal Investigator & Institution: Wagner, Edward K.; Professor of Virology; Molecular Biology and Biochem; University of California Irvine Irvine, Ca 926977600

  Timing: Fiscal Year 2002; Project Start 15-MAY-1978; Project End 31-JAN-2006

  Summary: The differential stability of interactions between kinetic classes of HSV promoters and the basal transcriptional machinery of the cell combined with virus-mediated compartmentalization of transcription machinery does much to explain the selective expression and repression of various kinetic classes of viral genes during the different phases of the productive replication cycle. We will expand and validate this model by accomplishing the following: 1. Analyze the biochemical interaction between a class of strict late promoters that contain a downstream activating sequence (DAS), as exemplified by the UL38 promoter, and the DNA binding subunits (Ku) of the multifunctional cellular enzyme DNA-dependant phosphokinase (DNA-PK). A major feature of this investigation will be the use of cultured cells in which components of DNA-PK have been functionally deleted, and purified TFIID. 2. Choose model promoters to investigate other modes that HSV utilizes to directly stabilize the interaction between late promoters and the TFIID complex. HSV DNA micro-arrays will be developed for this study. 3. Investigate how the kinetic class-specific promoter structure of HSV transcripts influences the strength of binding of the pre-initiation complex to influence time of maximal expression. We will use purified TFIID for biochemical studies, as well as in situ hybridization methods for analysis of differential gene expression in individual cells. 4. Use cell culture and mouse pathogenesis models to study of the precise role of time and level of maximal expression of selected required viral genes. This work has been started with viruses expressing kinetic alterations in the major capsid protein (VP5). We will also study kinetic modifications of expression of the VP19 capsid protein, the virion trans- activating protein, and the immediate-early ICP 27 promoter.

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- **Project Title: CORE--LABORATORY**

  Principal Investigator & Institution: Coombs, Robert W.; Associate Professor; University of Washington Grant & Contract Services Seattle, Wa 98105

Timing: Fiscal Year 2002

Summary: The purpose of the Laboratory Core is to provide virology laboratory support and services for the three Research Projects. Specifically, these services include screening to determine eligibility requirements, supervising the collection of specimens for monitoring virological markers of disease progression and regression of CMV, HSV and HIV. These studies will be conducted through the Laboratory Core at the University of Washington, the University of Rochester and the University of Nairobi. In addition, should the need arise over the course of the Program Project. Viral DNA detection procedures for studies of opportunistic infections in HIV-infected women due to the hepatitis C virus **herpes virus** type 6 (HHV-6) and type 8 (HHV-8/HKSV) are available in the Virology Division at the University of Washington. A diverse virological laboratory base is important for elucidating the pathogenesis of HIV infection in women. The specific goals of the Clinical Retrovirology Laboratory Core are as follows: 1. To coordinate the clinical virology activities of the University of Washington and affiliated institutions for the development and support of complementary research projects in HIV-1 shedding and diversity (Project I: Drs. Frenkel, Coombs and Mullins), CMV as a co-factor for HIV-1 shedding (Project III. Drs. Hitti, Cohn and Cohen). 2. To maintain and develop the facilities, equipment and staffing needed for an infrastructure to accommodate these complementary research projects. Virological procedures to accomplish the above purpose and goals are certified (NIAID-sponsored Virology Quality Assurance Program; CDC; CAP) or peer reviewed and include: i) HIV-1/2 antibody assays include EIA to detect antibodies to viral antigens and recombinant antigens; immunoblotting to detect antibodies to specific HIV proteins such as p24, gp41 and gp120/160; HSV-1/-2 antibody detection (screening). ii) Quantitative determinations of HIV-1 RNA in body tissues, oral fluid, genital secretions and blood (Projects I, II and III). iii) Determination of HIV total DNA by polymerase chain reaction (PCR) amplification using a novel quantitative-competitive PCR-EIA (QC-PCR- EIA) and by a Taq polymerase-based real-time PCR assay (Project I, II, III). iv) Quantification of HIV-1 unintegrated episomal 2-LTR DNA by in situ PCR and in situ hybridization (ISH) (Project II). Vi) Detection and quantification of CMV, HCV, and HSV DNA by TaqMan PCR (Project II).

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- **Project Title: CORE--VIROLOGY FACILITY**

  Principal Investigator & Institution: Borkowsky, William; New York University School of Medicine 550 1St Ave New York, Ny 10016

  Timing: Fiscal Year 2002

  Summary: The CFAR Virology Core consists of 3 units. One concentrates on bulk and quantitative HIV culture, measurement, resistance testing, phenotype analysis, and genotype analysis using the heteroduplex mobility assay and sequencing. The second quantitates HIV RNA in plasma or culture fluids by the Roche RT-PCR method. This lab is state licensed and has been accepted as a participant in the ACTG QA program. The third is a standard virology lab which detects the presence of herpes viruses (HSV, CMV, HHV6, VZV, and EBV) by culture and/or PCR, as well as other viruses such as HCV and JC by PCR. This lab is state licensed. The core offers these services to members of CFAR at reagent cost alone or without cost if the assay is being used to secure future funding. The services are also available to the non-CFAR AIDS community (e.g. other ACTG sites) at discounted prices.

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

- **Project Title: DNA/PROTEIN INTERACTION IN HERPES VIRUSES**

  Principal Investigator & Institution: Griffith, Jack D.; Professor; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002

  Summary: The Herpes viruses are large DNA viruses several of which infect human cells to cause a myriad of diseases some, severe. Combating these viruses will require knowing more about their life cycles. The initiation of DNA replication presents an attractive target for anti-viral approaches as it represents the earliest stage in the production of new virus. Herpes Simplex type l (HSV- l) infects human cells and is the best understood of the Herpes viruses. In this project, efforts will continue to focus on the action of viral and host proteins in the first stages of initiation of HSV- l replication, in particular UL9 protein which binds to the HSV-l origins and acts as a helicase, and ICP8, the general single strand DNA binding protein. A major focus will be on further characterizing the interactions of ICP8 and UL9 as they open and unwind the HSV-l origin. Analysis combining biochemical and electron microscopic (EM) studies will provide a detailed mechanism including how topoisomerase I drives the unwinding reaction and whether it binds directly to UL9. It is possible that host cell heat shock (chaperone) proteins help load UL9 onto the origins and this possibility will be explored. These studies will employ EM, biochemical assays, and surface plasmon resonance measurements to define the nature and structure of the protein complexes that form at the origins and initiate replication. Using plasmid DNA-protein complexes in which the origin is partially unwound by UL9 and ICP8, extracts from HSV-1 infected human cells and an HSV-l replisome generated in insect cells will be added to learn more about the subsequent steps of replication. The long-range goal is to reconstitute full HSV- l replication using plasmid templates in vitro. Activation of latent HSV- l and initiation of replication from latent genomes likely requires removal of nucleosomes from the origin. A GRE (glucocorticoid response element) has recently been identified in the HSV-l origin termed oriL and this may act to uniquely position nucleosomes over the UL9 binding sites in oriL, creating a molecular, hormone-sensitive switch. This will be tested using in vitro chromatin assembly and footprinting methods. High resolution EM will be utilized to determine the fine structure of several HSV- l DNA-protein complexes. A collaborative project with Dr. Kenney of this program project will explore many of these same questions in the EBV system.

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- **Project Title: EBNA1-SPECIFIC CD4+T HELPER 1 CELLS**

  Principal Investigator & Institution: Bickham, Kara; Lab/Cell Physiol & Immunology; Rockefeller University New York, Ny 100216399

  Timing: Fiscal Year 2002; Project Start 01-JUL-2001; Project End 01-FEB-2003

  Summary: Epstein Barr virus (EBV) is a gamma **herpes virus** that latently infects greater than 90% of the adult population. Despite a relatively benign course in most carriers, EBV has growth transforming potential and is associated with a number of malignancies, including nasopharyngeal carcinoma, Hodgkin's lymphoma and Burkitt's lymphoma. EBNA1 is a vital EBV latency antigen that maintains the viral episome and is found in all EBV-associated tumors. EBNA1-specific CD8+ T cell immunity is blocked by its glycine-alanine repeat domain, which prevents proteosomal processing for MHC class I. However, our laboratory recently showed that the normal host response to EBNA1 lies in the CD4+ TH1 T cell compartment. TH1 CD4+ T cells are known to be critical for resistance to tumors and viruses in mice. This project will characterize

EBNA1-specific CD4+ lymphocytes in several ways. First, we will optimize techniques to detect EBNA1 - specific responses using intracellular cytokine staining and real time PCR and thereby have methods to follow this immune response in patients with EBV-associated malignancies. Second, we will investigate the role of the antigen-presenting cell in the polarization of the CD4+ T cells to TH1 in vivo. We will describe the phenotype of the EBNA1- specific response in blood and tumor infiltrating lymphocytes from patients with EBV-associated Hodgkin's lymphoma and nasopharyngeal carcinoma to determine if EBNA1 immunity is reduced or changed to a TH2 response. Finally, we will learn to expand EBNA1 immunity in T cells from patients with EBV-associated malignancy, including if need be redirect established TH2 responses to TH1. These experiments will set the stage for clinical studies, most likely with dendritic cells pulsed with EBNA1, to manipulate the immune response in patients with EBV-associated malignancy.

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- **Project Title: ENZYMATIC MECHANISM OF HERPES VIRUS DNA REPLICATION**

  Principal Investigator & Institution: Lehman, I Robert.; Biochemistry; Stanford University Stanford, Ca 94305

  Timing: Fiscal Year 2003; Project Start 01-JUL-1988; Project End 31-DEC-2007

  Summary: (provided by applicant): The aim of this research is to understand (i) the mechanism of initiation of **herpes virus** DNA replication, (ii) the mechanism of inversion that occurs during **herpes virus** DNA replication and (iii) the factors that influence the development of viral latency in herpes virus-infected neuronal cells. We anticipate that these studies will provide us with an insight into the replication, recombination and latency of a significant class of human pathogens. The investigation will be organized along the following lines. A. Analysis of the stimulation of binding of multimeric origin binding protein (UL9 protein) to Ori-s, an origin of HSV-1 DNA replication, by the cellular hTid-1 DnaJ chaperone. B. Role of neural F box protein (NFB42) in HSV- 1 latency. 1. Ubiquitination and degradation of UL9 protein upon binding NFB4 2. Investigation of state of phosphorylation of UL9 protein on its interaction with NFB42. C. Role of endonuclease G in the initiation of sequence inversion in the HSV- 1 genome. 1. Studies of a sequence cleavage by endonuclease G. 2. Effect of HSV- 1 infection on levels of endonuclease G. 3. Cellular localization of endonuclease G pre- and post HSV-1 infection 4. Interaction of endonuclease G with other proteins. 5. Effect of suppression of endonuclease G on a-sequence-mediated recombination.

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

- **Project Title: GENE THERAPY FOR BRAIN TUMORS**

  Principal Investigator & Institution: Hochberg, Fred H.; Associate Professor; Massachusetts General Hospital 55 Fruit St Boston, Ma 02114

  Timing: Fiscal Year 2002; Project Start 15-AUG-1996; Project End 31-JUL-2005

  Summary: Malignant gliomas represent the single most costly and morbid neoplasm per capita. The prognosis for patients with these tumors has been largely unchanged by advances in surgery, radiation therapy and drug design. Our proposal provides an integrated effort to translate to clinical human trials laboratory advances in the design of **herpes virus** (HSV) vectors for the delivery of drug-enhancing genes to tumor cells. These effects build on achievements including over 35 publications over the past 2.5 years, the conduct of a human retroviral "gene-marking trial" and the design of three

human therapeutic trials Four Projects and four Cores are united , in collaboration with GMP vector facilities, as a resource for the brain-tumor Consortium (NABTT) to provide gene therapies of glioblastomas. Our studies explore vascular and migratory cell delivery systems (Project 4- Breakfield) of **herpes virus** and herpes-based amplicon vector systems. Studies are designed to provide high titers of HSV vector containing enzymes and herpes-based amplicon vector systems. Studies are designed to provide high titers of HSV vector containing enzymes which separately and in synergy activate pro-drugs including cyclophosphamide and irinotecan. Initial toxicity studies in Aoutus and Scientific Advisory meetings have resulted in the addition of two new scientific aims: We will track the delivery of vector, transgene and delivery cells using novel radiolabels in rodents and we will evaluate the Cytotoxic T Lymphocyte response to novel tumor antigens B-gal and OVA as distinguished from herpes vectors. In Aoutus and Human Trials we will distinguish from herpes vectors. In Aoutus and Human trials we will examine the local CTL responses that follow herpes vector transduction into brain. Human and in-vitro drug studies will be supported by for manufacture of polymeric pro-drug systems, and analysis and modeling for single and multiple activated drugs. All studies will be supported by histologic and immunohistochemical evaluations of gene expression and changes in tumor and surrounding brain, as well as the molecular characterization of tumors. Our program defines a rational and scientific means to evaluate and expand the potential of gen therapy for brain tumors.

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- **Project Title: GENERATION OF HERPES VIRUSES FOR IN VIVO OBSERVATION**

  Principal Investigator & Institution: Maul, Gerd G.; Professor; Wistar Institute Philadelphia, Pa 191044268

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

  Summary: (provided by applicant): The effect of viruses on the host can be observed at different levels of complexity and resolution depending on the technique used. The single-cell observation combined with various labeling techniques has provided great insight into host-virus interactions; however, the observations are made on fixed (dead) infected cells. We propose to develop an in vivo virus genome labeling system that will allow observation of virus genomes in live cells. Visualization of a viral genome in vivo requires tagging its DNA sequence. The construction of a "green" genome is possible by labeling a DNA tag in the viral genome as it enters the nucleus or before packaging with green fluorescent protein (GFP). Cells inducibly producing the GFP-fusion protein to bind to the DNA tag will be generated to assemble a system where upon virus entry into the nucleus or during packaging the viral genome is rendered "green" through very tight binding of the DNA tag and the reporter protein. These genomes can be visualized by confocal microscopy and documented in a time-resolved fashion by time-lapse microscopy. We propose to produce DNA-tagged recombinant herpes simplex virus and mouse cytomegalovirus. To complete the system, we will develop cell lines that inducibly produce GFP-labeled DNA-binding protein, where HSV-1 and MCMV can replicate and which are useful as quiescent ("latent") virus containing cultured cell model systems. Such a new system would recognize single viral genomes directly in the live cells and obviate in situ hybridization. The "green" viral genomes will open up new lines of inquiry into the dynamics of virus entry into the nucleus, the sequence of degradation by endonucleases and/or retention in a nuclease-resistant episome, replication and segregation by multiple observation of single cells or populations during quiescence, affinity immune separation of quiescent viral genomes and identification of viral genomes by immunoelectron microscopy.

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- **Project Title: GENETIC AND BIOCHEMICAL STUDIES OF THE HSV IE-O GENE**

  Principal Investigator & Institution: Silverstein, Saul J.; Professor; Microbiology; Columbia University Health Sciences New York, Ny 10032

  Timing: Fiscal Year 2002; Project Start 01-DEC-1993; Project End 30-NOV-2003

  Summary: The eight human herpes viruses share the ability to initiate a primary infection in a specific target tissue and to subsequently sequester themselves in a latent form. The viruses that compose this family are grouped into three classes on the basis of the site of where their primary infection occurs and where they are found during latency. Two members of this family Epstein Barr and Kaposi's Sarcoma have been implicated in the generation of tumors in humans. Regulation of gene expression from these large double-stranded DNA containing viruses results from a temporally ordered cascade of gene expression. This grant is concerned with regulation of gene expression in cells infected with herpes simplex virus (HSV), the prototype for the alphaherpesviridae. It is the expression of immediate early (IE) genes that is responsible for coordinate regulation of HSV gene expression. This laboratory has focused its efforts on characterizing the activities of IE gene products. In particular we have studied the gene products of the IE-O, IE-4 and IE-27 loci. These analyses have revealed novel functions for both ICPO and ICP27, and demonstrated that ICPs 4 and 27 interact. The novel feature of ICP27 that will be studied in this application is its RNA- dependent shuttling activity. We will continue our studies of these gene products using genetic and biochemical approaches to examine the effects of mutations to the sequences encoding these proteins. These studies will add to the understanding of how these viruses interact with their host and what the consequences of virus specified protein-protein and host-virus interactions are.

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- **Project Title: HERPES SIMPLEX VIRUS AS AN AIDS VACCINE VECTOR**

  Principal Investigator & Institution: Knipe, David M.; Higgins Professor; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2002

  Summary: The goal of this project is to use herpes simplex virus (HSV) as a vaccine vector to express simian immunodeficiency virus (SIV) proteins as a new approach to elicit immunity against SIV in inoculated animals. We have isolated three HSV-1 recombinants that express SIV env protein. In this application we want to exploit several recent important observations that promise approaches to make better to promise approaches to make better vectors. We propose to make HSV type 2 recombinant strains that express SIV and HIV env and gag from rev-independent mutant genes provide by Dr. George Pavlakis. Our hypothesis is that herpesviruses can be genetically modified to provide safe viral vectors for AIDS vaccines that possess some of the same biological properties as AIDS viruses. First, herpes viruses, like HIV replication-defective HSV strains seem to induce durable immune responses in mouse model systems. Second, herpes viruses activate a strong cellular immune response without the risk of killing T cells. Thus, our hope is that the herpesvirus recombinant vectors can induce a robust cellular response against AIDS virus antigens that is continually activated and eliminated any HIV or SIV infected cell soon after infection. In this application our specific aims are 1) To construct and characterize HSV-2 recombinant strains that are replication-defective and express SIV env and gag from rev-independent genes, 2) To

construct and characterize HSV-2 thymidine kinase-negative recombinant strains that are replication-competent and express SIV env and gag, 3) To identify HSV- 2 genes other than TK whose inactivation leads to HSV-2 mutant strains that are attenuated, but competent for establishment of and reactivation from latent infection in mice, 4) To use the mutant strains identified in specific aim 3 and to construct HSV-2 recombinant strains that are attenuated, replication-competent and latency competent and express SIV env and gag, and 5) To isolate HSV-2 recombinant strains expressing human immunodeficiency virus (HIV) gag and/or env.

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

- **Project Title: HERPES SIMPLEX VIRUS ENTRY INTO CELLS OF NEURAL ORIGIN**

  Principal Investigator & Institution: Eisenberg, Roselyn J.; Professor; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2002; Project Start 01-JUL-2002; Project End 30-JUN-2003

  Summary: Herpes simplex viruses (HSVs) cause a variety of human diseases, including cold sores, eye and genital infections, neonatal infections and encephalitis. The nervous system plays a central role in the pathogenesis of HSV. Both serotypes of the virus, HSV-1 (the oral form) and HSV-2 (the genital form) establish life-long latent infections within sensory ganglia. In addition, the nervous system is the major target of morbidity and mortality resulting from herpetic encephalitis and neonatal herpes. The central role of the neuron in the pathogenesis of HSV argues for experimental approaches that focus on this aspect of HSV infection. This proposal concerns the mechanism by which HSV enter cells of neural origin to initiate infection. Of the eleven virion-encoded glycoproteins, four, including gB, gD and a complex of gH-gL, are essential for virus entry. A fifth, gC though not essential, is important for facilitating initial attachment by binding to cell surface heparan sulfate proteoglycans (HSPG). A major function of gD is to interact with specific cellular receptors. One of these, called **herpes virus** entry mediator or HVEM, is a member of the tumor necrosis factor receptor (TNFR) superfamily of membrane proteins and is found primarily on T cells and other cells of the immune system. Recently, two additional mediators that allow HSV entry into otherwise non-permissive cells have been identified. Both are orphan receptors with the Ig superfamily of proteins and are homologues of the human polio-virus receptor (hPVR). They have been termed human polio-virus related receptors 1 and 2, or hPRR1 and hPRR2. We found that soluble hPRR1 binds saturably and specifically to soluble forms of gD and to gD in virions No other virion glycoproteins are needed for this interaction. Furthermore, binding of hPRR1 depends on gD conformation but does not involved the N-glycans of gD. Thus, like HVEM, hPRR1 satisfies our expectations for the properties of a bona-fide gD-receptor. We hypothesize that hPRR1 is a major receptor for HSV on cells of neural origin. To test this hypothesis, two specific aims are proposed: 1) to characterize the interaction between purified forms of gD and hPRR1; and 2) to examine the gD-receptor interaction in viruses, cells, and tissues of human neural origin.

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- **Project Title: HERPES VIRUS GLYCOPROTEINS IN CELL BINDING AND ENTRY**

  Principal Investigator & Institution: Harrison, Stephen C.; Professor; Children's Hospital (Boston) Boston, Ma 021155737

  Timing: Fiscal Year 2002; Project Start 15-JUN-2001; Project End 30-APR-2006

Summary: (provided by applicant): Our long term goal is to help understand how Herpes Simplex viruses-1 and -2 (HSV-1 and HSV-2) bind to human cells and gain entry into those cells by membrane fusion. These viruses cause health problems in humans, which they persistently infect for life; most commonly causing oral and occular lesions (HSV-1) and genital lesions (HSV-2). We propose experiments designed to determine the atomic structure of the gD glycoprotein from the surface of HSV-1 (highly homologous to that of HSV-2) alone and in complex with three human cellular receptors. We also propose biochemical and structural experiments aimed at understanding changes in the structure of gD resulting from receptor binding and how these structural changes might impact other glycoproteins (gH/gL and gB) involved in viral entry into human cells. We also propose to design and test inhibitors of the virus-to-cell binding and experiments to examine the neutralization mechanism of a therapeutic antibody with the goal of improving its effectiveness.

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- **Project Title: HERPES VIRUS VECTORS AS VACCINES**

  Principal Investigator & Institution: Desrosiers, Ronald C.; Professor; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2002

  Summary: Predicted difficulties in achieving vaccine protection against HIV and SIV have more or less been borne out by vaccine trials in animal models. Our laboratory has demonstrated impressive protective effects of live- attenuated, deletion mutations of SIV as preventive vaccines. The live- attenuated approach has significantly out-performed other vaccine approaches in rhesus monkey models. Although we do not have definitive knowledge on the immunological basis for the protection, continued antigen expression resulting from viral persistence may be a key factor. A variety of studies have suggested that immunological memory is simply not sufficient to protect against pathogenic, difficult-to-neutralize strains of SIV that would be representative of primary isolates of HIV1. We will investigate whether persistent, vectored expression of SIV antigens resulting from infection by recombinant herpesvirus can match the live- attenuated approach for protective efficacy. The alpha herpesvirus, herpes simplex virus (HSV), and the gamma herpesvirus, rhesus monkey rhadinovirus (RRV), will be used in vaccine/challenge experiments in monkeys. viral genes that contribute to pathogenic potential will be removed from these herpesviruses and replaced by cassettes for expression of SIV genes. Viruses expressing SIV env, gag-pol and gal-pol + env will be compared for their capacity to protect against mucosal challenge by wild-type, disease-inducing strains of SIV. The properties of herpesviruses that utilize a constitutive SV40 promoter versus endogenous herpesviral promoters for vectored expression will be compared since a regulated herpesvirus promoter may be needed for high level persistence and maximal immune responses. The ability of replication competent versus replication defective strains of recombinant herpesviruses to elicit high-titer immune responses and protection will also be compared. The proposed studies are expected to define conditions that are needed to achieve solid vaccine protection against SIV by recombinant herpesviruses.

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- **Project Title: HERPESVIRAL ONCOGENESIS, LATENCY AND REACTIVATION**

  Principal Investigator & Institution: Raab-Traub, Nancy J.; Professor; Microbiology and Immunology; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

Timing: Fiscal Year 2002; Project Start 01-JUL-1983; Project End 31-JUL-2004

Summary: The Virology Program Project continues its focus on the identification of interactions between viral and cellular proteins in herpesvirus infection and the effects of viral infection on cellular growth control. The program encompasses diverse approaches to these questions that include detailed basic analyses of protein/DNA interactions and the development and analysis of biologic models of pathogenesis. In project l, Dr. Jack Griffith will continue his studies of herpes simplex virus (HSV) replication proteins, visualizing the UL-9 and ICP8 proteins to determine how they bind and open the lytic origin of replication. An in vitro HSV replication system will be reconstituted for detailed study and three-dimensional imaging of HSV protein/DNA complexes will be obtained. In project 2, Dr. Shannon Kenney will pursue her studies of the Epstein Barr virus (EBV) lytic origin of replication. She has previously shown that EBV BMRF1, the EBV polymerase processivity factor, functions as a transactivator and binds the downstream essential component in orilyt. In this project, she will identify cellular proteins that interact with BMRF1 and use an in vitro replication system to determine if transcriptional transactivation is coupled to replication. Working with Dr. Griffith, she will analyze the orilyt protein/DNA structure using electron microscopy. Dr. Steven Bachenheimer will, in Project 3, determine if HSV infection affects cell cycle progression by affecting cyclin dependent kinase activity and analyze viral infection in genetically altered rodent fibroblasts that lack the retinoblastoma protein. He will also determine the role of viral proteins in regulating E2F and cyclin kinase activity. In Project 4, Dr. Joseph Pagano, will analyze the relationship between the cell cycle and EBV expression during latent infection. This project will determine and identify viral proteins that are expressed in a cell cycle dependent fashion. The phosphorylation state of specific proteins and the effects of phosphorylation on protein function and protein/protein interactions will be determined. Dr. Eng Shang Huang will, in project 5, continue his studies of the effects of human cytomegalovirus (HCMV) on endothelial and monocyte cell function. He has previously shown that HCMV induces expression of interleukin 1beta, NFkappaB, and SP1, and that many of these effects are mediated by binding glycoprotein B (gB) to a cellular receptor. In these studies, he will determine the effects of virus infection and gB binding on expression of cytokine and adhesion molecules and determine if infected cells secrete factors that affect endothelial cell function. He will also clone the gB receptor and define the signaling process that is upregulated by gB binding. In project 6, Dr. Nancy Raab- Traub, P.I., will characterize EBV latent membrane protein LMP1-induced transformation in transgenic mice and in rodent fibroblasts. She will analyze the molecular interactions of LMP1 with cellular proteins, determine which cellular pathways mediate LMP1 transformation, and identify complementing pathways that contribute to oncogenesis. Overall, the program project will continue to dissect the viral/cellular molecular interactions that occur during viral infection and determine how specific molecular events underlie **herpes virus** pathogenesis.

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- **Project Title: HERPESVIRUS PERSISTENCE AND ONCOGENICITY**

  Principal Investigator & Institution: Shenk, Thomas E.; Professor & Howard Hughes Investigator; Molecular Biology; Princeton University 4 New South Building Princeton, Nj 085440036

  Timing: Fiscal Year 2002; Project Start 30-SEP-2000; Project End 31-JUL-2005

  Summary: Changes in cellular biochemical pathways are fundamental to herpesvirus persistence and oncogenicity. We will employ new global approaches to identify viral

genes that modulate cellular pathways and to identify the pathways that are altered, and then we will elucidate the mode of action of these altered pathways within the infected cell. Our approach will be comparative. The program will include the study of viruses in each of the three families of herpesviruses: alpha, herpes simplex type 1 virus and pseudorabies virus; beta, human cytomegalovirus; and gamma, Epstein- Barr virus and Kaposi sarcoma-associated **herpes virus.** Some herpes viruses contribute to human cancers (Epstein-Barr virus and Kaposi sarcoma-associated herpesvirus), while others are not known to do so. Consequently, our program will compare tumor viruses with closely related non-tumor viruses. The long-term objective of the program is to better understand the mechanisms by which herpesviruses persist and contribute to oncogenesis in the infected host. We will search for additional viral genes that mediate persistence and oncogenicity, and we will study the mechanism of action of new genes that are identified. We also will identify cellular genes whose level of expression change after infection, and test the hypothesis that some of these altered cellular genes influence the outcome of the virus-host interaction, contributing to the persistence and/or oncogenicity of the viruses. The individual research projects are as follows. Project 1, Roizman. Comparative role of cellular functions in herpes simplex type 1 virus infection. Project 2, Enquist Comparative alpha-herpesvirus (herpes simplex type 1 virus and pseudorabies virus) infection of the nervous system. Project 3, Shenk: Viral and cell gene function in human cytomegalovirus replication and latency. Project 4, Moore: Viral and cellular gene regulation in Kaposi sarcoma-associated herpesvirus-associated tumors. Project 5, Kieff: Epstein-Barr virus and cell gene expression in latency and oncogenesis.

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- **Project Title: HERPESVIRUSES IN AIDS ASSOCIATED ORAL DISEASE**

  Principal Investigator & Institution: Webster-Cyriaque, Jennifer Y.; Assistant Professor; Dental Ecology; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 01-JUL-2000; Project End 30-JUN-2005

  Summary: This study addresses the molecular epidemiology of oral herpes viral infection in AIDS and seeks to understand the impact of these infections in terms of viral molecular pathogenesis and modulation of host response. Herpes viruses cause persistent infections and are shed into the oral cavity during immunosuppression resulting in increased morbidity and in the presence of AIDS defining oral lesions. The objective of these studies is to discern the prevalence of herpes viruses in saliva, blood, and oral disease, looking specifically at Hairy Leukoplakia (HLP) and (HIV) associated salivary gland disease to distinguish the character of infection, and to understand how the viruses modulate the host environment to cause these pathologies. The central hypothesis of this application is that herpes viral burdens vary with changes in immune status and drug regimen and that shedding and infection in the oral cavity results in pathologies such as HLP and HIVSGD that are a direct result of modulation of the cellular environment by these herpes viral pathogens. This study will determine whether herpes viral prevalence varies with changes in immune status and anti-AIDS drug regimen, based on a cross sectional studies that correlate herpes viral prevalence in tissue samples from diseased and non diseased oral tissues, saliva and blood to clinical parameters documented in patients charts from samples taken 1989/1990 and in present day specimens. Viral prevalence in these various specimens will be determined by quantitative polymerase chain reaction. Further, this study will determine if a **herpes virus** is the etiologic agent of HIVSGD and characterize the infection at the level of DNA

and gene expression. If these candidate organisms do not contribute to HIVSGD we will attempt to isolate the agent using representational differential display and then characterize that infection. This study will determine how Epstein-Barr virus manipulates cellular gene expression to result in characteristic phenotypic changes detected in HLP and correlate these molecular findings with clinical parameters determined in the first AIM. The proposed work is multidisciplinary incorporating principles of viral pathogenesis, clinical research design and oral epidemiology. These studies will serve to advance the knowledge of oral herpes viral pathogenesis and will be carried out in collaboration with individuals who are leaders in the aforementioned three areas. Further, involvement in these studies will enhance the candidate's prior training in oral medicine and microbiology while equipping her with tools to perform meaningful studies centered around patient oriented clinical research.

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- **Project Title: HERPESVIRUSES IN VESTIBULAR NEURITIS**

  Principal Investigator & Institution: Vrabec, Jeffrey; Otorhinolaryn & Communica Scis; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2002; Project Start 01-MAY-2001; Project End 30-APR-2004

  Summary: (provided by applicant): Vestibular neuritis is one of the most common causes of vertigo. The etiology is unknown, though it is widely assumed to be a viral illness. This project intends to investigate the role of herpes simplex virus (HSV) and varicella zoster virus (VZV) in the pathogenesis of vestibular neuritis. These viruses are selected for study for several reasons. First, they are known to establish latent infection in the vestibular ganglion. Second, reactivation of latent **herpes virus** can result in acute dysfunction of a cranial nerve as is seen in acute facial paralysis in Bell's palsy (HSV) and Ramsay Hunt syndrome (VZV). Third, vestibular symptoms occur in conjunction with acute facial palsy in a minority of cases. Finally, inoculation of animals with HSV can produce acute vestibular dysfunction. Some surgeons remove the vestibular ganglion when performing vestibular neurectomy to treat patients with chronic vertigo. Excised surgical specimens from patients with the pre-operative diagnosis of vestibular neuritis, Meniere's disease and other miscellaneous chronic vestibulopathies will be analyzed for the presence of **herpes virus** DNA using contemporary molecular diagnostic techniques. The prevalence of each virus in the ganglion will be compared with the prevalence in a randomly selected group of cadavers. A significant increase in the prevalence of one or both viruses in the vestibular neuritis group would constitute a firm epidemiological link between the virus and the disease. The sub-aims of the project will attempt to quantify the number of ganglion cells harboring latent virus and the number of copies of the viral genome per ganglion in the study and control groups. Experimental evidence suggests the potential for reactivation is proportional to the percentage of ganglion cells infected and the viral load per cell. This information can help determine why some individuals with latent virus in the vestibular ganglion develop clinical symptoms due to reactivation and some do not.

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- **Project Title: HUMAN GAMMA HERPES VIRUS DNA VACCINES**

  Principal Investigator & Institution: Dittmer, Dirk; Oklahoma Medical Research Foundation Oklahoma City, Ok 73104

  Timing: Fiscal Year 2002

Summary: Human gamma herpesviruses include Epstein-Barr virus (EBV or HHV- 4) and Kaposi's Sarcoma herpesvirus (KSHV or HHV-8). Both are oncogenic and have a chronic latent phase of infection, which leaves humans hosts infected for life. We hope to adapt the current knowledge of these viruses to develop DNA vaccines. Our purpose is to facilitate the elimination or relative suppression of Kaposi's sarcoma (especially in AIDS patients), as caused by KSHV, and of the latent EBV infection found in normals or expressed in some lymphomas, Hodgkin's disease, nasopharyngeal carcinomas, post-transplant lymphoproliferative disease, and infectious mononucleosis. These are over 150 gene products from which to select the targets for a DNA vaccine, as measured by the number of open reading frames in EBV and KSHV. We plan to begin this project (Specific Aim 1) by constructing DNA vaccines directed against four viral gene products, the TSAs ("tumor specific antigens"): LANA (latency associated nuclear antigen) and v-cyclin form KSHV and LMP-1 ((latent membrane protein) and LMP-2A from EBV. The immunogenicity and optimal vaccination strategy will be evaluated and developed in Balb/c mice (Specific Aim 2), where suppression of the transformed phenotype is expected using appropriately engineered vectors with, the 10(3) cell line. (Additional modifications may be needed for LMP-2A, which is the only one of the four TSAs not known to be oncogenic.) Finally, in preparation for future human studies we will test the DNA vaccines in non-human primates (Specific Aim 3). The suppression of EBV-induced lymphomas by the DNA vaccines will be assessed in Cotton top tamarins. Similarly, the acceleration of KSHV elimination will be assessed in DNA vaccine immunized Rhesus macaques. This experience and the immunologic evaluations performed will hopefully be preparatory for a successful trial of one or more of these gamma **herpes virus** vaccines in man.

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- **Project Title: IMMUNE REGULATION OF CNS VIRAL RECRUDESCENCE**

  Principal Investigator & Institution: Bergmann, Cornelia C.; Associate Professor; Neurology; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

  Timing: Fiscal Year 2002; Project Start 15-MAY-2001; Project End 31-MAR-2006

  Summary: (provided by applicant): A variety of human viruses, including herpes viruses, hepatitis B virus and HIV, produce acute infections followed by persistence or recrudescence. However, the mechanism(s) regulating persistence and recrudescence depend on a balance between viral replication and the host immune response. Viral tropism and antigenic load provide additional determinants in this complex scheme. This proposal examines the contribution of cell mediated and humoral immunity in controlling recrudescence of a neurotropic virus following initial clearance. Infection of immunocompetent mice induces an acute encephalomyelitis, followed by persistence without infectious virus. During acute infection cell mediated immunity, predominantly the CD8+ T cells, are crucial in controlling virus replication within the central nervous system (CNS). However, in the absence of B cells, these effector functions do not suffice to suppress virus to undetectable levels, thereby allowing virus reactivation. Importantly, transfer of anti-viral antibody (Ab) prevents virus reactivation, implicating a crucial role for Ab and/or B cells in controlling persistence. However, analysis of virus specific T cells using class I tetramet technology revealed that the percentage of virus specific CD8+ T cells in the CNS is reduced compared to immunocompetent mice. In addition, there is no increase in virus specific T cells during reactivation. These data suggested that CD8+ T cells may be functionally impaired or exhausted due to increased antigen load. This proposal distinguishes between the requirement(s) for potent CD8+ T

cell function vs Ab in controlling virus reactivation in a persistently infected host. The contribution of both neutralizing and non neutralizing Ab, Fc receptor (FcR) activity and complement are examined by Ab transfers and using mice deficient in FeR. These experiments will determine the mechanism of Ab mediated prevention of virus reactivation in an Ab deficient milieu. The possibility that the absence of Ab and/or B cells results in defective CD8+ T cell priming, ultimately leading to exhaustion during recrudescence is tested by functional and phenotypic analysis of CD8+ T cells during priming and recrudescence. Intervention via transfer of protective Ab or CD8+ T cells activated in vitro will determine if functionally impaired CD8+ T cells can be overcome. These experiments may have direct implications for therapeutic interventions during persistent viral infections. Finally, virus reactivation will be tested in an Ab deficient mouse with a normal B cell compartment. These experiments will distinguish between the possibilities of an Ab independent effect of B cells and a CD8+ T cell defect related to the absence of B cells. This proposal will provide insight into the immunological regulation of both virus recrudescence and the CNS as a target organ.

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- **Project Title: INDIVIDUAL DIFFERENCES IN ANXIETY: NEUROPEPTIDE-Y**

  Principal Investigator & Institution: Primeaux, Stefany D.; None; Lsu Pennington Biomedical Research Ctr 6400 Perkins Rd Baton Rouge, La 70808

  Timing: Fiscal Year 2003; Project Start 02-AUG-2003; Project End 01-AUG-2005

  Summary: (provided by applicant): The proposed experiments will investigate individual differences in anxiety and the role of neuropeptide Y (NPY) in these differences. In addition, the relationship of NPY to anxiety and the anxiolytic and sedative effects of ethanol. In the proposed experiments, individual differences in anxiety levels will be determined by % time spent on the open arms of the elevated plus maze, and differences in NPY mRNA levels and NPY receptor densities will be assessed 'anxious' and 'non-anxious' rats. AIM 2 will investigate the effects of **herpes virus** mediated overexpression and underexpression of amygdalar NPY on anxiety-related behaviors in the elevated plus maze test. A time course of **herpes virus** mediated increases and decreases in NPY gene expression and NPY like immunoreactivity will be assessed using in situ hybridization and radioimmunoassays. Overexpression of amygdalar NPY is expected to reduce anxiety in this test. AIM 3 will investigate the effects of **herpes virus** mediated overexpression and underexpression of NPY on the anxiolytic and sedative effects of ethanol preference. Increased amygdalar NPY gene expression is expected to potentiate the anxiolytic and sedative effects of ethanol. Decreased amygdalar NPY gene expression is expected to attenuate the anxiolytic and sedative effects of ethanol.

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- **Project Title: INTERCELLULAR TRANSPORT OF HSV-1 IN CORNEAL EPITHELIUM**

  Principal Investigator & Institution: Hegstrom, Carol D.; Public Hlth Bio & Epidemiology; University of California Berkeley Berkeley, Ca 94720

  Timing: Fiscal Year 2002; Project Start 01-JUL-2002

  Summary: The goal of this proposal is to define the mechanisms involved in cell-to-cell transmission of HSV-1 during recurrent herpetic infection of the corneal epithelium. Recurrent herpetic infection of the cornea is a leading cause of blindness in humans. Understanding the mechanisms of cell-to-cell spread of virus in the cornea will be

important in preventing this disease. The first specific aim is to identify factors in corneal epithelial cells that are utilized by the virus for cell-to-cell spread, such as proteins associated with cell junctions. The second aim is to target viral gene products involved cell-to-cell spread. The third aim focuses on identifying morphologic changes in infected corneal cells during cell-to-cell spread. The last aim is to develop and implement a culture system of viral infection that models the natural conditions of the eye to study the spread of virus from infected sensory neuron axons to corneal epithelial cells. Human corneal epithelial cells in culture will be inoculated with herpes simplex virus type. 1. Specific inhibitors of host proteins associated with cell junctions will be administered and their effects on cell-to-cell spread of virus determined. Mutant strains of **herpes virus** will be used to clarify specific viral gene products essential for viral spread. Morphological changes in the infected corneal cells will be monitored by light, confocal and electron microscopy. Finally, a novel culture system that models recurrent herpetic infection of cornea in vivo will be developed. Understanding how virus is spread cell-to-cell in the eye and the specific host and viral genes involved will be important for the development of effective treatments for recurrent corneal herpetic infection.

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- **Project Title: LASSA AND NIPAH VIRUS INTERFERON-ANTAGONISTS**

  Principal Investigator & Institution: Basler, Christopher F.; Assistant Professor; Microbiology; Mount Sinai School of Medicine of Nyu of New York University New York, Ny 10029

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 29-SEP-2004

  Summary: (provided by applicant): Lassa virus (an arenavirus) and Nipah virus (a paramyxovirus) are important emerging pathogens capable of causing lethal disease in humans. Lassa and Nipah viruses are also of concern as possible agents of biowarfare or bioterrorism, with Lassa virus being a category A bioterrorism agent and Nipah virus a category C bioterrorism agent. Despite their increasing importance, little is known about the determinants of virulence of these viruses. A major component of the innate immune response to viruses is the type I interferon (IFN) system, and for this reason, many viruses have developed methods of circumventing the host IFN response. The viral factors which disrupt the IFN-response, IFN-antagonists, are known to be important virulence factors for some viruses, including influenza and herpes viruses. The mechanisms by which the IFN response of the host is blocked vary, and many of the components of the type I IFN system are targeted by at least one known viral encoded IFN-antagonist. Based on data from numerous other viruses, it is very likely that Lassa and Nipah viruses will also encode IFN-antagonists. Because IFN-antagonist proteins are critical for virulence, they are attractive as targets for mutagenesis in the development of live, attenuated vaccines. Further, antiviral drugs that target IFN-antagonists should impair viral replication and might be used to potentiate other antiviral therapies including treatment with interferon. This proposal seeks to (1) clone genes encoding individual Lassa and Nipah virus proteins to permit transient expression; (2) screen individual proteins from Lassa virus and Nipah virus for type I interferon-antagonist function using transfection-based functional assays; and (3) determine the level at which the identified IFN antagonists alter the host interferon response.

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- **Project Title: MECHANISM AND INHIBITION OF HERPES REPLICATION**

  Principal Investigator & Institution: Kuchta, Robert D.; Associate Professor; Chemistry and Biochemistry; University of Colorado at Boulder Boulder, Co 80309

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-AUG-2004

  Summary: (provided by applicant): Herpes viruses comprise a large family of complex, double-stranded DNA viruses, a number of which are serious human pathogens. Herpes DNA replication requires a group of virally encoded proteins, and is the target of several antiviral drugs. However, the mechanism of Herpes DNA replication is remarkably complex and not well understood. The long term goal of these studies is to understand the mechanism of Herpes DNA replication at the level of individual enzymes. The studies in this proposal will focus on one of the key reactions in DNA replication, the initiation of new strands of DNA by the DNA primase/helicase complex and subsequent transfer of the primer to the Herpes DNA polymerase. The specific aims of this proposal are: 1. Obtain a detailed understanding of the mechanism of primer synthesis within the context of the primase/helicase complex. Three aspects of primase activity will be examined; how primase recognizes a potential primer synthesis site, the mechanistic coupling between the primase and helicase activities, and the fate of primase synthesized primers. 2. Develop a detailed understanding of the fidelity of primase. The mechanism(s) by which Herpes primase misincorporates NTPs, as well as the frequency and spectrum of misincorporation will be determined. 3. Elucidate the mechanism of primase-coupled DNA polymerase activity. How primase-synthesized primers are transferred between the primase and polymerase as well as the effects of the polymerase on primase activity will be ascertained. 4. Determine how primase interacts with both the base and sugar of the incoming NTP by examining the interaction of primase with NTP analogs. The data from these studies will be combined and used to direct the synthesis of novel and highly specific inhibitors of primase. To accomplish these aims, a variety of steady-state kinetic approaches will be employed. These approaches will be augmented with studies using photoactivateable crosslinking reagents along with a selection-based methodology to provide insights into the interaction of the enzyme with substrates and products. Additionally, a number of novel nucleotides will be synthesized to provide a thorough understanding of how the enzyme interacts with the incoming NTP.

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- **Project Title: MECHANISM OF LATENCY OF HERPES SIMPLEX VIRUS**

  Principal Investigator & Institution: Fraser, Nigel W.; Professor; Microbiology; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2002; Project Start 01-AUG-1986; Project End 31-AUG-2006

  Summary: (provided by applicant) Herpes Simplex virus (HSV) can cause a wide range of diseases, including skin lesions, which are common, encephalitis which is rare, an HSV infection of the eye, which is a leading cause of blindness in the USA (400,000 cases). The seroprevalence of HSV in the U.S. adult population is very high (approximately 70%). **Herpes virus** infections are characterized by the ability of the virus to form latent infections in the nervous system. It is this ability, which leads to recurrent episodes of the disease causing much human suffering, which is the focus of our application. The overall goal of this proposal is to understand the mechanism of HSV latency using both a mouse model system and tissue culture studies. We have previously used a mouse model system of HSV latency to study physical state of the latent viral genome, and to initiate studies on viral gene expression during latency.

From our data, we have formulated models for the mechanism of HSV-1 latency. We now wish to continue to refine these models using the techniques of molecular virology. The program consists of three scientific projects, and an administrative and two scientific cores. The scientific projects are titled: 1. Gene Expression during HSV-1 Latency and Reactivation; 3. The Role of Cellular Transcription Factors in the Regulation of HSV-1 Latency and Reactivation; 4. Herpes Simplex Virus and Neuronal Cell Interactions. Successful completion of these studies will permit the mechanisms of HSV latency to be described in more detail, allowing formulation of new strategies for the prevention of latency and recurrence. In addition, it is anticipated that the knowledge gained will continue to be of use to the fields of gene therapy and cancer therapy in the nervous system, and continue to provide more patentable findings.

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- **Project Title: NOVEL IMMUNE BASED THERAPIES FOR MULTIPLE MYELOMA**

  Principal Investigator & Institution: Anderson, Kenneth C.; Professor of Medicine; Dana-Farber Cancer Institute 44 Binney St Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-AUG-1998; Project End 30-JUN-2003

  Summary: The work outlined in this program project grant focuses on novel strategies to achieve long term disease free survival and potential cure of myeloma. We believe this is possible only with 1. achievement of minimal residual disease (MRD) status using high dose therapy; and 2. use of novel immunological approaches to treat MRD. This program is comprised of 4 Projects and 3 Cores which interact on both a scientific and clinical level to achieve this goal. In Project 1 we will concentrate on the reasons for failure of allogeneic transplant in this disease, specifically by investigating the biology of the graft-versus myeloma effect. As a result of this work, it is expected that antigen-specific T cells will be generated for subsequent use in the clinical trial setting to eradicate MRD that remains after allogeneic transplant. Project 2 will be dedicated to improving the results of autologous transplantation in myeloma by 1) developing technologies to provide tumor-free autografts and 2) identifying methods to generate and expand anti-myeloma specific autologous T cells ex vivo for adoptive transfer and treatment of MRD post autografting. In Project 3 we will determine the feasibility the inducing an active immune response against myeloma antigens such as DF3 in preclinical models and use this information to undertake clinical trials of vaccination in myeloma. This will be coupled with adoptive therapies to treat MRD post allografting and autografting as outlined in Projects 1 and 2. Project 4 will similarly attempt to induce an immune response to a recently discovered, potentially important tumor-specific virus, namely Human **Herpes Virus** 8 (HHV8) in myeloma. Administrative and Clinical Support (A) and Biostatistical (B) Cores will assist design, conduct, analysis and reporting of laboratory and clinical studies. Molecular Biology and Immune Assessment Core (C) will assess MRD in myeloma and provide immunological monitoring after these novel therapies. To ensure its success, we have assembled a highly diverse yet interactive collaborative team of molecular biologists, immunologists, transplant biologists, and clinicians with a long track record of successful collaboration and with extensive translational experience to drive our basic science discoveries to clinical experimentation.

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

- **Project Title: OCULAR INFECTION WITH THE HERPES VIRUSES**

  Principal Investigator & Institution: Margolis, Todd P.; Associate Professor; To Be Determined; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 01-DEC-1993; Project End 30-JUN-2004

  Summary: Recurrent infection with herpes simplex virus (HSV) may affect up to one-third of the world's population. In addition, recurrent corneal disease due to HSV is the leading cause of infectious corneal blindness in developed countries. An important concept in understanding the pathophysiology of disease due to HSV is that the virus establishes a latent infection in neurons, and that recurrent disease is due to reactivation of the virus from this latent state. Arriving at a solution for the problem of recurrent HSV disease will undoubtedly depend on an improved understanding of the molecular mechanisms that regulate latent infection with HSV. The overall goal of the proposed research is to identify neuronal signaling pathways and transcription factors that play a role in the establishment of herpes simplex virus (HSV) latent infection. Nerve growth factor, glial-cell-derived growth factor and artemin, potent neurotrophic factors that trigger intracellular signaling pathways important for neuronal survival, will be examined for their possible roles in promoting the establishment of HSV latent infection. Transgenic mice will be used to determine whether establishment of latent infection is due, in part, to the host neuron's ability to modulate expression of the key HSV immediate early (IE) regulatory genes, ICPO, ICP4 and ICP27. The gene expression profiles of two populations of ganglionic neurons with very different outcomes of HSV infection will be studied in order to identify host genes that are differentially expressed and may play a role in the establishment of latent infection. Finally, a neuronal cDNA expression library will be screened for host cell gene products that influence expression of key viral regulatory genes. These gene products will then be tested for their ability to repress HSV IE promoter activity in transient assays and HSV productive infection in vitro. Taken together, these studies will begin to elucidate mechanisms by which neurons survive HSV infection to become reservoirs of latent virus responsible for recurrent disease.

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

- **Project Title: OPIOID BINDING TO U51: A HUMAN HERPES VIRUS PROTEIN**

  Principal Investigator & Institution: Bidlack, Jean M.; Professor; Pharmacology and Physiology; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2002; Project Start 27-SEP-2001; Project End 31-AUG-2004

  Summary: (provided by the applicant) The human **herpes virus** (HHV)-6 and HHV-7 are viruses that infect the human central nervous system and T lymphocytes. HHV-6, which is closely related to HHV-7 at the genetic level, is frequently associated with disease, particularly in immunocompromised persons and persons with AIDS. Both HHV-6 and HHV-7 express a 7-transmembrane G-protein coupled receptor, U51, which has been identified as an opioid receptor homologue, sharing greater than 50 percent sequence similarity with the Kappa opioid receptor. HHV-6 and -7 U51 share greater sequence similarity with the Kappa, mu and delta opioid receptors than with any other cloned protein. HHV-6 U51 is a chemokine receptor, which binds the chemokine RANTES, and other beta chemokines, such as eotaxin, monocyte chemoattractant protein 1, 3, and 4. While HHV-7 U51 probably binds beta chemokines, this has not been definitely proven and will be addressed in the proposed studies, which will examine the interactions of opioids with both HHV-6 U51 and HHV-7 U51. The overall hypothesis to

be tested is that the U51 protein, which binds chemokines and is a homologue of the human Kappa opioid receptor, will bind some opioids, and that these opioids will activate the U51 receptor and regulate the binding and function of RANTES. The following specific aims will be tested: 1) Determine if opioids will inhibit the binding of the chemokine [125I]RANTES to the HHV-6 and HHV-7 U51 protein; 2) Determine if opioids activate the U51 protein, as measured with the [35S]GTPgammaS binding assay; and 3) Determining if opioids modulate RANTES-induced stimulation of [35S]GTPgammaS binding. This proposal qualifies for a Cutting Edge Basic Research Award because if opioids bind to the chemokine receptor U51, this finding would demonstrate a common receptor for both beta chemokines and opioids. In addition, because HHV-6 and -7 infect both T lymphocytes and cells of the human central nervous system, this could result in the expression of a novel opioid receptor that is only present in the human neurons and T lymphocytes.

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

- **Project Title: PLASTICITY IN THE AUDITORY SYSTEM**

  Principal Investigator & Institution: Snyder, Russell L.; Associate Adjunct Professor; Otolaryngology; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 01-JAN-1999; Project End 31-DEC-2003

  Summary: (from the application): The proposed research will examine the physiological and anatomical plasticity in the central and peripheral auditory systems following the removal of restricted (1 mm) spiral ganglion (SG) sectors in adult and newborn cats. Such lesions produce focal, highly restricted hearing losses without changing the overall tuning or sensitivity of the basilar membrane and allow the acute effects of focal hearing losses to be determined and compared to their chronic effects. In the proposed experiments we will determine the physiological effects by mapping the tonotopic organization of the inferior colliculus (IC) and primary auditory cortex (AI) before, immediately after, and long after restricted SG lesions both unilateral and bilateral. Our data demonstrate that acute unilateral lesions result in immediate alterations in the tonotopic organization of IC and AI neurons; they produce expansions of representations of acoustic edge frequencies. These expansions are comparable to those in published studies using chronic lesions and indicate that some of that reorganization occurs immediately (within minutes of the lesion) before any anatomical or experience-dependent changes can occur. We will determine the anatomical effects of SG lesions in adults lesioned adults or as neonates by making focal injections of direct (e.g., neurobiotin) and transsynaptic (e.g. Herpes simplex virus) tracers into intact sectors of the SG and labeling not only the direct projections of SG neurons but also their indirect (transsynaptic) projections. Previous experiments suggest that direct projections will be most profoundly altered after neonatal lesions, but the effects of both chronic adult and neonatal lesions on transsynaptic projecions, have never before been described and will be of major importance. An understanding of the critical role sensory input plays in the development and maintenance of auditory system organization is essential to any analysis of auditory function. These studies provide insight into the processes by which the auditory nervous system accommodates early acquired as well as late-onset hearing losses. They also provide insight into the time course and nature of the topographic spread of (herpes viruses within the auditory system, the major cause of congenital deafness in humans.

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

- **Project Title: REACTIVATED HSV-1 DISEASE IN IMMUNE COMPROMISED HOSTS**

  Principal Investigator & Institution: Goade, Diane E.; Associate Professor; Internal Medicine; University of New Mexico Albuquerque Controller's Office Albuquerque, Nm 87131

  Timing: Fiscal Year 2002; Project Start 01-APR-2001; Project End 31-MAR-2006

  Summary: (Provided by the Applicant) **Herpes virus** infection is a very common recurrent health problem in humans, especially immuno suppressed individuals. After resolution of primary infection, a state of latency develops that persists until death. Environmental stimuli such as UV lead to periodic recrudescence of disease. The investigators have recently developed a powerful murine model of reactivated HSV disease of epithelium that is stimulated by a minimum UV exposure. This very closely mimics HSV epithelium disease in man, permitting study of cutaneous HSV-1 reactivation in a relevant experimental system. The studies proposed in this application will use this model to test the hypothesis that reactivated HSV-1 disease is due to a disruption in local cytokine balance, and disease resolution requires local cutaneous immunologic changes. They propose to study the immunopathology of HSV disease reactivation and suggest new treatments and vaccine strategies. They hypothesize that UV exposure results in secretion of soluble factors by keratinocytes that ultimately alter the TH1/TH2 balance which induces HSV from reactivation. Lack of CD4 responses in CD4 depleted animals then permit severe and prolonged disease. They propose that modulation of local immune factors including IL-12 and IFN-gamma alter the reactivation process and that differences of components of the local immune systems impact susceptibility to HSV-1 infection. Studies will be done in immune competent mice and in mice depleted of CD4 which yields reactivated HSV disease in a manner very similar to human HSV disease in HIV infected hosts. Specifically, they will characterize the immune response to HSV-1 at the local cutaneous level and to define the context of interplay of cytokines and immune cells during reactivated cutaneous HSV-1 disease; determine the role of infiltrating T lymphocytes in primary and reactivated disease in normal versus immune compromised models; and determine efficacy of genomic vaccine candidates in prevention of primary infection and in attenuation of reactivated disease.

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

- **Project Title: SORTING AND ASSEMBLY OF THE HSV-1 TEGUMENT PROTEIN VHS**

  Principal Investigator & Institution: Wilson, Duncan W.; Professor; Developmtl & Molecular Biology; Yeshiva University 500 W 185Th St New York, Ny 10033

  Timing: Fiscal Year 2002; Project Start 01-APR-1999; Project End 31-JAN-2004

  Summary: The Herpes viruses are responsible for a large number of human diseases. All Herpes viruses possess a proteinaceous layer termed tegument which lines the inner surface of the viral envelope. Correct assembly of tegument and envelope is essential for the production of an infectious virus particle, and thus for the progression of disease. However, little is known of how tegument proteins recognize and bind to specific cellular membranes, nor how they ensure their assembly into the maturing virion. This proposal will investigate membrane and tegument sorting information present within the Herpes simplex virus (HSV) tegument protein vhs. We will identify the cytoplasmic organelle which binds vhs, and determine the role of this association in the HSV life cycle. Sequences responsible for vhs/organelle binding will be identified, and we will

determine which regions of vhs ensure incorporation of this protein into the mature virus. Information obtained from this study will help in the design of agents able to interfere with vhs assembly into the HSV particle, reducing the virulence of this serious human pathogen.

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

- **Project Title: SPECIFICITY OF HEPARAN SULFATE FOR HERPES INFECTION**

  Principal Investigator & Institution: Liu, Jian; Medicinal Chemistry and Natural Products; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 15-JUL-2001; Project End 31-MAY-2005

  Summary: (provided by applicant) The long term goal of this project is to understand the roles of cell surface heparan sulfate in contributing herpes simplex viral infection. Heparan sulfate is a highly sulfated polysaccharide with very complicated saccharide sequences, and is present on the mammalian cell surface and in the extracellular matrix in a large quantity. Although heparan sulfate is a known important cell-surface molecule involved in assisting **herpes virus** infection for a long time, the relationship between the saccharide structure and its role in assisting herpes viral infection is poorly understood. We propose to conduct a series of biochemical studies to elucidate the structural specificity of the 3-O-sulfated heparan sulfate, which is generated by three different heparan sulfate 3-O-sulfotransferase (3-OST) isoforms, for the binding to herpes envelope glycoprotein D (gD). In particular, we plan to carry out the following projects: 1. Isolation and characterization of the gD-binding oligosaccharides generated by isoform 3 (3-OST-3). We plan to prepare the gD-binding oligosaccharide by incubating purified 3-OST-3 enzyme with a heparan sulfate oligosaccharide library. The gD-binding oligosaccharide will be purified using anion exchange HPLC and gD-affinity column. The structure of the gD-binding oligosaccharide will be determined by chemical and enzymatic degradation approaches coupled with matrix assisted laser desorption/ionization mass spectrometry. We also plan to examine the effect of the purified gD-binding oligosaccharide on viral entry into the cell using a cell-based assay. 2. Characterization of the structures of the gD-binding sites generated by isoform 2 and isoform 4 (3-OST-2 and 3-OST-4). We plan to express and purify 3-OST-2 and 3-OST-4 enzymes. We will also determine the structures of the gD-binding sites within 3-OST-2 and 3-OST-4 modified heparan sulfate. Both 3-OST-2 and 3-OST-4 have recently proved to assist herpes simplex virus 1 entry into the cells, suggesting that 3-OST-2 and 3-OST-4 provide binding sites for gD. In addition, studies of the distribution of 3-OST-2 and 3-OST-4 revealed that both enzymes are highly expressed in human brains. We speculate that **herpes virus** may utilize 3-OST-2 and 3-OST-4 modified heparan sulfate to infect human brains.

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

- **Project Title: SUBVERSION OF HOST ANTIVIRAL DEFENSES BY HHV8 VIRF**

  Principal Investigator & Institution: Offermann, Margaret K.; Associate Professor; Medicine; Emory University 1784 North Decatur Road Atlanta, Ga 30322

  Timing: Fiscal Year 2002; Project Start 02-JUL-1998; Project End 30-APR-2003

  Summary: Human **herpes virus** 8 (HHV8) is a recently identified gamma **herpes virus** that is associated with and most likely the etiologic agent of both Kaposi's sarcoma (KS) and primary effusion lymphomas. These conditions occur primarily in patients infected with HIV, suggesting that immunosuppression, cytokine dysregulation, or other factors

associated with HIV infection may be important factors in the pathogenesis of these diseases, perhaps by altering the host-viral interaction in latently infected cells. The HHV8 genome encodes vIRF, a gene product that has homology to the interferon regulatory factor (IRF) family of transcription factors, a group of related transcription factors that regulate expression of interferon and other antiviral, immunomodulatory and growth regulatory genes. The investigators have demonstrated that vIRF inhibits responses to type I and type II interferons and blocks IRF-1-mediated transcription. This suggests that vIRF joins a number of viral proteins that specifically target components of the host antiviral responses and could further compromise the immunologic status of patients who are already compromised by infection with HIV. Furthermore, IRF-1 is a tumor suppressor gene, and vIRF may contribute to the malignant transformation of HHV8 infected cells in part by inhibiting IRF-1 function. The investigators will investigate the mechanism(s) by which vIRF alters interferon responses and affects gene transcription. They will examine the sensitivity of specific IFN-responsive genes to inhibition by vIRF. They have demonstrated that the inhibition of IRF-1-regulated transcription by vIRF is not a consequence of competition for DNA binding, indicating that the mechanism differs from the competition for binding to the IRF site that occurs in response to IRF2. The investigators have determined that the transactivation domain of IRF-1 is targeted by vIRF, and they propose to refine their analysis of elements within IRF-1 that are affected by vIRF. They will also determine whether the elements in vIRF that are responsible for inhibition of IFN responses are the same or distinct from those that inhibit IRF-1-mediated responses. They will identify and characterize proteins that are involved in vIRF-mediated inhibitory responses. They will extend their studies from in vitro systems to KS lesions and primary effusion lymphoma cells using reagents generated in their laboratory. These studies should offer insight into the mechanism of action by which HHV8-encoded vIRF subverts host antiviral responses and contributes to malignant transformation in HIV infected patients.

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

- **Project Title: TARGETTING DIFFUSE LIVER METASTASES WITH HERPES VIRUS**

  Principal Investigator & Institution: Tanabe, Kenneth K.; Massachusetts General Hospital 55 Fruit St Boston, Ma 02114

  Timing: Fiscal Year 2002; Project Start 07-JAN-2000; Project End 31-DEC-2003

  Summary: Current therapuetic modalities for patients with liver metastases are clearly inadequate. To date, virtually all cancer gene therapy research using viruses have focused on replication- incompetent viruses. However, replication-competent herpes simplex virus type 1 (HSV) holds promise as a potentially effective oncolytic agent. The principal anti-tumor activity of replication-competent HSV results from viral replication within tumor cells, resulting in cell destruction, as well as production of progeny virions that can directly infect adjacent tumor cells. In addition, HSV thymidine kinase activation of the prodrug ganciclovir enhances the antitumor activity. The strategy of restricting HSV replication to cancer cells represents a novel paradigm. The hypotheses to be examined are 1) HSV can be genetically modified to restrict its replication to CEA-expressing cells; 2) Treatment of diffuse liver metastases with intrasplenic administration of HSV will result in significant tumor reduction with limited spread of viral infection; and 3) Pre-existing immunity to HSV will limit spread of viral infection without reducing anti-tumor efficacy. In Specific Aim 1 construction of an HSV mutant (designated HSVceaalpha) will be completed. This vector is engineered such that an immediate-early gene that is critical for HSV replication is regulated by the human CEA promoter, thereby limiting HSVceaalpha replication to CEA-expressing cells. The ability

of HSVceaalpha to replicate and cause cytopathic effects will be examined in primary cultures of normal human tissues, CEA- positive and CEA- negative colon carcinomas, and in human skin xenografts. In Specific Aim 2 the efficacy and toxicity of treating liver metastases with replication-conditional HSV will be examined. Several complementary assays will be used to detect HSV replication in tumor and non-tumor tissues after intrasplenic HSV administration to mice bearing diffuse liver metastases. The effects of viral dose, systemic ganciclovir administration, and initial tumor volume on spread of viral infection and animal surivival will be measured. In Specific Aim 3 we will analyze the effect of the host immune system on treatment of liver metastases with replication-conditional HSV. We will first examine how pre-existing immunity influences both the spread of HSV infection after treatment of liver metastases and the anti- tumor efficacy. We will subsequently examine the effect of individual components of the immune system on viral spread and anti-tumor efficacy. In concert, these studieds will provide a basis for development of clinical trials with HSV.

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

- **Project Title: THERAPEUTIC EFFECTS OF CD40L IN ACUTE LYMPHOBLASTIC LEUK**

  Principal Investigator & Institution: Brenner, Malcolm K.; Professor; Pediatrics; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2002; Project Start 30-SEP-1998; Project End 31-JUL-2004

  Summary: Amplified production of immunostimulatory molecules by tumor cells offers an attractive way to generate specific immune responses in vivo. The investigator has demonstrated the feasibility of this approach in neuroblastoma patients, using an adenoviral vector to transduce autologous tumor cells with IL-2. The research proposed here builds on that experience to test IL-2 and the costimulator molecule CD40 ligand in CD40+ blast cells from patients with ALL. Preliminary data in a murine model suggests that combined expression of CD40L and IL-2 does enhance the anti-tumor effect over results seen with either molecule alone. However, primary ALL blasts are difficult to transduce with adenoviral or other available vectors, leading the investigator to develop a **herpes virus** vector for this purpose. The subject of this project is a phase I clinical trial. Aim 1 tests the safety and immunogenicity of herpes virus-IL-2 transduced autologous lymphoblasts, while Aim 2 tests cells transduced with a herpes-CD4OL vector. In Aim 3, the goal will be to administer a fixed dose of IL-2 transduced cells with an escalating dose of CD4R0L-transduced cells to test the central hypothesis of this project, that in vivo immune responses against leukemia cells can be greatly enhanced by co-administering autologous blasts that express both stimulatory molecules. The results will permit a reliable assessment of the safety of this strategy, as well as the likelihood of amplifying human immune responses to putative leukemia specific antigens.

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

- **Project Title: TOPICAL THERAPY FOR HSV-2 INFECTION OF THE GENITAL TRACT**

  Principal Investigator & Institution: Howett, Mary K.; Professor; Pennsylvania State Univ Hershey Med Ctr 500 University Dr Hershey, Pa 17033

  Timing: Fiscal Year 2002

  Summary: Genital **herpes virus** infection is caused by infection of male or female genital tissues by herpes simplex virus type 2 (HSV-2) or less frequently by herpes simplex

virus type 1 (HSV-1). This proposal will focus on HSV-2. Infection in the female can target the labial surfaces, the vagina and the cervix. Adjacent areas of buttock skin also may be infected. Infection may occur as a primary event, usually as a result of sexual transmission. Following primary infection, virus most often enters latency in sacral ganglia and can serve as a source of recurrent infection. Primary infection is usually more severe, but recurrent infections may occur over a number of years and serve as a potent source of transmittable virus. Incidence of this virus infection is extremely high. Immunosuppressed patients are at grave risk for replication of this virus at all tissues and can suffer life-threatening sequelae. The current mainstay of therapy for HSV- 2 infection is Acyclovir, a potent nucleotide analogue specifically phosphorylated and incorporated into DNA in HSV-infected cells. Intravenous, oral and topical formulations of this compound have therapeutic benefit. In addition, certain detergent based spermicides have proven anti-virucidal activity for HSV. Studies in the previous three years of this Program Project have shown that C31G (C14/C16) and an alkyl sulfate microbicide can each inactivate HSV-2. Importantly, SDS has been shown to prevent HSV-2 infection in an in vivo model of infection in the mouse vaginal and SDS and C31G have been shown to inactivate HSV-2 and prevent infection in a human vaginal xenograft model. Our specific aims in the next phase of this grant will include: 1) continue to employ three model systems for HSV-2 growth to determine the toxicity and efficacy of non-formulated and formulated microbicidal compounds: a) in vitro assay of HSV-2 by plaque formation in monkey kidney epithelial cells and primary human vaginal keratinocytes; b) in vivo assay by vaginal inoculation of Swiss-Webster, outbred mice, c) in vivo assay by inoculation of human, vaginal xenografts growing in immunocompromised mice; 2) compare the kinetics and natural history of HSV-2 infection following inoculation of either normal, human, vaginal xenografts or human vaginal xenografts expressing the complete repertoire of viral genes from HPV-11; and 3) determine if acute of subclinical HSV-2 infection of human vaginal xenografts growing in nude mice, SCID mice or SCID mice that have been reconstituted with human lymphoreticular cells, alters the complexity of cells in the xenografts that serve as potential targets for HIV infection.

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

- **Project Title: VIRUS CHROMOSOME STRUCTURE: ROLE IN DEVELOPMENT**

  Principal Investigator & Institution: Feiss, Michael G.; Professor; Microbiology; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 01-AUG-1994; Project End 31-AUG-2006

  Summary: (provided by applicant): Bacteriophage Lambda is an excellent model system for studying virion assembly for the large DNA viruses, including the herpes, pox and adenoviruses. These viruses assemble empty protein shells into which the viral chromosome is packaged. In addition, during DNA packaging of many lambdoid phages and the herpes viruses, long end-to-end polymers of viral DNA are cut at specific sites to generate unit-length molecules.Viral DNA is selected for packaging from a DNA pool that also includes host sequences. This recognition is governed by the interactions of viral packaging proteins with a set of protein binding sites on the viral DNA. How protein-DNA interactions orchestrate packaging is best understood for. We propose to further define these DNA-protein interactions, which have broad implications for virus DNA recognition. We also seek to understand the mechanism of an assembly catalyst that aids recognition steps.While the functioning of the viral DNA packaging enzyme, terminase, has been extensively studied, the role of the shell, especially the shell's portal vertex, has not. We propose experiments on the portal's role

in packaging, and seek to define the portal's binding site for terminase. As part of this work we plan to examine the roles of several proteins involved in shell assembly. This work will generate purified packaging proteins and assemblages suitable for structural analysis. Structural information about packaging proteins is crucial for understanding the wealth of genetic information and to assist in design of further studies on the functioning of these proteins.The mechanism of how DNA is translocated into the shell is not understood in any virus system. We propose molecular studies on a series of mutants that have defects in DNA packaging, including DNA translocation. We will also look at the ability of terminase to move DNA, and to pursue a structural analysis of functional domains of terminase.

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 "herpes virus" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for herpes virus in the PubMed Central database:

- **Herpes viruses hedge their bets.** by Stumpf MP, Laidlaw Z, Jansen VA.; 2002 Nov 12; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=137573

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 herpes virus, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "herpes virus" (or

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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.

[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.

synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for herpes virus (hyperlinks lead to article summaries):

- **1,3-Dihydroxyacridone derivatives as inhibitors of herpes virus replication.**
  Author(s): Akanitapichat P, Lowden CT, Bastow KF.
  Source: Antiviral Research. 2000 February; 45(2): 123-34.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10809021

- **A case of classic Kaposi's sarcoma in a Japanese man: detection of human herpes virus 8 (HHV-8) infection by means of polymerase chain reaction and immunofluorescence assay.**
  Author(s): Yamada Y, Funasaka Y, Nishioka E, Okuno T, Ichihashi M.
  Source: The Journal of Dermatology. 2000 June; 27(6): 391-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10920585

- **A mu-capture immunoassay for detection of human herpes virus-6 (HHV-6) IgM antibodies in human serum.**
  Author(s): Nielsen L, Vestergaard BF.
  Source: Journal of Clinical Virology : the Official Publication of the Pan American Society for Clinical Virology. 2002 August; 25(2): 145-54.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12367648

- **A novel approach to cancer therapy using an oncolytic herpes virus to package amplicons containing cytokine genes.**
  Author(s): Carew JF, Kooby DA, Halterman MW, Kim SH, Federoff HJ, Fong Y.
  Source: Molecular Therapy : the Journal of the American Society of Gene Therapy. 2001 September; 4(3): 250-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11545616

- **A role for MHC class I down-regulation in NK cell lysis of herpes virus-infected cells.**
  Author(s): Huard B, Fruh K.
  Source: European Journal of Immunology. 2000 February; 30(2): 509-15.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10671206

- **A sero-epidemiological study of herpes virus type 1 and 2 infection in Israel.**
  Author(s): Isacsohn M, Smetana Z, Rones ZZ, Raveh D, Diamant Y, Samueloff A, Shaya M, Mendelson E, Slater P, Rudenski B, On EB, Morag A.
  Source: Journal of Clinical Virology : the Official Publication of the Pan American Society for Clinical Virology. 2002 February; 24(1-2): 85-92.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11744432

- **Absence of HBV and HCV, HTLV-I and -II, and human herpes virus-8 activation after allogeneic RBC transfusion in patients with advanced HIV-1 infection.**
  Author(s): Asmuth DM, Kalish LA, Laycock ME, Murphy EL, Mohr BA, Lee TH, Gallarda J, Giachetti C, Dollard SC, van der Horst CM, Grant RM, Busch MP; Viral Activation Transfusion Study Group.
  Source: Transfusion. 2003 April; 43(4): 451-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12662277

- **Absence of human herpes virus 8 in semen from healthy Danish donors.**
  Author(s): Kelsen J, Tarp B, Obel N.
  Source: Human Reproduction (Oxford, England). 1999 September; 14(9): 2274-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10469694
- **Altered cytokine production after human herpes virus type 6 infection.**
  Author(s): Arena A, Liberto MC, Iannello D, Capozza AB, Foca A.
  Source: New Microbiol. 1999 October; 22(4): 293-300.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10555198

- **Amnestic syndrome after lung transplantation by human herpes virus-6 encephalitis.**
  Author(s): Bollen AE, Wartan AN, Krikke AP, Haaxma-Reiche H.
  Source: Journal of Neurology. 2001 July; 248(7): 619-20.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11518006

- **An update on herpes virus infections in graft recipients.**
  Author(s): Ketteler M, Kunter U, Floege J.
  Source: Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association. 2003 September; 18(9): 1703-6. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12937213

- **Antibodies to human herpes virus type 8 (HHV8) in general population and in individuals at risk for sexually transmitted diseases in Western Sicily.**
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  Source: Human Pathology. 1999 October; 30(10): 1269-70.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10534180

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  Author(s): Galieni P, Moschettini D, Donati D, Tozzi M, Valensin PE, Lauria F.
  Source: Haematologica. 2001 July; 86(7): 782-3.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11454544

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  Author(s): Atedzoe BN, Menezes J, D'Addario M, Xu J, Ongradi J, Ahmad A.
  Source: Journal of Leukocyte Biology. 1999 November; 66(5): 822-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10577515

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  Author(s): Matta H, Sun Q, Moses G, Chaudhary PM.
  Source: The Journal of Biological Chemistry. 2003 December 26; 278(52): 52406-11. Epub 2003 October 15.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14561765

- **Multiple co-infections (Mycoplasma, Chlamydia, human herpes virus-6) in blood of chronic fatigue syndrome patients: association with signs and symptoms.**
  Author(s): Nicolson GL, Gan R, Haier J.
  Source: Apmis : Acta Pathologica, Microbiologica, Et Immunologica Scandinavica. 2003 May; 111(5): 557-66.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12887507

- **No association between Langerhans cell histiocytosis and human herpes virus 8.**
  Author(s): Slacmeulder M, Geissmann F, Lepelletier Y, Fournet JC, Brousse N, Thomas C, Donadieu J, Gessain A.
  Source: Medical and Pediatric Oncology. 2002 September; 39(3): 187-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12210448

- **No evidence of parvovirus B19, Chlamydia pneumoniae or human herpes virus infection in temporal artery biopsies in patients with giant cell arteritis.**
  Author(s): Helweg-Larsen J, Tarp B, Obel N, Baslund B.
  Source: Rheumatology (Oxford, England). 2002 April; 41(4): 445-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11961176

- **Non-herpes virus infections after stem cell transplantation and anti-viral immunity.**
  Author(s): Chakrabarti S.
  Source: Transplantation Proceedings. 2003 February; 35(1): 509-10.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12591508

- **Nuclear export of herpes virus RNA.**
  Author(s): Sandri-Goldin RM.
  Source: Curr Top Microbiol Immunol. 2001; 259: 2-23. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11417125

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  Author(s): Gomez RS, Carneiro MA, Souza LN, Victoria JM, de Azevedo WM, De Marco L, Kalapothakis E.
  Source: Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 2001 May; 91(5): 552-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11346734

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  Author(s): Freitas RB, Monteiro TA, Linhares AC.
  Source: Revista Do Instituto De Medicina Tropical De Sao Paulo. 2000 November-December; 42(6): 305-11.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11136516

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  Author(s): Stocher M, Leb V, Bozic M, Kessler HH, Halwachs-Baumann G, Landt O, Stekel H, Berg J.
  Source: Journal of Clinical Virology : the Official Publication of the Pan American Society for Clinical Virology. 2003 January; 26(1): 85-93.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12589838

- **Polymorphous light eruption: is herpes virus the culprit?**
  Author(s): Baby O.
  Source: Photodermatology, Photoimmunology & Photomedicine. 2002 June; 18(3): 162.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12207684

- **Positron emission tomography imaging for herpes virus infection: Implications for oncolytic viral treatments of cancer.**
  Author(s): Bennett JJ, Tjuvajev J, Johnson P, Doubrovin M, Akhurst T, Malholtra S, Hackman T, Balatoni J, Finn R, Larson SM, Federoff H, Blasberg R, Fong Y.
  Source: Nature Medicine. 2001 July; 7(7): 859-63.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11433353

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  Author(s): Lin WC, Moore JO, Mann KP, Traweek ST, Smith C.
  Source: Leukemia & Lymphoma. 1999 April; 33(3-4): 377-84. Review.
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  Author(s): Pancheva S, Dundarova D, Remichkova M.
  Source: Z Naturforsch [c]. 2002 September-October; 57(9-10): 902-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12440731

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  Author(s): Schmidt CA, Oettle H, Peng R, Binder T, Wilborn F, Huhn D, Siegert W, Herbst H.
  Source: Leukemia Research. 2000 October; 24(10): 865-70.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10996205

- **Pretransplantation human herpes virus 8 seropositivity as a risk factor for Kaposi's sarcoma in kidney transplant recipients.**
  Author(s): Cattani P, Nanni G, Graffeo R, Capuano M, Cerimele F, La Parola IL, Diociaiuti A, Pozzetto U, Cerimele D, Fadda G, Castagneto M.
  Source: Transplantation Proceedings. 2000 May; 32(3): 526-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10812097

- **Quantitation of human herpes virus 8 DNA in paraffin-embedded biopsies of HIV-associated and classical Kaposi's sarcoma by PCR.**
  Author(s): Bezold G, Messer G, Peter R, Flaig M, Sander C.
  Source: Journal of Cutaneous Pathology. 2001 March; 28(3): 127-30.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11168763

- **Reactivation of herpes virus after surgery for epilepsy in a pediatric patient with mesial temporal sclerosis: case report.**
  Author(s): Bourgeois M, Vinikoff L, Lellouch-Tubiana A, Sainte-Rose C.
  Source: Neurosurgery. 1999 March; 44(3): 633-5; Discussion 635-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10069600

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  Author(s): Morel Y, Schiano de Colella JM, Harrop J, Deen KC, Holmes SD, Wattam TA, Khandekar SS, Truneh A, Sweet RW, Gastaut JA, Olive D, Costello RT.
  Source: Journal of Immunology (Baltimore, Md. : 1950). 2000 October 15; 165(8): 4397-404.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11035077

- **Replication-competent herpes virus NV1020 as direct treatment of pleural cancer in a rat model.**
  Author(s): Ebright MI, Zager JS, Malhotra S, Delman KA, Weigel TL, Rusch VW, Fong Y.
  Source: The Journal of Thoracic and Cardiovascular Surgery. 2002 July; 124(1): 123-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12091817

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  Author(s): Advani SJ, Chung SM, Yan SY, Gillespie GY, Markert JM, Whitley RJ, Roizman B, Weichselbaum RR.
  Source: Cancer Research. 1999 May 1; 59(9): 2055-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10232586

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  Author(s): Arena A, Iannello D, Gazzara D, Speranza A, Bonina L, Mastroeni P.
  Source: Intervirology. 2001; 44(4): 250-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11509888

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  Author(s): Cristiano K, Wirz M, Gentili G.
  Source: Vox Sanguinis. 2001 July; 81(1): 52-3.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11520418

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  Author(s): Barnett FH, Rainov NG, Ikeda K, Schuback DE, Elliott P, Kramm CM, Chase M, Qureshi NH, Harsh G 4th, Chiocca EA, Breakefield XO.
  Source: Cancer Gene Therapy. 1999 January-February; 6(1): 14-20.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10078959

- **Seroprevalence of anti-human herpes virus-6 IgG antibody in children of Bangkok, Thailand.**
  Author(s): Bhattarakosol P, Pancharoen C, Mekmullica J, Bhattarakosol P.
  Source: Southeast Asian J Trop Med Public Health. 2001 March; 32(1): 143-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11485077

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  Author(s): Challine D, Roudot-Thoraval F, Sarah T, Laperche L, Boisson B, Mauberquez S, Dubernet F, Rigot P, Lefrere F, Mercier B, Brossard Y, Rouet F, Girot R, Loiseau P, Girard D, Claquin J, Loty B, Lerable J, Mariotti M, Pawlotsky JM, Lefrere JJ.
  Source: Transfusion. 2001 September; 41(9): 1120-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11552068

- **Seroprevalence of human herpes virus 8 in different Eritrean population groups.**
  Author(s): Enbom M, Tolfvenstam T, Ghebrekidan H, Ruden U, Grandien M, Wahren B, Linde A.
  Source: Journal of Clinical Virology : the Official Publication of the Pan American Society for Clinical Virology. 1999 December; 14(3): 167-72.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10614853

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  Author(s): Stroh C, Held J, Samraj AK, Schulze-Osthoff K.
  Source: Oncogene. 2003 August 14; 22(34): 5367-73.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12917639

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  Author(s): Pereira DB, Antoni MH, Danielson A, Simon T, Efantis-Potter J, Carver CS, Duran RE, Ironson G, Klimas N, Fletcher MA, O'Sullivan MJ.
  Source: Journal of Psychosomatic Research. 2003 March; 54(3): 237-44.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12614833

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  Author(s): Jha R, Narayen G, Sinha S, Kadeer K, Prasad KN.
  Source: Transplantation Proceedings. 2003 February; 35(1): 284-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12591401

- **The equine herpes virus 4 thymidine kinase is a better suicide gene than the human herpes virus 1 thymidine kinase.**
  Author(s): Loubiere L, Tiraby M, Cazaux C, Brisson E, Grisoni M, Zhao-Emonet J, Tiraby G, Klatzmann D.
  Source: Gene Therapy. 1999 September; 6(9): 1638-42.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10490775

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  Author(s): Liu L, Eby MT, Rathore N, Sinha SK, Kumar A, Chaudhary PM.
  Source: The Journal of Biological Chemistry. 2002 April 19; 277(16): 13745-51. Epub 2002 February 05.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11830587

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  Author(s): Sun Q, Matta H, Chaudhary PM.
  Source: Blood. 2003 March 1; 101(5): 1956-61. Epub 2002 October 24.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12406869

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  Author(s): Sun Q, Zachariah S, Chaudhary PM.
  Source: The Journal of Biological Chemistry. 2003 December 26; 278(52): 52437-45. Epub 2003 October 16.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14563855

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  Author(s): Allen UD, Tellier R, Doyle J, Petric M, Wasfy S, Kumar P, Calderwood S, Freedman M, Saunders F.
  Source: Bone Marrow Transplantation. 2001 September; 28(5): 473-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11593320

- **Unusual presentation of herpes virus infections in renal transplant recipients exposed to high mycophenolic acid plasma concentrations.**
  Author(s): Smak Gregoor PJ, van Gelder T, van Riemsdijk-van Overbeeke IC, Vossen AC, IJzermans JN, Weimar W.
  Source: Transplant Infectious Disease : an Official Journal of the Transplantation Society. 2003 June; 5(2): 79-83.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12974788

- **Verrucous herpes virus infection in human immunodeficiency virus patients.**
  Author(s): Fagan WA, Collins PC, Pulitzer DR.
  Source: Archives of Pathology & Laboratory Medicine. 1996 October; 120(10): 956-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12046608

- **World wide interest in herpes virus-associated lymphoproliferation in humans.**
  Author(s): Murphy JK.
  Source: American Journal of Clinical Pathology. 2000 January; 113(1): 153.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10660436

CHAPTER 2. NUTRITION AND HERPES VIRUS

Overview

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

Finding Nutrition Studies on Herpes Virus

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 "herpes virus" (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 "herpes virus" (or a synonym):

- **Functional measurements of [Ca2+] in the endoplasmic reticulum using a herpes virus to deliver targeted aequorin.**
  Author(s): Departamento de Bioquimica y Biologia Molecular y Fisiologia, Universidad de Valladolid y CSIC, Spain. talonso@cpd.uva.es
  Source: Alonso, M T Barrero, M J Carnicero, E Montero, M Garcia Sancho, J Alvarez, J Cell-Calcium. 1998 August; 24(2): 87-96 0143-4160
- **Histological lesions in vascular tissues of bovine herpes virus type 4-infected rabbits.**
  Author(s): Veterinary Medical Research Institute of the Hungarian Academy of Sciences, P.O. Box 18, H-1581 Budapest, Hungary. laci@novell.vmri.hu
  Source: Egyed, L Baska, F Vet-Microbiol. 2003 January 2; 91(1): 1-10 0378-1135
- **Increased susceptibility of peripheral blood mononuclear cells to equine herpes virus type 1 infection upon mitogen stimulation: a role of the cell cycle and of cell-to-cell transmission of the virus.**
  Author(s): Faculty of Veterinary Medicine, Laboratory of Virology, Ghent University, Salisburylaan 133, B-9820, Merelbeke, Belgium.
  Source: van der Meulen, Karen M Nauwynck, Hans J Pensaert, Maurice B Vet-Microbiol. 2002 April 22; 86(1-2): 157-63 0378-1135

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 herpes virus; 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:

- **Minerals**

  Selenium
  Source: WholeHealthMD.com, LLC.; www.wholehealthmd.com
  Hyperlink:
  http://www.wholehealthmd.com/refshelf/substances_view/0,1525,10055,00.html

CHAPTER 3. CLINICAL TRIALS AND HERPES VIRUS

Overview

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

Recent Trials on Herpes Virus

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

- **Seroprevalence of Kaposi's Sarcoma Herpes Virus in the United States**

  Condition(s): Kaposi's Sarcoma; Herpesviridae Infection

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Cancer Institute (NCI)

  Purpose - Excerpt: This study will investigate patterns of Kaposi's sarcoma **herpes virus** (KSHV) in the United States and its potential impact on the U.S. population. KSHV is a newly discovered virus that is strongly associated with Kaposi's sarcoma and primary effusion lymphoma. The high prevalence of KS and KSHV among HIV-infected homosexual men suggests sexual contact as a primary mode of transmission. Reports of non-sexual transmission in parts of Africa and the Mediterranean where Kaposi's sarcoma is endemic, and the identification of viral DNA in saliva and other bodily fluids, however, indicate the virus is also transmitted non-sexually. This study will: - Compare the prevalence of KSHV among different demographic groups in the United States - Examine the association between KSHV and high risk behaviors such as drug use (marijuana and cocaine), sexual behavior (age at first sexual intercourse and number of sexual partners), and medical risk factors (herpes simplex virus II, hepatitis B and hepatitis C) - Estimate the prevalence of KSHV in the United States. Data and blood samples for the study will be taken from the NHANES III survey. NHANES is a program of periodic surveys conducted by the Centers for Disease Control and Prevention's National Center for Health Statistics. The survey is designed to provide national estimates of health status for the United States non-institutionalized civilian

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

population by means of household interviews, standardized physical examinations, and blood sample collection and testing. NHANES III-the seventh in a series of national examination studies-was conducted from 1988 to 1994. This study will use the HANES data to identify risks associated with a KSHV-positive blood test in the survey population. The study plans to include all 19,754 participants (67% of the 29,314 participants originally examined) for whom blood samples were collected and remain available.

Study Type: Observational

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00026728

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 "herpes virus" (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 4. PATENTS ON HERPES VIRUS

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 "herpes virus" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on herpes virus, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Herpes Virus

By performing a patent search focusing on herpes virus, 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 herpes virus:

- **(Poly)peptides which represent the epitopes of the human herpes virus type 8**

  Inventor(s): Haas; Jurgen (Munich, DE), Schatz; Octavian (Altomunster, DE)

  Assignee(s): Biotrin International Properties Limited (mount Merrion, Ir)

  Patent Number: 6,669,939

  Date filed: February 8, 2001

  Abstract: The present invention relates to (poly)peptides, which are recognized by anti-HHV8 antibodies of HHV-8 infected patients, whereby these (poly)peptides are not naturally occurring HHV-8 proteins. The present invention further relates to polymers, comprising at least two identical or different peptides according to the invention as well as conjugates, comprising said peptides and/or polymers thereof. Furthermore, this invention provides mixtures, comprising said peptides and/or polymers thereof, which are used to detect anti-HHV-8 antibodies with high sensitivity and specificity. In addition, the present invention relates to a diagnostic kit, comprising said peptides, polymers and/or mixtures thereof, which can be used for the detection of anti-HHV-8 antibodies and for the diagnosis of an HHV-8 infection, respectively.

  Excerpt(s): The present invention relates to (poly)peptides that are recognized by anti-HHV-8 antibodies of HHV-8 infected patients. By definition, these (poly)peptides shall not comprise naturally occurring HHV-8 proteins. The invention further relates to polymers containing two or more (identical or different) inventory peptides as well as conjugates comprising the inventory peptides and/or polymers thereof. Further we describe mixtures comprising the inventory peptides and/or polymers thereof that are particularly suited for use in procedures to detect anti-HHV-8 antibodies with high sensitivity and specificity. In addition, the present invention relates to a diagnostic kit comprising the inventory peptides, polymers and/or mixtures thereof for the detection of anti-HHV-8 antibodies or diagnosis of HHV-8 infection, respectively. The human herpesvirus 8 (HHV-8), also known as Kaposi sarcoma associated herpesvirus (KSHV) is the purported etiological agent of Kaposi's sarcoma and certain B cell lymphomas. Kaposi's sarcoma (KS) is the most frequent tumor in AIDS patients, affecting 20-30% of all patients during the course of their HIV infection. In the U.S., the incidence of KS in this risk group is 20,000fold higher than in the general population [1]. In some geographic areas, e.g. in Mediterranean countries or in Africa, the incidence in the general population is significantly higher. The production of VEGF (vascular endothelial growth factor) is significantly increased in tumor tissue leading to continued angiogenesis and, hence, an extreme vascularization. Already years ago, epidemiological analyses gave hints that an infectious agent might be involved in the development of KS [1, 3]. Using a new PCR technique, Chang and Moore isolated from KS biopsies DNAs from a hitherto unknown human.gamma.-2 herpesvirus [4]. This virus was called KSHV (Kaposi sarcoma associated herpesvirus) or HHV-8 (human herpesvirus 8), respectively. Its 140 kb genome has been recently cloned and sequenced [5].

  Web site: http://www.delphion.com/details?pn=US06669939__

- **Anti-herpes virus and cytomegalovirus polyurea oligomers**

  Inventor(s): Cardin; Alan D. (Cincinnati, OH), Jackson; Richard L. (Cincinnati, OH), Mullins; Michael J. (Midland, MI)

  Assignee(s): Merrell Pharamaceuticals Inc (bridgewater, Nj), The Dow Chemical Company (midland, Mi)

  Patent Number: 6,232,349

  Date filed: January 7, 1993

  Abstract: The oligomers of the present invention are polyureas, polycarbonates, polyesters or polyamides having a number average molecular weight of <10,000. These oligomers are water-soluble, have a rigid backbone with a predictable anion spacing, and are, pharmaceutically-acceptable. The oligomers are useful for the treatment and/or diagnosis of HSV and HCMV.

  Excerpt(s): Research worldwide is currently underway to develop treatments and cures for Herpes Simplex Virus (HSV) Types 1 and 2. Both HSV Types 1 and 2 show a predilection for infection of the ectodermal tissues wherein such infections by the virus cause lesions in the skin, oral cavity, vagina, conjunctiva, and the nervous system. Generally, infection by HSV Type 1 (HSV1) is associated with oral, facial and ocular lesions. Infection by HSV Type 2 (HSV2) generally results in genital and anal lesions. HSV infections left untreated often lead to blindness, neonatal deaths, and encephalitis. HSV Type 2 infections are at an epidemic portion in the U.S. from venereal transmission. Greater than some twenty million persons are presently afflicted with the disease in this country with new cases and recurrences exceeding half a million annually. The annual cost of HSV infections results in a substantial economic loss to diagnose and treat. Epidemiological control of HSV is poor because the majority of the population, up to 90%, has been exposed to the virus. Man serves as the natural host for HSV Types 1 and 2 infections whereby the virus is transmitted during close personal contact. Initial or primary infections by HSV Types 1 and 2 are contracted through breaks in the mucus membrane. In the healthy carrier the virus can be isolated in the tears, saliva, vaginal and other secretions, even during the absence of overt disease. From the mucus membrane they are able to replicate and spread to the regional lymph nodes. Occasionally these viruses can infect cells of the haemopoietic system and cause viremia. Part of the difficulty in treating HSV infections results from the ability of these viruses to persist in a latent, or quiescent form. When the primary infection subsides or recedes, the virus generally resides in a latent form in the sensory nerve ganglia which innervate the site of primary infection. In ocular or oral infections with HSV Type 1, the virus generally resides in the trigeminal ganglia. In HSV Type 2 the virus generally resides in the sacral ganglia serving the genitalia and lower abdoman. The determinative period of latency of the HSV virus is unknown, other than this period can be upset by heat, cold, sunlight, hormonal and emotional disturbances, or by immunosuppressive agents, resulting generally in a recurrent infection.

  Web site: http://www.delphion.com/details?pn=US06232349__

- **Aqueous solvent based encapsulation of a bovine herpes virus type-1 subunit vaccine**

  Inventor(s): Campos; Manuel (Stonington, CT), Clark; H. Fred (Philadelphia, PA), Frenchick; Patrick J. (Gurnee, IL), Moser; Charlotte A. (Bensalem, PA), Offit; Paul A. (Bala Cynwyd, PA), Speaker; Tully J. (Philadelphia, PA)

  Assignee(s): Pfizer Inc. (new York, Ny)

  Patent Number: 6,270,800

  Date filed: April 21, 1998

  Abstract: A microencapsulated subunit component from bovine herpes virus-1 (BHV-1) is disclosed. Vaccines, kits, and methods for using the same to vaccinate a member of a bovine species are also disclosed.

  Excerpt(s): The present invention relates to microencapsulated vaccines. More particularly, the present invention relates to novel microcapsules having an anisotropic salt membrane encapsulating an aqueous or substantially aqueous core together with an immunogenic composition. The microcapsules are prepared by the interfacial reaction, in aqueous medium, of Lewis acid and base wall-forming reactants. More particularly, the present invention relates to a subunit component of bovine herpes virus-1 (BHV-1) so encapsulated. Microencapsulation is a process by which a relatively thin coating can be applied to dispersions of small particles of solids or droplets of liquids, thus providing a means for converting liquids to solids, altering colloidal and surface properties, providing environmental protection, and controlling the release characteristics or availability of coated materials. Several of these properties can be attained by macropackaging techniques; however, the uniqueness of microencapsulation is the smallness of the coated particles and their subsequent use and adaptation to a wide variety of dosage forms and product applications. Heretofore, known feasible methods for producing microcapsules on an industrial scale have often involved the use of organic solvents. However, the use of organic solvents may present environmental and safety problems. In addition, it is often difficult to remove all the organic solvent from the microcapsules, thus leaving organic contaminants. It has been proposed to use microcapsules as a means of delivering vaccine. Two broad types of antigen delivery systems have been studied for their capacity to enhance immunity: solid (or porous) microcapsules and microcapsules with a core region surrounded by a physically distinct wall. Solid microcapsules may be prepared by a variety of processes including coacervation of colloids (Kwok, K.K., et al., 1991, Pharm. Res. 8:341-344), precipitation of proteins by physical means (e.g., phase separation) (Santiago, N., et al., 1993, Pharm. Res. 10:1243-1247) or chemical agents (e.g., acid chlorides) (Levy, M. C., et al., 1991, J. Pharm. Sci. 80:578-585.), or solvent evaporation techniques that surround aqueous dispersions with polyester films (Singh, M., et al., 1991, Pharm. Res. 8:958-961). Wall/core systems shown useful for antigen delivery include liposomes (Gerlier, D., et al., 1983, J. Immunol. 131:490), ISCOMS (Claassen, I., and Osterhaus, A., 1992, Res. Immunol. 143:531-541) and proteosomes (Gould-Fogerite, S., and Mannino, R., 1992, Liposome Technology, Vol. III, Gregoriadis, G. (ed.), CRC Press, Boca Raton, Fla.; Miller, M. D., et al., 1992, J. Exp. Med. 176:1739-1744).

  Web site: http://www.delphion.com/details?pn=US06270800__

- **Controlling immune response to specific antigens**

  Inventor(s): Curiel; David T. (Birmingham, AL), Mountz; John D. (Birmingham, AL), Zhang; Huang-Ge (Birmingham, AL)

  Assignee(s): Uab Research Foundation (birmingham, Al)

  Patent Number: 6,689,605

  Date filed: January 2, 2000

  Abstract: One major problem with adenovirus gene therapy has been the T-cell mediated immune response elicited by inoculation of adenovirus, which leads to rapid clearance of the virus and loss of transgene expression. In the instant invention, the immune response to a virus is prevented by pre-treatment with adenovirus, adenoassociated virus or **herpes virus** infected antigen-presenting cell (APC) expressing Fas ligand with induced T-cell tolerance. Administration of AdCMVLacZ after tolerance resulted in prolonged expression of LacZ in tolerized animals compared to control treated animals. In control, but not tolerized animals, there was proliferation of CD3.sup.+ T-cell in the spleen in response to AdCMVLacZ treatment. Tolerance induction is also indicated by decreased production of interferon-.gamma. and IL-2 by peripheral T-cells isolated from treated animals after stimulation with the adenovirus infected APCs. T-cell tolerance is specific for the virus as the T-cell responses to an irrelative virus, mouse cytomegalovirus (MCMV) remained unimpaired. The instant invention utilizes virus specific T-cell tolerance, which is induced by APCs that co-express Fas ligand and virus antigens. The instant invention involves novel vectors and methods to induce tolerance to a viral vector gene therapy and prolong expression of a transgene in a viral host.

  Excerpt(s): This invention relates generally to gene therapy. More specifically, the invention relates to suppressing immune system response to antigens expressed on an infected host cell. The proper function of the immune system of an organism is to attack and neutralize materials which are perceived as being foreign to that organism. T-cells are one component of the immune system. T-cells can become activated to specific antigens, and function to directly destroy materials which display that antigen, and they also function to sensitize other components of the immune system to the presence of that antigen. While a properly functioning immune system is vital to the health of an organism, in some instances there is a need for the selective inhibition of an immune response to particular materials. For example, viral vectors, such as adenovirus, are employed in genetic therapies to introduce genetic material and products into an organism. One problem encountered with the use of such viral vectors is that they can provoke an immune response in the organism. This immune response can destroy the viral vector, and those host cells which are intentionally infected by the vector, as well as therapeutic gene products produced by the action of the vector. Furthermore, immune system "memory" provides a lasting response to this vector; hence, readministration of the material will be ineffective. Therefore, there is a need for a method whereby the immune response to a selected viral vector may be blocked or destroyed. Suppression of immune response is also desirable in the instances of autoimmune disease. As is known, such disease results when the immune system of an organism inappropriately recognizes an organ or tissue of that organism as being foreign, and commences an immune response against it. If this immune response can be blocked, the autoimmune disease can be controlled. Immune suppression is also needed in those instances where organs are transplanted. Immune system suppressing drugs are sometimes employed in the foregoing situations; however, such drugs produce a generalized suppression of the immune system, which leaves a patient open to a number of infections. It would

therefore be advantageous if immune response to a specific antigen could be suppressed and/or an immune suppressed zone of tissue created within an organism.

Web site: http://www.delphion.com/details?pn=US06689605__

- **Detection and quantification of human herpes virus 7 by enzymic amplification**

  Inventor(s): Emery; Vincent C (London, GB), Griffiths; Paul (London, GB)

  Assignee(s): Royal Free Hospital School of Medicine (london, Gb)

  Patent Number: 6,331,417

  Date filed: January 8, 1998

  Abstract: The present invention relates to an isolated nucleic acid molecule comprising: (i) a primer protion consisting of a contiguous sequence of from 10 to 50 nucleotides capable of hybridizing to (a) the target nucleic acid molecule represented by SEQ ID NO:1, or (b) to the complementary stand thereof; and optional (ii) a further portion comprising from 1 to 25 nucleotides joined to and immediately 5' to the 5' end of the primer portion.

  Excerpt(s): This invention relates to a method for detecting and quantifying the presence of human herpesvirus 7 (HHV-7) in a sample, and to nucleic acid sequences useful in such a method. The inventors have identified a sequence of HHV-7 DNA that is unique to this virus and not found in other related viral genomes although it codes for a protein that has some sequence homology with the product of KA3L gene of HHV6. The unique sequence is a 193 base pair fragment of HHV-7 DNA, and was identified by digestion of purified HHV-7 DNA with a restriction endonuclease, followed by cloning the restriction fragments into a plasmid vector. Using the sequence of this 193 base pair "target" fragment, it has been possible to synthesise a variety of primers that hybridise to it over part of its length. These can be used in Polymerase Chain Reaction (PCR), including nested PCR reactions, to amplify the 193 base pair fragment. The inventors have also prepared a mutant DNA control sequence based on the 193 base pair fragment. This construct has internal substitutions that provide an additional restriction site (for the restriction endonuclease SmaI) that is absent from the target sequence. Primers suitable for construction of the mutant sequence by PCR amplification have also been synthesised.

  Web site: http://www.delphion.com/details?pn=US06331417__

- **Gamma-herpes virus DNA and methods of use**

  Inventor(s): Patience; Clive (Beverly, MA)

  Assignee(s): Biotransplant, Inc. (charlestown, Ma)

  Patent Number: 6,461,811

  Date filed: July 7, 2000

  Abstract: Isolated polynucleotides and polypeptides derived from the genome of swine gamma-herpesviruses are disclosed, including recombinant cells and vectors encoding such polypeptides and expressing such polynucleotides. Use of the novel polynucleotides as probes of the swine genome is also described. Assay methods employing antibodies against the isolated polypeptides are also disclosed.

Excerpt(s): The present invention relates to newly identified polynucleotides, polypeptides, and fragments thereof encoded by porcine gamma-herpesvirus sequences, and methods of using the porcine gamma-herpesvirus nucleic acids and polypeptides. Organ procurement currently poses one of the major problems in solid organ transplantation, since the number of patients requiring transplants far exceeds the number of organs available. One means of eliminating the shortage of donor organs for allotransplantation is to develop the technologies required to transplant non-human organs into humans, i.e., xenotransplantation. The development of clinical xenotransplantation will also allow for the transplantation of non-human cells and tissues. A potential problem lies in the fact that human and animal organs may be of very different size, depending on the species serving as donor, and on the possibility of infection due to microorganisms present in the donor tissues and having an ability to infect humans. Consequently, one strain of the domesticated pig, denoted miniature swine (Sus scrofa), appears suitable for such transplants because of its similar size to humans (see below). Furthermore, any use of pigs as organ donors in xenotransplantation would obviate problems associated with the consideration of non-human primates as donors. Xenografts from non-human primates, for example, present considerable risk of transmission of pathogens and the consequent development of emerging infections. In addition, several pathogens that cause disease are known to infect both humans and non-human primates, for example, in the transmission of HIV from the chimpanzee to humans. Furthermore, chimpanzees and orangutans, the closest non-human primates phylogenetically, are endangered species and far too rare to be considered for organ transplantation purposes. Baboons are too small to be an appropriate donor for most organ transplants. Even the largest baboons weigh less than 40 kg. In addition, the gestation times and productivity of primates would not allow a commercially significant generation of source animals.

Web site: http://www.delphion.com/details?pn=US06461811__

- **Herpes virus proteinase and methods of assaying**

  Inventor(s): Gibson; D. Wade (Baltimore, MD), Welch; Anthony R. (Sunnyvale, CA)

  Assignee(s): Johns Hopkins University (baltimore, Md)

  Patent Number: 6,406,902

  Date filed: June 2, 2000

  Abstract: A **herpes virus** proteinase has been found to be encoded by a member of a family of four nested genes in simian cytomegalovirus. Another member of the nested genes encodes the assembly protein precursor, which is a substrate for the proteinase. Homologous genes are found in other herpes viruses. Cleavage sites recognized by the proteinase are identified in cytomegalovirus and are found to be highly conserved in other herpes viruses. Substrates, inhibitors, assay kits, and methods of assaying are provided which rely on the proteinase and its activity.

  Excerpt(s): This invention relates to the area of herpes virology. More particularly, it relates to a new enzyme and the use of that enzyme as a target for anti-viral therapy. Herpes viruses are large double stranded DNA viruses that are responsible for a number of human diseases including chicken pox, shingles, fever blisters, salivary gland virus disease, and infectious mononucleosis. The seven human herpes viruses that have been described thus far are HSV-1, HSV-2, cytomegalovirus (CMV), Epstein-Barr Virus (EBV), varicella zoster virus (VZV), HHV-6, and HHV-7. Maturation of **herpes virus** particles is believed to occur through the formation of a procapsid structure, which

acquires DNA and an envelope to become an infectious virion. A **herpes virus** group-common protein referred to as the assembly protein in CMV, and as p40, VP22a, NCP-3, and ICP35e in HSV-1, is an abundant constituent of the **herpes virus** procapsid. The assembly protein is phosphorylated and proteolytically processed from a precursor molecule. It is absent from the mature virion, although its fate is unknown. These characteristics of the assembly protein have suggested an analogy between it and the bacteriophage scaffolding protein, which is an essential component for phage assembly but is not found in mature virus particles (Gibson et al. (1991) J. Virol. 64:1241-1249).

Web site: http://www.delphion.com/details?pn=US06406902__

- **Herpes virus vectors and their uses**

  Inventor(s): Boursnell; Michael Edward Griffith (Cambridge, GB), Brenner; Malcolm Keith (Memphis, TN), Dilloo; Dagmar (Dusseldorf, DE), Inglis; Stephen Charles (Cambridge, GB)

  Assignee(s): Cantab Pharmaceutical Research Limited (cambridge, Gb), St. Jude Children's Research Hospital (memphis, Tn)

  Patent Number: 6,344,445

  Date filed: October 18, 1996

  Abstract: A process of treating a human or non-human animal cell to introduce heterologous genetic material into said cell and express said material in said cell, comprises (a) providing a recombinant herpesviral vector which is an attenuated or replication-defective and non-transforming mutant herpesvirus, and which carries heterologous genetic material, and (b) transducing human or non-human animal cells selected from: hemopoietic cells, malignant cells related to blood cells, and malignant or non-malignant CD34+cells; by contacting said cells with said virus vector to transduce said cells and express said genetic material. Among applications of the technique is modification of hemopoietic cells by transfer of genes, e.g. to generate tumor immunogens from malignant cells.

  Excerpt(s): This invention relates to viral vectors and methods for their use, especially for example for transducing cells, for example malignant cells of hemopoietic lineage, and for inducing the expression of foreign genetic material in such cells. The invention also relates to pharmaceutical compositions based on such viral vectors, to the production of cells infected with such viral vectors, to pharmaceutical preparations based on such cells, and to their use for administration to humans and to non-human animals in order to achieve expression of foreign genetic material in vivo. Methods according to the invention can be used for example in cancer immunotherapy. Recombinant viral vectors are among several known agents available for the introduction of foreign genes into cells so that they can be expressed as protein. A central element is the target gene itself under the control of a suitable promoter sequence that can function in the cell to be transduced. Known techniques include non-viral methods, such as simple addition of the target gene construct as free DNA; incubation with complexes of target DNA and specific proteins designed for uptake of the DNA into the target cell; and incubation with target DNA encapsulated for example in liposomes or other lipid-based transfection agents. A further option is the use of recombinant virus vectors engineered to contain the required target gene, and able to infect the target cells and hence carry into the cell the target gene in a form that can be expressed. A number of different viruses has been used for this purpose including retroviruses, adenoviruses, and adeno-associated viruses.

Web site: http://www.delphion.com/details?pn=US06344445__

- **Herpes virus vectors for dendritic cells**

  Inventor(s): Chain; Benjamin (London, GB), Coffin; Robert Stuart (London, GB)

  Assignee(s): Biovex Limited (london, Gb)

  Patent Number: 6,641,817

  Date filed: August 6, 2001

  Abstract: An attenuated **herpes virus** capable of efficiently infecting a dendritic cell without preventing antigen processing occurring within the infected cell. The attenuated **herpes virus** and dentrictic cells infected with the virus are useful in immunotherapeutic methods of treating disease.

  Excerpt(s): The present invention relates to attenuated herpes simplex viruses capable of efficiently infecting dendritic cells. It also relates to the use of such viruses in immunotherapy approaches to the treatment of disease. Dendritic cells (DCs) are the most potent antigen presenting cells and are efficient at inducing responses even to antigens to which the immune system has become tolerant. Thus for tumour immunotherapy, in which an immune response is raised against a tumour, the use of DCs may be ideal if they were made to present tumour specific antigens. DCs might also be used to present antigens derived from infectious agents such as bacteria, viruses or parasites, providing protective or therapeutic vaccines for such diseases. However effective transfer of antigens into DCs for any of these targets has proved the greatest problem with this approach. To provide a realistic chance of generating a therapeutic immune response against a tumour antigen or other disease related antigen, several conditions have to be met. Firstly, it is necessary to identify molecules whose expression is tumour or disease specific (or at least selective), and which can therefore serve as the target for an immune response. This task has proved very difficult for the majority of common tumours, but is solved in for example the case of cervical cancer by the presence, in most cases, of the viral oncogenes E6 and E7, and for other tumours, good candidate antigens are beginning to be identified. For example the MUC-1 gene product is over, expressed in a number of tumours, including 90% of ovarian cancers. Various other tumour associated antigens have also been identified, any of which might be used in an immunotherapy treatment of cancer. Secondly, following the identification of the antigen/antigens, it is necessary to deliver the antigens in an immunogenic form to the immune system. To generate the cellular immune response critical for tumour rejection, this means the proteins must either be delivered inside the cytoplasm of a host cell (a difficult task for high molecular weight protein antigens) or synthesized by the host cells themselves after gene delivery or DNA immunisation. Viral vectors which have been considered for this purpose include vaccinia, adenoviruses, or retroviruses.

  Web site: http://www.delphion.com/details?pn=US06641817__

- **Immortal cell line derived from grouper Epinephelus coioides and its application therein**

  Inventor(s): Chi; Shau-Chi (Taipei, TW)

  Assignee(s): National Science Council (taipei, Tw)

  Patent Number: 6,436,702

  Date filed: November 30, 1999

  Abstract: The present invention describes (1) an immortal cell line derived from grouper and a method for establishing the cell line; (2) methods for mass producing and purifying aquatic viruses using the immortal cell line from grouper; (3) an anti-NNV antibody and a method for producing the anti-NNV antibody; and (4) a vaccine of NNV and a method for protecting fish against NNV infection. The present immortal cell line is derived from the grouper and is susceptible to the viral families of Birnaviridae such as Infectious Pancreatic Necrosis Virus (IPNV); Herpesviridae such as Eel **Herpes Virus** Formosa (EHVF); Reoviridae such as Hard Clam Reovirus (HCRV); and Nodaviridae such as Nervous Necrosis Virus (NNV).

  Excerpt(s): The present invention relates to an immortal cell line (GF-1) derived from the fin tissue of grouper Epinephelus coioides and the method of establishing the GF-1 cell line. The GF-1 cell line is susceptible to a number of aquatic viruses, including, but not limited to, Infectious Pancreatic Necrosis Virus (IPNV), Eel **Herpes Virus** Formosa (EHVF), and Nervous Necrosis Virus (NNV). This invention also relates to the method of mass producing and purifying the aquatic viruses using an immortal cell line from grouper such as the GF-1 cell line as a host. Additionally, this invention relates to an anti-NNV antibody and the method of producing the anti-NNV antibody. Finally, this invention relates to a vaccine of NNV and the method for protecting fish against NNV infection. Nervous necrosis virus (NNV), a pathogen found in many varieties of hatchery-reared marine fish, has caused mass mortality of such fish at their larval or juvenile stages. NNV belongs to the family Nodaviridae. Fish nodaviruses isolated from different species (such as SJNNV, BFNNV, JFNNV, TPNNV, RGNNV, GNNV etc.) are closely related to each other owing to the high similarity of the conserved region of their coat protein genes. NNV, also named as fish encephalitis virus (FEV) and piscine neuropathy nodavirus (PNN), is an unenveloped spherical virus with particles sized between 25 and 34 nm. The virus is characterized by vacuolation of the nerve tissues. Viral Nervous Necrosis (VNN) disease has been found in many countries under various names such as viral fish encephalitis, fish encephalomyelitis, cardiac myopathy syndrome. The hosts of NNV include many species of marine fish, for example: parrotfish, sea bass, turbot, grouper, stripped jack, tiger puffer, berfin flounder, halibut, barramundi, and spotted wolffish. According to the statistics shown in 1993, approximately 159 fish cell lines have been established which have demonstrated a capacity for growing fish viruses (Fryer and Lannan, J. Tissue Culture Method (1994), 10:57-94). Most of these cell lines are derived from the tissues of freshwater fish. There are only thirty-four cell lines which are originated from marine fish. Although some of the fish cell lines, which include RTG-2, CHSE-214, BF2, SBL, FHM, EPC, have been tested for the susceptibility of fish nodavirus, none of these cells lines has shown cytopathic effects (CPE) after viral inoculations.

  Web site: http://www.delphion.com/details?pn=US06436702__

- **L-.beta.-dioxolane uridine analogs and their pharmaceutical compositions**

  Inventor(s): Cheng; Yung-Chi (Woodbridge, CT), Chu; Chung K. (Athens, GA), Qu; Fucheng (Lawrenceville, NJ)

  Assignee(s): The University of Georgia Research Foundation (athens, Ga), Yale University (new Haven, Ct)

  Patent Number: 6,274,589

  Date filed: July 29, 1999

  Abstract: The present invention relates to the discovery that certain.beta.-L-dioxolane nucleoside analogs which contain a uracil base, and preferably, a 5-halosubstituted uracil base, exhibit unexpectedly high activity against Epstein-Barr virus (EBV), Varciella-Zoster virus (VZV) and **Herpes Virus** 8 (HV-8). In particular, the compounds according to the present invention show potent inhibition of the replication of the virus (viral growth) in combination with very low toxicity to the host cells (i.e., animal or human tissue). Compounds are useful for treating EBV, VZV and HV-8 infections in humans.

  Excerpt(s): This invention relates to novel L-.beta.-Dioxolane Uridine nucleoside analogs and their use in the prevention and treatment of Epstein-Barr virus, Varicella-Zoster virus and Kaposi's Sarcoma virus, also known as HV-8. As human bacterial infections have become more manageable and treatable through the use of increasingly available antibiotic agents, viral infections have remained a more difficult and less treatable target. Emphasis in finding agents to treat viral infections has remained a high priority. Epstein-Barr virus (EBV is an important human pathogen, related to herpes simplex virus (HSV). Elliot Kieff, Virology Third Edition, Edited by B. N. Fields, D. M. Knipe, P. M. Howley, et al. Epstein-Barr Virus and Its Replication. Chapter 74. Pp 2343-2396 and Alan B. Rickinson and Elliot Kieff, Ibid. Chapter 75, pp. 2397-2446. EBV is a lymphotrophic member of the genus Lumphocryptovirus, and belongs to the sub-family gammaherpesvirinae. Another new member of human virus also belonging to this family is Kaposi's sarcoma-associated **herpes virus** (KSHV/HHV8). Chang, et al., Science, 266:1865-1869 (1994); Cesarman, et al., N. Eng. J. Med., 332:1186-1191 (1995); Soulier, et al., Blood, 86:1276-1280 (1995). There are two subtypes of EBV identified and their genomes are nearly identical, but there is no clear relationship between EBV associated diseases and EBV sub-types. Abdul-Hamid, et al., Virology, 190: 168-175 (1992) and Sample, et al., J. Virol. 64:4084-4092 (1990). The lytic EBV genome is a linear, double-stranded, 172 Kbp DNA composed of 60 mol % guanine and cytosine. The genome has been sequenced and it was found to be capable of encoding a number of virus specified proteins, which include several enzymes involved in virus DNA synthesis during lytic infection of EBV. In vitro, EBV infection is generally limited to B-lymphocytes, although epithelial cells can also be infected. Sixbey, et al., Nature, 306:480-483 (1983). In humans, the virus genome can be detected in B-lymphocytes and T-lymphocytes as well as epithelial cells. The EBV genome replicates lytically in the linear form and can also be latent as supercoiled circular DNA. The expression of the EBV genome in lytic infected cells is very different from latent infected cells. EBV specified DNA plymerase, Dnase and dTbd kinase are only expressed in cells upon lytic DNA replication. Cell culture studies indicated the essential role of EBV specified DNA polymerase for EBV DNA replication during lytic infection, but not for the maintenance of supercoiled EBV DNA in latent infected cells. A unique set of EBV proteins including EBVNA 1 and sometimes, EBNA LP, 2, 3A, 3B, 3C, LMP1 as well as LMP2 is expressed in latent infected or transformed cells. Elliot Kieff, Virology, Third Edition, Edited by B. N. Fields, D. M. Knipe, P. M. Howley, et al. Epstein-Barr Virus and Its Replication.

Chapter 74. Pp 2343-2396 and Alan B. Rickinson and Elliot Kieff, Ibid. Chapter 75, pp. H2397-2446.

Web site: http://www.delphion.com/details?pn=US06274589__

- **Method for treating herpes virus**

  Inventor(s): Ratcliff; Perry A. (Scottsdale, AZ)

  Assignee(s): Vortech, Inc. (las Vegas, Nv)

  Patent Number: 6,287,551

  Date filed: November 3, 2000

  Abstract: A solution or gel composition containing activated chlorine dioxide and phosphates, such as disodium hydrogen phosphate, sodium dihydrogen phosphate, trisodium phosphate, and sodium monofluorophosphate, is disclosed for treating **herpes virus.** The preferred concentration ranges are between about 0.005% to about 2.0% chlorine dioxide, and between about 0.02% to about 3.0% of a phosphate compound. The phosphate compound retards escape of chlorine dioxide in the pH range of 6.0 to 7.4, at which pH chlorine dioxide becomes activated and releases sufficient chlorine dioxide to reduce motility and become lethal to the involved micro-organisms.

  Excerpt(s): The present invention is directed to a method and composition for destroying Human Immuno Virus (HIV) and other bacterial and fungus viral forms and the present invention is directed to a related method and composition which provide lubricity, stops vaginal itching and destroys HIV. More particularly, the present invention relates to the use of activated stabilized chlorine dioxide in conjunction with a phosphate compound to destroy HIV and other viral forms and wherein the phosphate compound provides stability and serves as a surfactant or nonsudsing detergent to reduce surface tension on mucosal tissues assisting in the exposure of the epithelial covering to the activated chlorine dioxide. Thiols, particularly the volatile sulfur compounds such as hydrogen sulfide, methylmercaptan and dimethylsulfide, are recognized in the current literature as being major contributors to the penetration of bacterial toxins through the epithelial barrier into the underlying basal lamina and connective tissue. A. Rizzo, Periodontics, 5:233-236 (1967); W. Ng and J. Tonzetich, J. Dental Research, 63(7):994-997 (1984); M. C. Solis-Gaffar, T. J. Fischer and A. Gaffar, J. Soc. Cosmetic Chem., 30:241-247 (1979); I. Kleinberg and G. Westbay, J. Periodontal, 63(9): 768-774 (1992). The penetration of this barrier makes possible the invasion of antigenic substances such as viral and bacterial toxins and bacteria into the underlying substrate. Thus, by removing the volatile sulfur compounds and maintaining the epithelial barrier there is a reduction in the penetration capacity of antigens and microbiota (A. Rizzo, Periodontics, 5:233-236 (1967); W. Ng and J. Tonzetich, J. Dental Research, 63(7): 994-99.7 (1984); M. C. Solis-Gaffar, T. J. Fischer and A. Gaffar, J. Soc. Cosmetic Chem., 30:241-247 (1979)) as well as the destruction of the motility and the death of bacterial and viral forms. Studies done in the mouth have demonstrated that the penetration of bacteria takes place in the presence of the volatile sulfur compounds, resulting in initiation of the inflammatory reaction including initiation of the complement cascade. I. Kleinberg and G. Westbay, J. Periodontal, 63(9): 768-774 (1992). Initiation of the inflammatory reaction and development of the complement cascade leads to an eightfold increase in the cell division or mitosis of epithelial cells in the attachment apparatus of the gingiva. W. O. Engler, S. P. Ramfjiord and J. J. Hiniker, J. Periodont., 36:44-56 (1965). Because the epithelia of other orifices, and particularly

vaginal epithelium, are very similar to the gingival epithelium, reactions similar to those described above for the gingival epithelium occur in all other parts of the body, as demonstrated by the occurrence of vaginitis and endometriosis of the vagina. Examples of such bacteria which may appear in any bodily orifice include Porphyromonas (formerly known as Bacteroides) gingivitis. Actinobacillus actinomycetemcomitans, and Pseudomonades.

Web site: http://www.delphion.com/details?pn=US06287551__

- **Method for treating infectious viral diseases**

  Inventor(s): Kronis; K. Anne (Tampa, FL), Lezdey; Darren (Indian Rocks Beach, FL), Lezdey; John (Indian Rocks Beach, FL)

  Assignee(s): Alphamed Pharmaceutical Corp. (clearwater, Fl)

  Patent Number: 6,468,557

  Date filed: January 5, 2001

  Abstract: The present invention provides for the treatment of an individual suffering from infections from **herpes virus** or human papilloma virus by utilizing a cromolyn compound. The treatment includes the use of a corticosteroid or L-lysine that can be administered separately or in combination.

  Excerpt(s): The present invention relates to the treatment of infectious viral diseases. More particularly, there is provided the treatment of viral infections caused by herpes simplex virus (HSV) or human papilloma virus (HPV) with a cromolyn compound. There are two immunologic types of herpes simplex virus (HSV), HSV-1 and HSV-2. HSV-1 commonly causes herpes labialis and keratitis. HSV-2, usually genital, is transmitted primarily by direct contact with lesions, most often venereally, and also produces skin lesions. Shingles is believed to be a result of HSV infection.

  Web site: http://www.delphion.com/details?pn=US06468557__

- **Method of treating tumorigenic disease**

  Inventor(s): Chou; Joany (Chicago, IL), Roizman; Bernard (Chicago, IL)

  Assignee(s): Arch Development Corporation (chicago, Il)

  Patent Number: 6,340,673

  Date filed: April 1, 1999

  Abstract: The present invention relates to methods of treatment of programmed cell death (apoptosis) through the use of the HSV-1 gene.gamma.sub.1 34.5 or the product of its expression, ICP34.5. The gene and its expression have been demonstrated to be required for HSV-1 neurovirulence, and in particular, to act as an inhibitor of neuronal programmed cell death which allows for viral replication. Use of the gene therapy, or the protein itself, can be expected to result in inhibition of programmed cell death in various neurodegenerative diseases. This invention also relates to novel vectors for gene therapy, including modified **herpes virus.** Methods are presented for conducting assays for substances capable of mimicing, potentiating or inhibiting the expression of.gamma.sub.1 34.5 or the activity of ICP34.5. Also, methods are disclosed for the treatment of tumorogenic diseases, including cancer, and for treatment of herpes and

other viral infections using inhibitors of.gamma.sub.1 34.5 expression or ICP34.5 activity.

Excerpt(s): The present invention is directed to methods for blocking or delaying programmed cell death, for delivery of gene therapy to specific cells, and for treatment of cancer and other tumorgenic diseases, as well as treatment of viral infections, through the potentiation of programmed cell death in tumor or viral host cells. The present invention is also directed to assays for candidate substances which can either inhibit, or potentiate programmed cell death. In the last decade there has been increasing acceptance in the scientific community of the idea that cells may actually be internally programmed to die at a certain point in their life cycle. As an active cellular mechanism programmed cell death, is or apoptosis, has several important implications. First, it is clear that such an active process can provide additional means of regulating cell numbers as well as the biological activities of cells. Secondly, mutations or cellular events which potentiate apoptosis may result in premature cell death. Third, a form of cell death which is dependent on a specific active cellular mechanism can at least potentially be suppressed. Finally, an inhibition of preprogrammed cell death would be expected to lead to aberrant cell survival and could be expected to contribute to oncogenesis. In general, apoptosis involves distinctive morphological changes including nuclear condensation and degradation of DNA to oligonucleosomal fragments. In certain circumstances it is evident that apoptosis is triggered by or is preceeded by changes in protein synthesis. Apoptosis appears to provide a very clean process for cellular destruction, in that the cells are disposed of by specific recognition and phagocytosis prior to bursting. In this manner cells can be removed from a tissue without causing damage to the surrounding cells. Thus, it can be seen that programmed cell death is crucial in a number of physiological processes, including morphological development, clonal selection in the immune system, and normal cell maturation and death in other tissue and organ systems.

Web site: http://www.delphion.com/details?pn=US06340673__

- **Methods and compositions for the large scale production of recombinant adeno-associated virus**

  Inventor(s): Dong; Jianyun (Birmingham, AL), Frizzell; Raymond A. (Birmingham, AL)

  Assignee(s): Uab Research Foundation (birmingham, Al)

  Patent Number: 6,686,200

  Date filed: August 31, 1993

  Abstract: This invention provides novel methods and compositions for use in the efficient and large-scale production of recombinant adeno-associated virus (AAV). Described herein are new producer cell lines, recombinant adenovirus or **herpes virus** vectors and AAV constructs. Also disclosed are particularly advantageous methods of using such materials to produce recombinant AAV virions using only the efficient process of viral infection, without requiring transfection steps. The AAV produced may be used in a variety of embodiments including, for example, for transferring exogenous genes into human cell lines and for use in human gene therapy regimens.

  Excerpt(s): The present invention relates generally to the fields of molecular biology and gene transfer and particularly concerns recombinant adeno-associated virus (AAV). The invention provides novel methods and compositions, including cell lines, recombinant AAV and adenovirus or **herpes virus** vectors, for use in the efficient and large-scale

production of adeno-associated virus. The AAV production methods described herein do not require a transfection step. The resultant AAV may be used in a variety of embodiments including, for example, for transferring exogenous genes into human cell lines and for use in human gene therapy regimens. There are currently more than 4,000 known genetic disorders which lack fully effective therapies. In recent years the prospect of using gene therapy to treat such diseases has become to be viewed as a realistic goal. The ultimate form of gene therapy requires the integration of a wild-type gene able to correct the genetic disorder into the host genome, where it can co-exist and replicate with the host DNA. The expression of the gene should be regulated at a level that can best compensate for the defective gene. In the most ideal circumstances, the disease would be cured for life by one or a few treatments, with no serious side effects. There have been several experimental approaches to gene therapy proposed to date, but each suffer from their particular drawbacks (Mulligan, 1993). Firstly, there are basic transfection methods in which DNA containing the gene of interest is introduced into cells non-biologically, for example, by permeabilizing the cell membrane physically or chemically. This approach is limited to cells that can be temporarily removed from the body and can tolerate the cytotoxicity of the treatment, i.e. lymphocytes. Furthermore, the efficiency of gene integration is very low, on the order of one integration event per 1,000 to 100,000 cells, and expression of transfected genes is often limited to days in proliferating cells or weeks in non proliferating cells.

Web site: http://www.delphion.com/details?pn=US06686200__

- **Production of recombinant proteins using herpes virus promoters and VP16 transactivators**

  Inventor(s): Highkin; Maureen Katherine (St. Louis, MO), Hippenmeyer; Paul Jerome (St. Louis, MO)

  Assignee(s): G. D. Searle & Co. (chicago, Il)

  Patent Number: 6,635,478

  Date filed: April 30, 1996

  Abstract: Stable cell lines are produced to express high levels of a gene product of interest using VP16, a herpes simplex virus transactivator, and a promoter from herpes simplex virus which is a target for VP16. The transactivator and promoter are introduced to a cell line separately using antibiotic resistance genes as selectable markers on separate vectors.

  Excerpt(s): This invention pertains to production of recombinant proteins and more particularly to a means of heterologous gene transactivation. The ability to efficiently produce recombinant proteins in mammalian cell culture is critical for the production of both research agents and commercial products. Several approaches and host vector systems for the production of recombinant proteins have been reviewed (Kaufman, Genetic Engineering, Principles and Methods, vol. 9, J. K, Setlow, ed., Plenum Press, New, York, 1987; Warren et al., Recombinant DNA Technology and Applications, A. Prokop, R. Bajpai and C. Ho, eds., McGraw Hill, New York, 1990). These systems include use of high copy episomal vectors such as bovine papillomavirus (Howley et al., Methods in Enzymology, vol. 101, Academic Press, New York, 1983), amplifiable vectors such as those containing the dihydrofolate reductase gene (Kaufman,supra), the asparagine synthetase gene (Andrulis, Molecular Cell Genetics, vol. 17, 1985) or the ornithine decarboxylase gene (McConlogue, Gene Transfer Vectors for Mammalian Cells. 1987) or strong constitutive promoters such as the simian virus 40 promoter

(Mulligan et al., Science. vol. 209, pp. 1422-1427, 1980) or the human cytomegalovirus major early promoter (Boshart et al., Cell, vol. 41, pp. 521-530, 1985). All of these systems rely upon the levels of endogenous transactivators in the particular cell type to stimulate transcription of the promoters used to construct the expression vectors. An alternative approach to high level production would be to engineer cells with a specific transcriptional activator or transactivator. If the transactivator has a specific target promoter, then the target promoter can be linked to a gene of interest and inserted into the engineered cell. The amount of target protein produced from that cell would depend on several parameters. First, the inherent specific activity of the transactivator will be a factor in the amount of transcription from the target promoter. In addition, the amount of transactivator produced by the target cell will affect the amount of transactivation. For instance, in Chinese hamster ovary cells (CHO) there is a low level of endogenous glucocorticoid receptor/transactivator present. Transfection of a plasmid that requires the glucocorticoid receptor/transactivator results in very little expression from that plasmid. However, if the cells are first engineered to express high levels of the glucocorticoid receptor/transactivator, then high level expression from the same plasmid is obtained (Israel et al., Nuc. Acids Res., vol. 17, pp. 4589-4606, 1989). Therefore, the amount of transactivation depends on the amount of transactivator in the cell. The amount of transactivator will depend on the promoter used to drive expression of the transactivator and the site of the integration of the cassette in the host cell. Thirdly, the amount of target vector in a particular cell will influence how many copies will be transactivated. The site of integration of the target promoter may also play a role in the expression of the activated promoter.

Web site: http://www.delphion.com/details?pn=US06635478__

- **Recombinant vaccine containing feline herpes virus type 1 particularly for treating feline infectious peritonitis**

  Inventor(s): Audonnet; Jean-Christophe Francis (Lyons, FR), Baudu; Philippe Guy Nicolas (Lyons, FR), Riviere; Michel Albert Emile (Ecully, FR)

  Assignee(s): Merial (lyons, Fr)

  Patent Number: 6,387,376

  Date filed: March 21, 2000

  Abstract: The recombinant live vaccine comprises, as vector, a feline herpesvirus comprising and expressing at least one nucleotide sequence encoding a polypeptide, this sequence being inserted into the ORF5 and/or ORF2 sites. Polyvalent vaccine formula and feline herpesvirus DNA fragments.

  Excerpt(s): The present invention relates to vaccines, preferably for cats, produced from recombinant feline herpesviruses, and to the methods for obtaining and preparing these recombinant viruses. In particular, the present invention relates more particularly to the feline herpesvirus recombinants comprising an expression cassette for one or more foreign genes. Feline infectious rhinotracheitis is caused by feline herpesvirus type 1 (FHV-1). Feline herpesvirus (FHV-1) is classified in the Alphaherpesviridae family. Feline infectious rhinotracheitis is a disease which is very widespread in cats and, in practice, all medicated cats are vaccinated against this viral condition. There are currently several vaccines for preventing infectious rhinotracheitis. These vaccines are either of the attenuated live type, or of the inactivated type (whole virus or purified subunits). The attenuation of the live vaccines currently used has been obtained by repeated passages on cells, and the cause of their attenuation is not known.

Furthermore, these vaccines exhibit, in general, a residual virulence and are for this reason administered via the parenteral (subcutaneous or intramuscular) route rather than via the intranasal route (which would nevertheless be the preferred route given the local replication of this virus). Inactivated vaccines exhibit good safety, but their weak immunogenicity requires multiple injections in order to induce a satisfactory protection. Moreover, domestic cats are exposed to numerous other diseases, and the development of a vaccinal vector which can express various antigens of feline pathogenic agents would make it possible to simplify and improve the efficacy of vaccination programmes.

Web site: http://www.delphion.com/details?pn=US06387376__

- **Stabilization of herpes virus preparations**

  Inventor(s): Loudon; Peter Thomas (Cambridge, GB), Varley; Claire Alison (Cambridge, GB)

  Assignee(s): Cantab Pharmaceuticals Research Ltd (cambridge, Gb)

  Patent Number: 6,258,362

  Date filed: April 26, 1999

  Abstract: Stabilized dried pharmaceutical compositions dispersible in aqueous liquid or injection comprise (i) virus e.g. for use as a vaccine or vector, preferably a herpesvirus, e.g. attenuated or genetically disabled infectious herpes simplex virus or varicella zoster virus, (ii) polysaccharide, e.g. dextran, and/or a source of mixed aminoacids of vegetable or bacterial origin, (iii) a buffer, and (iv) a mono- or oligo-saccharide or derivative thereof.

  Excerpt(s): This invention relates to preparations of viruses, e.g. for vaccine or other pharmaceutical or research use, to their stabilisation, and to processes of producing such preparations, as well as to their use, e.g. as vaccines or as virus vectors. It is known to freeze and/or lyophilise viable virus preparations for laboratory or vaccine use in order to preserve their activity. Numerous methods are known for producing live virus preparations, e.g. herpesvirus preparations, for vaccine and other purposes.

  Web site: http://www.delphion.com/details?pn=US06258362__

- **Sugar modified oligonucleotides that detect and modulate gene expression**

  Inventor(s): Cook; Philip Dan (Vista, CA), Kawasaki; Andrew M. (Oceanside, CA)

  Assignee(s): Isis Pharmaceuticals, Inc. (carlsbad, Ca)

  Patent Number: 6,307,040

  Date filed: September 23, 1997

  Abstract: Compositions and methods are provided for the treatment and diagnosis of diseases amenable to modulation of the production of selected proteins. In accordance with preferred embodiments, oligonucleotides and oligonucleotide analogs are provided which are specifically hybridizable with a selected sequence of RNA or DNA wherein at least one of the 2'-deoxyfuranosyl moieties of the nucleoside unit is modified. Treatment of HIV, **herpes virus,** papillomavirus and other infections is provided.

  Excerpt(s): This invention relates to the design, synthesis and application of nuclease resistant oligonucleotides which are useful for antisense oligonucleotide therapeutics,

diagnostics, and research reagents. Sugar modified oligonucleotide which are resistant to nuclease degradation and are capable of modulating the activity of DNA and RNA are provided. Methods for modulating the production of proteins utilizing the modified oligonucleotide of the invention are also provided. It is well known that most of the bodily states in mammals including infectious disease states, are affected by proteins. Such proteins, either acting directly or through their enzymatic functions, contribute in major proportion to many diseases in animals and man. Classical therapeutics has generally focused upon interactions with such proteins in efforts to moderate their disease causing or disease potentiating functions. Recently however, attempts have been made to moderate the actual production of such proteins by interactions with molecules that direct their synthesis, intracellular RNA. By interfering with the production of proteins, it has been hoped to effect therapeutic results with maximum effect and minimal side effects. One approach for inhibiting specific gene expression is the use of oligonucleotide and oligonucleotide analogs as antisense agents.

Web site: http://www.delphion.com/details?pn=US06307040__

- **Treatment of chronic viral infections with M. vaccae**

  Inventor(s): Rook; Graham A. W. (London, GB), Stanford; Cynthia A. (Kent, GB), Stanford; John L. (Kent, GB)

  Assignee(s): Stanford Rook Limited (london, Gb)

  Patent Number: 6,596,282

  Date filed: September 13, 2001

  Abstract: The present invention provides the use of an M. vaccae preparation for the manufacture of a medicament for use in the treatment of a chronic viral infection, excluding an HIV infection. Chronic viral infections include HPV infection, such as HPV infection associated with cervical dysplasia, **herpes virus** infection, subacute sclerosing pan-encephalitis and hepatitis virus infection.

  Excerpt(s): The present invention relates to the use of M. vaccae in the treatment of viral infections, particularly chronic viral infections. British Specification No. 2156673 (International Patent Specification WO85/03639) describes immunotherapeutic agents comprising killed cells of M. vaccae. These agents are useful in the immunotherapy of mycobacterial disease, especially tuberculosis and leprosy. It is stated that use of this immunotherapeutic agent facilitates the removal of the persisting bacilli responsible for tuberculosis or leprosy which, as is well known, it is difficult to remove by chemotherapy alone. International Patent Specification PCT/GB85/00183 (WO85/05034) describes compositions for the alleviation of the symptoms of, and for the treatment or diagnosis of, arthritic disease which comprise as active ingredient the whole organism of M. vaccae. It is stated that the preparations of M. vaccae are useful for the treatment of various autoimmune diseases and especially arthritic conditions including rheumatoid arthritis, ankylosing spondylitis or Reiter's syndrome.

  Web site: http://www.delphion.com/details?pn=US06596282__

Patent Applications on Herpes Virus

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 herpes virus:

- **4-hydroxycinnoline-3-carboxyamides as antiviral agents**

  Inventor(s): Larsen, Scott D.; (Kalamazoo, MI), Nair, Sajiv K.; (Kalamazoo, MI), Vaillancourt, Valerie A.; (Kalamazoo, MI)

  Correspondence: Andrew M. Solomon; Pharmacia & Upjohn Company; Global Intellectual Property; 301 Henrietta Street; Kalamazoo; MI; 49001; US

  Patent Application Number: 20020042397

  Date filed: March 15, 2001

  Abstract: Certain novel 4-hydroxycinnoline-3-carboxyamides. The compounds are particularly effective in the treatment or prevention of viral infections, particularly infections caused by herpes viruses including herpes simplex virus types 1 and 2, human **herpes virus** types 6, 7 and 8, varicello zoster virus, human cytomegalovirus or Epstein-Barr virus.

  Excerpt(s): This application claims the benefit of the following provisional application: U.S. Ser. No. 60/190976, filed Mar. 21, 2000. The present invention provides novel cinnolines, which are useful as antiviral agents (e.g. as agents against viruses of the herpes family). The herpesviruses comprise a large family of double stranded DNA viruses. They are also a source of the most common viral illnesses in man. Eight of the herpes viruses, herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), varicella zoster virus (VZV), human cytomegalovirus (HCMV), epstein-Barr virus (EBV), and human herpes viruses 6, 7, and 8 (HHV-6, HHV-7, and HHV-8), have been shown to infect humans.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Composition for treatment of malignant tumors**

  Inventor(s): Dechant, Richard Frederick; (Sacramento, CA)

  Correspondence: Richard Frederick Dechant; 500 Dunbarton Circle; Sacramento; CA; 95825; US

  Patent Application Number: 20020188013

  Date filed: May 2, 2001

  Abstract: A unique composition for treatment of malignant tumors and **herpes virus** infections is composed of resorcinol, camphor, and sodium sulfathiazole dissolved in propylene glycol. This composition is easy to apply, and at cocentrations used, causes no apparent side effects.

  Excerpt(s): The Merck Index, Ninth Edition, Merck & Co., Rahway N.J., page 1058, No. 7951, 1976. The present invention is related to the chemical treatment of cancer. Malignant tumors sensitive to the composition are attacked via the blood stream and/or

[10] This has been a common practice outside the United States prior to December 2000.

the lymph system, or by direct contact. I originally formulated this composition to treat infections caused by streptococcus and staphlococcus bacteria. By chance I discovered it had properties for treating melanomas, carcinomas, internal malignant tumors, and vesicles caused by herpes simplex and zoster viruses, all of which are sensitive to this composition. When the composition is applied to the skin or to sensitive mucous membranes there are no deleterious side effects other than a slight 10 to 15 second stinging sensation.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Compositions and methods for the treatment of viral disorders**

  Inventor(s): Faller, Douglas V.; (Weston, MA)

  Correspondence: Ronald I. Eisenstein; Nixon Peabody Llp; 101 Federal Street; Boston; MA; 02110; US

  Patent Application Number: 20010009922

  Date filed: January 8, 2001

  Abstract: This invention relates to compositions and methods for the treatment of virus infections and other viral-associated disorders. Compositions comprise an inducing agent and an anti-viral agent. The inducing agent induces the expression of a cellular or viral product, such as viral thymidine kinase, increasing the sensitivity of proliferating cells to the anti-viral agent. Typical anti-viral agents are nucleoside analogs such as ganciclovir that inhibit viral replication. Methods involve administration of therapeutically effective amounts of the inducing agent with the anti-viral agent to destroy virus-infected cells. Viral infections that can be treated include infections by herpes viruses such as Kaposi's-associated **herpes virus** and Epstein-Barr virus, HIV infections and HTLV infections. These compositions and methods are particularly effective against episomal and latent infections in proliferating cells.

  Excerpt(s): This invention relates to compositions and methods for the treatment of viral disorders. Treatment involves administration of an inducing agent, to induce expression of a product in a virus-infected cell, and an anti-viral agent, that acts on the expressed product to destroy the virus-infected cell. A growing number of cellular disorders such as neoplastic malignancies have been found to contain viral genetic sequences or virus particles in the anomalous cells. For a large number of these disorders, the presence of the virus is believed to be causative or at least contributory instrument. Representative members of many of the known families of viruses have been found in such cells including members of the herpes family of viruses, the polyomaviruses and the hepatitis viruses. Epstein-Barr virus (EBV), a 172 kb **herpes virus,** is often found intimately associated with both mature and immature B cells and is believed to be involved to some degree in infectious mononucleosis, African Burkitt's lymphoma (BL) and nasopharyngeal carcinoma. EBV undergoes lytic replication after initial infection of oropharyngeal epithelia. The linear form genome is duplicated, packaged into the viral capsid and extruded from the cell by budding or lysis. One hundred viral proteins are synthesized during this lytic stage of the virus life cycle. In contrast, normal B cells incubated with EBV in vitro are efficiently immortalized and develop into continuously growing lymphoblastoid cell lines (LCIs). The cellular events that regulate these distinct outcomes are as yet unclear.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Detection of human herpes virus 6 (HHV6)**

  Inventor(s): Cunningham, Anthony Lawrence; (New South Wales, AU), Ratnamohan, Vigneswary Mala; (New South Wales, AU)

  Correspondence: Nixon & Vanderhye, PC; 1100 N Glebe Road; 8th Floor; Arlington; VA; 22201-4714; US

  Patent Application Number: 20040018488

  Date filed: July 31, 2003

  Abstract: The present invention relates to methods for detecting viral pathogens, particularly human **herpes virus** 6 (HHV6), preferable using polymerase chain reaction (PCR) techniques. The present invention also relates to primer sequences useful in these methods. In a first aspect, the present invention consists in an isolated nucleic acid molecule complementary to and specific for human **herpes virus** 6 (HHV6) DNA including a sequence selected from the group consisting of 5' CTTCTGTTTTACAGGAGT (SEQ ID NO:1). 5'ACAATTGCCATTTCGGGGAAGTAC (SEQ ID N0:2), and functionally equivalent sequences. A method for detecting HHV6 in a sample suspected of containing HHV6, the method comprising the steps of: (a) optionally amplifying viral DNA present in the sample by polymerase chain reaction techniques using outer primers complementary to the viral DNA; (b) adding to the sample or to the sample having undergone optional amplification step (a), a pair of inner oligonucleotide primers complementary to and specific for HHV6 DNA, wherein the inner primers comprise the sequences 5'AAGCTTGCACAATGCCAAAAAACAG and 5'CTCGAGTATGCCGAGACCCCAATC, or functionally equivalent sequences; (c) carrying out polymerase chain reaction techniques on the sample so as to amplify the HHV6 DNA spanned by the inner primers present in the sample: and (d) detecting the amplified HHV6 DNA.

  Excerpt(s): The present invention relates to methods for detecting viral pathogens, particularly human **herpes virus** 6 (HHV6), using polymerase chain reaction (PCR) techniques. Other herpesviruses, including human **herpes virus** 6 (HHV6), reactivate during periods of intense immunosuppression. Infection with HHV6 is usual in the first one to three years of life and a minority develop exanthem subitum during primary infection. HHV6 antibody levels tend to decrease in adults over 30 years of age and may reach undetectable levels. Two major subspecies of HHV6, variants A and B, have been distinguished on genetic, antigenic and biological characteristics. Reactivation of HHV6 (variant B) has been reported in bone marrow, renal and liver transplant patients and has been associated with hepatitis severe interstitial pneumonitis and encephalitis. Serologic evidence has been reported for simultaneous reactivation of CMV and HHV6 after renal transplantation and there have been reports of dual infection with CMV and either HHV6 or HHV7 in transplant patients. Prospective studies of the role of HHV6 in febrile disease following renal transplantation and the potential interaction between CMV and HHV6 reactivation in causing disease are lacking. Viral markers which can accurately predict CMV/HHV6 disease, the need for antiviral therapy, and likelihood of successful response in renal transplant recipients is an important clinical priority. Buffy coat cultures have been a more reliable predictor of CMV disease in renal transplantation than detection in urine. More recently, detection of CMV DNA in plasma or quantification in urine or buffy coat have been shown to be predictive of disease in liver, renal transplant or HIV infected patients. HHV6 DNA has been detected in sera from immunosuppressed patients with HIV infection or undergoing bone marrow transplantation. The present inventors have examined prospectively reactivation or infection with CMV and HHV6 detected as viral DNA by polymerase

chain reaction (PCR) in serum and urine, to determine the relative contributions of the two viruses towards disease during renal transplantation and to consider whether active infection of both viruses together may predict either the frequency or severity of disease.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Diagnosis and treatment of herpes infections**

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  Patent Application Number: 20010049113

  Date filed: May 30, 2001

  Abstract: Methods and compositions for treating or preventing virus infections by interfering with the activity or function of Ras, the Ras pathway, the ERK pathway, MEK1/2, PKR or eIF-2.alpha., includes the use of agents which inhibit Ras or otherwise modulate anti-PKR activity. Also, a method of diagnosing such virus infections includes the use of cell lines that have an activated Ras pathway, including cell lines which have been transformed with a gene that activates the Ras pathway. The virus infections may be **herpes virus** infections and HSV-1 or HSV-2 infections in particular.

  Excerpt(s): This application claims the priority benefit of U.S. Provisional Patent Application No. 60/207,337 filed on May 30, 2001. The present invention relates to the field of treatment of viral infections and **herpes virus** infections in particular. The present invention also relates to the field of detection and diagnosis of the presence of **herpes virus** in a specimen. The herpes family of viruses comprises viruses whose genomes consist of a single double-stranded DNA molecule. Herpes simplex viruses (HSV) are members of this family, and are known commonly for their association with cold sores (HSV-1) and genital herpes infections (HSV-2) [1]. Within this family are also varicella-zoster virus, cytomegalovirus, Epstein-Barr virus and various other human herpes viruses (HHV) such as HHV-6, HHV-7 and HHV-8 [2].

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **EHV-1 vectors**

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  Patent Application Number: 20020090716

  Date filed: March 18, 2002

  Abstract: The invention relates to manipulation of equine **herpes virus** for use in gene therapy and in particular to modifications of the virus so that it can carry heterologous material and furthermore, preferably, be replication deficient so that the virus cannot replicate in the target tissue.

  Excerpt(s): The invention relates to a method of virus manipulation; means therefor and products thereof which have particular, but not exclusive, application in gene therapy/vaccine development. Human gene therapy virus vectors constructed to date

are derived from adenovirus, retrovirus, parvovirus and herpesvirus families. With the exception of retroviruses, all have been derived from viruses originally isolated from humans. In nearly every case the vectors used in both ex and in vivo work have been derived from virus mutants originally created to study gene function, rather than to act as gene delivery systems. A virus-derived vector capable of efficient gene delivery to human epithelial mucosal cells would have a wide range of uses in human gene therapy, for example delivery of a correct copy of the cystic fibrosis trans-membrane regulator protein to the lung or a range of human tumour suppressor genes to tumours of the lung and colon or additionally as a vaccine delivery vehicle to induce muscosal immunity. Although adenoviruses have proved to be popular because of ease of growth of stocks to high titre, they have many problems, as viruses which are replication incompetent in cell culture have caused tissue damage and respiratory disease in patients treated with such vectors (1,2). Furthermore, adenovirus vectors with further gene deletions to express proteins are in development, but these grow less well in culture than the original E1A (a gene essential for adenovirus replication in tissue culture) deletion mutants (3), which suggests production problems in the longer term. The compact nature of the adenovirus genome, in which many of the early regulatory genes are components of overlapping gene clusters, which are differentially spliced, makes it difficult to delete the coding region of single transcripts (4). Furthermore, adenoviruses have a packaging constraint which prevents the introduction of heterologous DNA sequences >8 Kbp. One of the biggest problems with adenoviruses resides in the lack of information on virus gene function in pathogenesis (5). It is very difficult to predict, at present, which genes might be deleted in order to create a completely replication defective virus in vivo. In addition, one of the major structural components of adenoviruses, the fibre, responsible for cell attachment, can itself cause a cytopathic effect (6).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Genetically engineered herpes virus for the treatment of cardiovascular disease**

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  Patent Application Number: 20020155432

  Date filed: November 28, 2001

  Abstract: The present invention provides methods of expressing a nucleic acid or producing a proteinaceous composition encoded by a nucleic acid in vascular and cardiovascular cells by administration of a herpesvirus vector. The present invention provides methods of producing a therapeutic benefit in vascular and cardiovascular tissue by administration of a herpesvirus vector. In additional aspects, the invention concerns combination therapies for vascular and cardiovascular diseases comprising administration of a herpesvirus vector and treatment with at least one addition pharmacological agent or surgical procedure.

  Excerpt(s): Priority is claimed to U.S. Provisional Patent Application No. 60/253,680, filed Nov. 28, 2000. The present invention relates generally to the fields of genetic therapy. More particularly, it concerns administration of a herpes simplex viral vector to produce a therapeutic benefit in vascular and cardiovascular tissue. In additional aspects, the invention concerns combination therapies comprising administration of a

herpes simplex viral vector and treatment with at least one additional pharmacological agent or surgical procedure, as well as use of surgical procedures and other targeting means to facilitate delivery of the herpes simplex virus vectors to vascular cells and tissues. Vascular disease remains the leading cause of death and disability in the Western world [McGovern et al., New Engl. J. Med. 334:884-890, 1996]. Current treatment strategies are primarily aimed at risk factor modification and/or mechanical remediation of critical lesions. Although these strategies are often effective, the ability to genetically alter the basic pathophysiologic defects within diseased vascular tissue would offer a new paradigm of therapy and possibly revolutionize the treatment of vascular disease. The feasibility of vascular gene transfer was first demonstrated in 1989 when it was shown endothelial cells (EC's) expressing the retrovirally transduced lacZ gene could adhere and function in porcine iliac arteries [Nabel et al., Science 244:1342-1344, 1989]. Since then, nearly one billion U.S. dollars annually have been spent to refine and improve systems of transfer vectors and delivery systems [Svensson et al., Curr. Opin. Cardio. 13:369-374, 1998].

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Herpes virus complementing cell line**

  Inventor(s): Metcalfe, Karen; (Wilmington, MA)

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  Patent Application Number: 20030049830

  Date filed: October 10, 2002

  Abstract: The present invention is directed to a cell line capable of supporting replication of a growth-defective Herpes Simplex Virus strain; specifically a replication-defective HSV-2 double mutant. Particularly disclosed is a cell line that expresses the ICP8 protein and the UL5 protein of Herpes Simplex Virus. This cell line is useful to propagate a replication-defective HSV-2 vaccine strain that contains mutations and/or deletions in the ICP8 and UL5 genes.

  Excerpt(s): This application claims priority to U.S. provisional application No. 60/196,801, filed Apr. 13, 2000. The present invention is in the fields of cellular and molecular biology. Specifically, The present invention is directed to a cell line useful for the growth of a mutant strain of Herpesvirus. Herpesviridae is a large family of enveloped linear dsDNA-containing animal viruses. Herpesviruses are morphologically similar. The virion (.about.120-200 nm diam.) contains a core (DNA wound around a central protein structure) within an icosahedral capsid (.about.100-110 nm diam.) comprising 12 pentameric and 150 hexameric capsomers. The viron is enclosed by a lipoprotein envelope bearing surface projections. The linear dsDNA genome characteristically contains repeated terminal and/or internal sequences.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Herpes viruses for immune modulation**

  Inventor(s): Coffin, Robert S.; (London, GB)

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  Patent Application Number: 20040022812

  Date filed: October 18, 2002

  Abstract: A method of stimulating an immune response in a human or animal subject, which method comprises administering to a subject in need thereof an effective amount of an attenuated **herpes virus** which:(i) lacks a functional vhs gene, or a functional equivalent thereof;(ii) lacks a functional ICP47 gene, or a functional equivalent thereof; and(iii) is incapable of expressing a substantial amount of functional ICP22, or a functional equivalent thereof, in mammalian dendritic cells.

  Excerpt(s): The present invention relates to attenuated herpes simplex viruses capable of efficiently infecting dendritic cells. It also relates to the use of such viruses in immunotherapy approaches to the treatment of disease. Dendritic cells (DCs) are the most potent antigen presenting cells and are efficient at inducing responses even to antigens to which the immune system has become tolerant. Thus for tumour immunotherapy, in which an immune response is raised against a tumour, the use of DCs may be ideal if they were made to present tumour specific antigens. DCs might also be used to present antigens derived from infectious agents, such as bacteria, viruses or parasites, providing protective or therapeutic vaccines for such diseases. However effective transfer of antigens into DCs for any of these targets has proved the greatest problem with this approach. To provide a realistic chance of generating a therapeutic immune response against a tumour antigen or other disease related antigen, several conditions have to be met. Firstly, it is necessary to identify molecules whose expression is tumour or disease specific (or at least selective), and which can therefore serve as the target for an immune response. This task has proved very difficult for the majority of common tumours, but is solved in for example the case of cervical cancer by the presence, in most cases, of the viral oncogenes E6 and E7, and for other tumours, good candidate antigens are beginning to be identified. For example the MUC-1 gene product is over expressed in a number of tumours, including 90% of ovarian cancers. Various other tumour associated antigens have also been identified, any of which might be used in an immunotherapy treatment of cancer. These include gp100, MART-1 tyrosinase, MAGE, CEA, PSA and many others. Further tumor associated antigens will no doubt continue to be discovered over time. Secondly, following the identification of the antigen/antigens, it is necessary to deliver the antigens in an immunogenic form to the immune system. To generate the cellular immune response critical for tumour rejection, this means the proteins must either be delivered inside the cytoplasm of a host cell (a difficult task for high molecular weight protein antigens) or synthesized by the host cells themselves after gene delivery or DNA immunisation. Viral vectors which have been considered for this purpose include vaccinia, adenoviruses, or retroviruses.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Herpes zinc finger motifs**

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  Patent Application Number: 20030186283

  Date filed: February 11, 2003

  Abstract: The present invention relates to a method for detecting an agent for use in the treatment of **herpes virus** infection and use of known agents, such as 2,2'-dithiobisbenzamide (DIBA) and azodicarbonamide (ADA), and unknown agents, which selectively eject zinc bound to a zinc finger protein, for the manufacture of a medicament for the treatment of herpesvirus infections.

  Excerpt(s): The present invention relates to a method for detecting an agent for use in the treatment of **herpes virus** infection and use of known and unknown agents for the manufacture of a medicament for the treatment of herpesvirus infections. A paradigm for the development of antivirals was based on the identification of agents that selectively eject zinc from retroviral zinc finger proteins. One such protein is the human immunodeficiency HIV-1 nucleocapsid protein NCp7, which is essential for early and late virus replication. NCp7 interacts with the viral RNA at a packaging site (1). This 55bp amino acid protein contains two zinc fingers, one of which is highly conserved among the retroviruses (reviewed in 2). The NCp7 CCHC zinc finger represents a rare conserved feature, absent in cellular proteins, against the extreme variation of other retrovirus components which suggests that mutation to resistance against reagents that target conserved zinc finger motifs may be difficult to achieve. Potent anti-HIV-1 agents that selectively target the NCp7 protein zinc finger by ejecting zinc have been identified which are non-toxic to cells (3,4). Huang et al. 1998 describe agents that target retroviral nucleocapsid protein zinc fingers without seriously affecting cellular zinc finger proteins. Specifically, the agents are 3-nitrosobenzamide (NOBA), disulfide benzamides (DIBAs or 2,2'-dithiobisbenzamides), dithiaheterocyclic molecules such as 1,2-dithiane-4,5-diol, 1,1-dioxide, cis(dithiane),.alpha.-carbonyl azoic compounds such as azodicarbonamide (ADA), and others. However, this document only discloses the agents' action on retroviruses and in particular nucleocapsid p7 (NCp7).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Immortal cell line derived from grouper Epinephelus coioides and its applications therein**

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  Patent Application Number: 20020164787

  Date filed: December 3, 2001

  Abstract: The present invention describes (1) an immortal cell line derived from grouper and a method for establishing the cell line; (2) methods for mass producing and purifying aquatic 10 viruses using the immortal cell line from grouper; (3) an anti-NNV antibody and a method for producing the anti-NNV antibody; and (4) a vaccine of NNV and a method for protecting fish against NNV infection. The present immortal cell line is

derived from the grouper and is susceptible to the viral families of Birnaviridae such as Infectious Pancreatic Necrosis Virus (IPNV); Herpesviridae such as Eel **Herpes Virus** Formosa (EHVF); Reoviridae such as Hard Clam Reovirus (HCRV); and Nodaviridae such as Nervous Necrosis Virus (NNV).

Excerpt(s): This application claims the priority of U.S. Provisional Application No. 60/110,699, filed on Dec. 3, 1998, which is incorporated herein by reference. The present invention relates to an immortal cell line (GF-1) derived from the fin tissue of grouper Epinephelus coioides and the method of establishing the GF-1 cell line. The GF-1 cell line is susceptible to a number of aquatic viruses, including, but not limited to, Infectious Pancreatic Necrosis Virus (IPNV), Eel **Herpes Virus** Formosa (EHVF), and Nervous Necrosis Virus (NNV). This invention also relates to the method of mass producing and purifying the aquatic viruses using an immortal cell line from grouper such as the GF-1 cell line as a host. Additionally, this invention relates to an anti-NNV antibody and the method of producing the anti-NNV antibody. Finally, this invention relates to a vaccine of NNV and the method for protecting fish against NNV infection. Nervous necrosis virus (NNV), a pathogen found in many varieties of hatchery-reared marine fish, has caused mass mortality of such fish at their larval or juvenile stages. NNV belongs to the family Nodaviridae. Fish nodaviruses isolated from different species (such as SJNNV, BFNNV, JFNNV, TPNNV, RGNNV, GNNV etc.) are closely related to each other owing to the high similarity of the conserved region of their coat protein genes. NNV, also named as fish encephalitis virus (FEV) and piscine neuropathy nodavirus (PNN), is an unenveloped spherical virus with particles sized between 25 and 34 nm. The virus is characterized by vacuolation of the nerve tissues. Viral Nervous Necrosis (VNN) disease has been found in many countries under various names such as viral fish encephalitis, fish encephalomyelitis, cardiac myopathy syndrome. The hosts of NNV include many species of marine fish, for example; parrotfish, sea bass, turbot, grouper, stripped jack, tiger puffer, berfin flounder, halibut, barramundi, and spotted wolffish.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **L-beta-dioxolane uridine analogs and methods for treating and preventing virus infections**

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  Patent Application Number: 20010018440

  Date filed: January 19, 2001

  Abstract: The present invention relates to the discovery that certain P-L-dioxolane nucleoside analogs which contain a uracil base, and preferably, a 5-halosubstituted uracil base, exhibit unexpectedly high activity against Epstein-Barr virus (EBV), Varciella-Zoster virus (VZV) and **Herpes Virus** 8 (HV-8). In particular, the compounds according to the present invention show potent inhibition of the replication of the virus (viral growth) in combination with very low toxicity to the host cells (i.e., animal or human tissue). Compounds are useful for treating EBV, VZV and HV-8 infections in humans.

Excerpt(s): This application is a continuation-in-part application of Ser. No. 08/749,263 filed Nov. 15, 1996. This invention relates to novel L-.beta.-Dioxolane Uridine nucleoside analogs and their use in the prevention and treatment of Epstein-Barr virus, Varicella-Zoster virus and Kaposi's Sarcoma virus, also known as HV-8. As human bacterial infections have become more manageable and treatable through the use of increasingly available antibiotic agents, viral infections have remained a more difficult and less treatable target. Emphasis in finding agents to treat viral infections has remained a high priority.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Ligand for herpes simplex virus entry mediator and methods of use**

  Inventor(s): Ware, Carl; (Solana Beach, CA)

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  Patent Application Number: 20030060605

  Date filed: September 28, 2001

  Abstract: A novel polypeptide ligand, p30, or LIGHT, for **herpes virus** entry mediator, HVEM, is provided. LIGHT is useful for modulating immune responses and in inhibiting infection and/or subsequent proliferation by herpesvirus. HVEM fusion proteins are also provided. Methods for treating subjects with lymphoid cell disorders, tumors, autoimmune diseases, inflammatory disorders or those having or suspected of having a herpesvirus infection, utilizing p30 and the fusion proteins of the invention, are also provided.

  Excerpt(s): This application is a continuation-in-part of U.S. Ser. No. 09/549,096, filed Apr. 12, 2000, which is a continuation-in-part of U.S. Ser. No. 08/898,234, filed Jul. 30, 1997 (now U.S. pat. No. 6,140,467), which claims priority to U.S. Ser. No. 60/051,964, filed Jul. 7, 1997, and which are incorporated herein by reference in their entirety for all purposes. The invention relates generally to compounds and methods useful in regulating immune responses and viral infection. Herpes simplex virus (HSV), types 1 and 2, causes recurrent infections that range in severity from benign to serious. HSV emerges from latency in neurons to infect the skin and other tissues in the presence of a competent cellular immune system. The D glycoprotein (gD) of HSV, a transmembrane protein located in the virion envelope, initiates infection by binding to cellular receptors (Spear et al. (1993) Viral Fusion Mechanisms. Ed. Bentz. CRC press, Boca Raton). Recently, a cellular protein used by HSV for infection was identified and given the term HSV entry mediator (HVEM) (Montgomery (1996) Cell 87:427). HVEM is a transmembrane type 1 protein with a cysteine-rich extracellular domain that exhibits significant homology with receptors for tumor necrosis factor (TNF)-related cytokines (Smith et al. (1994) Cell 76:959; Ware et al. (1995) in, Pathways of Cytolysis. Eds. Griffiths and Tschopp. Springer-Verlag, Basel). Many of the TNF superfamily members initiate a variety of cellular responses necessary to mount effective inflammatory and immune responses.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Lymphotropic agents and vectors**

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  Patent Application Number: 20020137186

  Date filed: February 4, 2002

  Abstract: Human **herpes virus** (HHV) 7 is capable of binding to the CD4 antigen and the HHV-7 or a binding protein derived therefrom is thus useful as a CD4-ligand for various therapeutic applications. HHV-6 or HHV-7 are lymphotropic and are thus useful as lymphotropic vectors for delivering DNA into lymphocytes.

  Excerpt(s): The present invention is generally in the field of targeted therapeutic agents. By one of its embodiments, the present invention concerns an agent which specifically binds to receptors on certain cells. By a second embodiment the present invention concerns vectors specifically targeted to certain cells. A specific aspect of the present invention concerns the prophylaxis and treatment of AIDS. The following are references considered to be relevant for the subsequent description.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Means of inducing durable immune responses**

  Inventor(s): Brockman, Mark; (Boston, MA), Knipe, David; (Auburndale, MA)

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  Patent Application Number: 20030215463

  Date filed: March 24, 2003

  Abstract: A replication defective **herpes virus** vector is described. The replication defective **herpes virus** vector has a deletion of at least a fragment of a U.sub.L29 gene that is replaced with a heterologous sequence encoding an antigen from a specific infectious disease agent. The vector can express said antigen. Prior HSV infection did not diminish the magnitude or the durability of the IgG antibody response generated by preferred replication-defective HSV-1 vectors. A method of inducing in a mammal an immune response against a specific infectious disease agent also is described. A recombinant replication defective mutant Herpes Simplex Virus as a vaccine is administered to a mammal to elicit in the mammal an immune response against the infectious disease causing agent.

  Excerpt(s): The present application claims the benefit of U.S. provisional application No. 60/366,977 filed Mar. 22, 2002, and which is incorporated herein by reference in its entirety. This invention relates to the construction of vectors that produce a durable protective immune response and may be used repeatedly and still obtain a strong immune response, regardless of prior host immunity. Herpes Simplex Virus (HSV) infection often results in a localized lesion within epithelial cells of the skin or a mucosal membrane. The innate immune response, consisting of macrophages, natural killer (NK) cells, cytokines, and complement proteins, may act to contain initial viral infection. NK cell-mediated lysis and numerous cytokines, including interleukin (IL)-12, IL-18, and gamma interferon and tumor necrosis factor-alpha, have been reported to affect HSV pathogenesis in mouse models of disease.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method for diagnosing and alleviating the symptoms of chronic fatigue syndrome**

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  Patent Application Number: 20020037501

  Date filed: October 3, 2001

  Abstract: A method for alleviating chronic fatigue syndrome with the administration of antiviral agents. Based on clinical tests, chronic fatigue syndrome is a persistent **herpes virus** infection including incomplete virus multiplication and thus administration of antiviral agents are shown to alleviate the symptoms associated with the disorder. Based on therapeutic trials, patients receiving the recommended antiviral treatment, have experienced significant reduction or elimination of the symptoms associated with chronic fatigue syndrome. A method of diagnosis of the chronic fatigue syndrome is further disclosed.

  Excerpt(s): This application is a continuation-in-part of U.S. application Ser. No. 09/663,729 filed Sep. 15, 2000, which is a continuation-in-part of U.S. application Ser. No. 09/177,942 filed Oct. 23, 1998, which, in turn, is a continuation-in-part and divisional of prior U.S. application Ser. No. 08/802,776 filed Feb. 18, 1997. This invention relates to a method of alleviating the symptoms associated with chronic fatigue syndrome through the use of antiviral agents. Chronic fatigue syndrome (CFS) is a disorder which, until recently, had no formalized name, received little attention and was believed by the majority of the medical community to be a psychological rather than medical disorder. However, as information about the disorder has been disseminated, the symptoms associated with the disorder, as well as the growing number of people afflicted with this disorder, have steadily increased to alarming proportions. In fact, CFS is being reported with increasing frequency throughout the world.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method of inhibiting formation of infectious microorganisms**

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  Patent Application Number: 20010020043

  Date filed: December 11, 2000

  Abstract: The present invention provides a method of inhibiting the formation of pseudorabies particles in a host cell. The method involves administering an effective amount of a poly-hydroxylated stilbene, particularly resveratrol, to a **herpes virus** infected host cell. The present invention also provides a method of reducing or inhibiting the growth of Neisseria gonorrhea and Neisseria meningiditis in vitro and in vivo. The method comprises administering a composition comprising a therapeutically effective amount of a tri-hydroxylated stilbene to a growth surface which has come into contact or could come into contact with the bacterium.

Excerpt(s): This application is a continuation in part of the co-pending, commonly assigned, U.S. patent application Ser. No. 09/145,039; filed Sep. 1, 1998. The present invention relates to methods of inhibiting replication of three pathogenic microorganisms, pseudorabies virus, Neisseria gonorrheae, and Neisseria meningiditis. Pseudorabies virus, a member of the Herpesvirus family, primarily affects swine. Because virus is present in the nasal and oral discharges of infected pigs, infection is usually transmitted between pigs by none to nose contact. Contaminated drinking water and feed buckets may also transmit disease. Clinical symptoms in pigs can vary from undetectable to death. The extent of the symptoms depends on the age and immune status of the animal at the time of infection, the virus dose, route of infection, and strain of virus. Young pigs may be severely affected with a 100% mortality in pigs under 2 weeks of age. Piglets may die suddenly or, prior to death, exhibit symptoms which include fever, loss of appetite, convulsions, and paddling. The severity of clinical signs decreases with age, and older pigs may only experience fever and inappetence of a few days duration.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Methods for delaying recurrence of herpes virus symptoms**

  Inventor(s): Smith, Michael H.; (St. Paul, MN)

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  Patent Application Number: 20020055517

  Date filed: August 17, 2001

  Abstract: Novel dosing regimens of resiquimod formulations are disclosed for delaying recurrence of herpetic lesions in patients affected with a **herpes virus** infection. Preferably, dosing regimens include administering a pharmaceutical formulation containing resiquimod to a herpetic lesion once a week for at least one week.

  Excerpt(s): The invention is directed to novel dosing regimens for the administration of resiquimod. In some embodiments, the invention is particularly advantageous for delaying recurrence of symptoms associated with infection by double-stranded DNA viruses such as herpes simplex virus types 1 (HSV-1) and 2 (HSV-2). Approximately 600,00 new cases of herpes simplex virus are diagnosed annually in the United States. The total number of people infected in the United States is estimated to be more than 40 million. Herpes simplex virus is composed of a double-stranded DNA nucleoprotein core surrounded by an icosahedral protein capsid, which in turn is enclosed in a lipid and glycoprotein outer envelope. It is a member of a family of eight known related human herpes viruses, including herpes simplex virus types 1 (HSV-1) and 2 (HSV-2), varicella-zoster virus (VZV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), human **herpes virus** 6 (HHV-6), human **herpes virus** 7 (HHV-7) and human **herpes virus** 8 (HHV-8). Many herpes viruses are capable of establishing latency in certain cell types, resulting in persistent infection.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Molecular vaccine linking intercellular spreading protein to an antigen**

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  Patent Application Number: 20040028693

  Date filed: August 8, 2003

  Abstract: Superior molecular vaccines comprise nucleic acids, including naked DNA and replicon RNA, that encode a fusion polypeptide that includes an antigenic peptide or polypeptide against which an immune response is desired. Fused to the antigenic peptide is an intercellular spreading protein, in particular a **herpes virus** protein VP22 or a homologue or functional derivative thereof. Preferred spreading proteins are VP22 from HSV-1 and Marek's disease virus. The nucleic acid can encode any antigenic epitope of interest, preferably an epitope that is processed and presented by MHC class I proteins. Antigens of pathogenic organisms and cells such as tumor cells are preferred. Vaccines comprising HPV-16 E7 oncoprotein are exemplified. Also disclosed are methods of using the vaccines to induce heightened T cell mediated immunity, in particular by cytotoxic T lymphocytes, leading to protection from or treatment of a tumor.

  Excerpt(s): The present invention in the fields of molecular biology, immunology and medicine relates to a chimeric nucleic acid, including DNA and viral RNA encoding a fusion protein and its use as a vaccine to enhance immune responses, primarily cytotoxic T lymphocyte (CTL) responses to specific antigens such as tumor or viral antigens. The fusion protein comprises an antigenic polypeptide fused to a protein that promotes intercellular transport and processing via the MHC class I pathway, such as the VP22 protein from herpes simples virus and related herpes viruses. Naked DNA vaccines have emerged as attractive approaches for vaccine development (for review, see (1-3)). Intradermal administration of DNA vaccines via gene gun represents a convenient way of delivering DNA vaccines into professional antigen presenting cells (APCs) in vivo. Professional APCs are a superior candidate for mediating presentation of an antigen encoded by such a DNA vaccine to T lymphocytes of the immune system. The "gene gun" strategy provides efficient delivery of DNA into epidermal bone marrow-derived APCs termed Langerhans cells, which move to draining lymph nodes where they enter the lymphatic system (Condon et al., 1996). The present inventors and their colleagues have successfully used this system of DNA delivery to test various intracellular targeting strategies (Chen et al., 2000; Ji et al., 1999); co-pending, commonly assigned U.S. patent applications U.S. Ser. Nos. 09/421,608; 09/501,097, 09/693,450 and No. 60/281,003). However, one limitation of DNA vaccines is their potency, since they do not have the intrinsic ability to amplify and spread in vivo as some replicating viral vaccine vectors do. The present inventors conceived a strategy that facilitates the spread of antigen may significantly enhance the potency of naked DNA vaccines.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Novel avian herpes virus and uses thereof**

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  Patent Application Number: 20020081316

  Date filed: June 14, 2001

  Abstract: The present invention provides a novel avian herpesvirus (NAHV) vector and recombinant vaccines made therefrom that are useful to immunize avian species against Marek's disease, infectious laryngotracheitis and Newcastle disease. Methods of immunizing an avian species against Marek's disease, infectious laryngotracheitis and Newcastle disease are also provided.

  Excerpt(s): This application is a continuation-in-part of U.S. Ser. No. 09/426,352, filed Oct. 25, 1999; which is a continuation of U.S. Ser. No. 08/804,372, filed Feb. 21, 1997, now U.S. Pat. No. 6,183,753, which is a continuation-in-part of application No. PCT/US95/10245, filed on Aug. 9, 1995, and U.S. Ser. No. 08/663,566, filed on Jun. 13, 1996, now U.S. Pat. No. 5,853,733, which is a continuation of U.S. Ser. No. 08/288,065 filed Aug. 9, 1994, now U.S. Pat. No. 5,961,982, which is a continuation-in-part of application No. PCT/US93/05681, filed on Jun. 14, 1993 and U.S. Ser. No. 08/023,610, filed on Feb. 26, 1993, now U.S. Pat. No. 5,928,648, which is a continuation-in-part of U.S. Ser. No. 07/898,087, filed Jun. 12, 1992. The disclosures of all publications, patents and patent applications are incorporated herein by reference. The present invention relates to recombinant herpesviruses and, more particularly to a novel avian herpesvirus (NAHV) suitable for use as a viral vector for vaccination of birds against disease. The ability to isolate DNA and clone such isolated DNA into bacterial plasmids has greatly expanded the approaches available to make viral vaccines. The methods used to make the present invention involve modifying cloned DNA sequences from various viral pathogens of animals, by insertions, deletions, single or multiple base changes, and subsequent insertions of these modified sequences into the genome of the virus. One utility of the addition of a foreign sequence is achieved when the foreign sequence encodes a foreign protein that is expressed during viral infection of the animal. The resulting live virus may then be used in a vaccine to elicit an immune response in a host animal and provide protection to the animal against disease. A virus with these characteristics is referred to as a viral vector, because it becomes a living vector that will carry and express the foreign protein in the host animal. In effect it becomes an elaborate delivery system for the foreign protein(s).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Novel feline cytokine protein**

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  Patent Application Number: 20020107366

  Date filed: February 22, 2002

Abstract: A novel feline cytokine protein having the activity to enhance the cytotoxic activity of feline cytotoxic T lymphocytes, a DNA sequence coding for said protein, a recombinant DNA for expressing said protein, an expression vector comprising said recombinant DNA, a transformant which is transformed with said expression vector, a process for preparing said protein by culturing said transformant, and an antibody against said protein are provided. The novel feline cytokine protein of the present invention is a heterologous dimer comprising FLAF p35 and FLAF p40 and can be used for treating feline infectious diseases such as feline **herpes virus** type 1 (FHV-1) or feline calicivirus (FCV).

Excerpt(s): The present invention relates to a novel polypeptide tide, a novel protein comprising a homologous dimer or a heterologous dimer of said polypeptide, a novel DNA coding for said peptide, a recombinant DNA molecule comprising said DNA, a transformant which is transformed with said recombinant DNA molecule, an antibody against said novel polypeptide or said novel protein, a process for preparing said novel polypeptide or said novel protein, and an agent for treating feline viral diseases comprising said novel protein or said novel antibody. More particularly, the present invention relates to a feline cytokine protein comprising two distinct novel polypeptides having an activity to damage virus-infected cells by activating feline cytotoxic T lymphocytes and a gene coding for said cytokine protein as well as a process for preparing said feline cytokine protein. A cat is such an animal that has been loved by humans as a pet from ancient times and, in modern times, called as Companion species, is becoming a member of a human society. On the other hand, a cat has hitherto greatly contributed to humans as an experimental animal in various fields such as medicine, pharmaceutics, animal husbandry veterinary and psychology, and in recent years, the contribution of a cat has further increased to be used in an effectiveness assay or safety test for drugs. With increasing social significance of a cat, there is a high interest in feline diseases, especially feline infectious diseases, and thus more efficacious method for treating these diseases is desired. Many feline viral diseases, attack of which often leads to serious conditions, are known. For example, an upper tracheal disease caused by feline **herpes virus** type 1 (FHV-1) or feline calicivirus (FCV) is acute and highly lethal. In addition to this, diseases caused by feline immunodeficiency virus, feline infectious peritonitis virus, feline parvovirus, etc. are also highly lethal and have been great concern. Although some prophylactic vaccines have been developed for these viral diseases, many of these vaccines are not fully efficacious due to diversity of viral serotype. Furthermore, once a cat is infected with virus and after the onset of viral diseases, vaccines are not substantially efficacious any more, and hence, protection from secondary bacterial infections with antibiotics, sulfonamides etc. or symptomatic treatment with vitamins or nutrients have primarily been carried out. That is, presently no efficacious medicaments are available for treating the viral diseases.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Pharmaceutical compositions comprising herpes virus entry receptor protein**

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  Patent Application Number: 20020102644

  Date filed: August 8, 2001

Abstract: The present invention provides isolated and purified polynucleotides that encode HVEM of mammalian origin, expression vectors containing those polynucleotides, host cells transformed with those expression vectors, a process of making HVEM using those polynucleotides and vectors, and isolated and purified HVEM.

Excerpt(s): This application is a continuation of U.S. application Ser. No. 09/333,279, which is a divisional of U.S. application Ser. No. 08/509,024, filed on Jul. 28, 1995, both of which are herein incorporated by reference in their entireties. The field of this invention is a **herpes virus** entry receptor (HVEM). More particularly, the field of the present invention is recombinant mammalian HVEM, polynucleotides encoding that HVEM, and methods of making recombinant HVEM. Glycosaminoglycan chains on cell surface proteoglycans serve as receptors for the binding of herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) to cells. Binding is not sufficient for entry, however: other cell surface components are necessary for virus entry, which occurs by fusion of the virion envelope with a cell membrane. For example, Chinese hamster ovary (CHO) cells express glycosaminoglycan chains to which HSV-1 and HSV-2 can bind, but are resistant to the entry of some HSV strains, particularly HSV-1(KOS).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Polynucleotide herpes virus vaccine**

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Patent Application Number: 20020147167

Date filed: April 16, 2001

Abstract: Genes encoding herpes simplex virus type 2 (HSV-2) proteins were cloned into eukaryotic expression vectors to express the encoded proteins in mammalian muscle cells in vivo. Animals were immunized by injection of these DNA constructs, termed polynucleotide vaccines or PNV, into their muscles. In a DNA titration, it was found that a single immunization of.gtoreq.0.5.mu.g of (one) PNV, gave >90% seroconversion by ten weeks post immunization. Immune antisera neutralized both HSV-2 and HSV-1 in cell culture. When animals were challenged with HSV-2, significant ($p<0.001$) protection from lethal infection was achieved following PNV vaccination. DNA constructs may be full-length, truncated and/or mutated forms and may be delivered along or in combination in order to optimize immunization and protection from HSV infection.

Excerpt(s): This application is a continuation-in-part of U.S. application Ser. No. (not yet known), filed Sep. 18, 1996, which is a continuation application of U.S. application Ser. No. 08/279,459, filed Jul. 22, 1994. A major obstacle to the development of vaccines against viruses, particularly those with multiple serotypes or a high rate of mutation, against which elicitation of neutralizing and protective immune responses is desirable, is the diversity of the viral external proteins among different viral isolates or strains. Since cytotoxic T-lymphocytes (CTLs) in both mice and humans are capable of recognizing epitopes derived from conserved internal viral proteins [J. W. Yewdell et al., Proc. Natl. Acad. Sci. (USA) 82, 1785 (1985); A. R. M. Townsend, et al., Cell 44, 959

(1986); A. J. McMichael et al., J. Gen. Virol. 67, 719 (1986); J. Bastin et al., J. Exp. Med. 165, 1508 (1987); A. R. M. Townsend and H. Bodmer, Annu. Rev. Immunol. 7, 601 (1989)], and are thought to be important in the immune response against viruses [Y.-L. Lin and B. A. Askonas, J. Exp. Med. 154, 225 (1981); I. Gardner et al., Eur. J. Immunol. 4, 68 (1974); K. L. Yap and G. L. Ada, Nature 273, 238 (1978); A. J. McMichael et al., New Engl. J. Med. 309, 13 (1983); P. M. Taylor and B. A. Askonas, Immunol. 58, 417 (1986)], efforts have been directed towards the development of CTL vaccines capable of providing heterologous protection against different viral strains. It is known that CTLs kill virally-infected cells when their T cell receptors recognize viral peptides associated with MHC class I and or class II molecules. These peptides can be derived from endogenously synthesized viral proteins, regardless of the protein's location or function within the virus. By recognition of epitopes from conserved viral proteins, CTLs may provide heterologous protection.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Production of therapeutic proteins in transgenic cereal crops**

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  Patent Application Number: 20030159182

  Date filed: August 29, 2002

  Abstract: There is provided a **herpes virus** vaccine produced in in the seeds of a cereal crop and a method of producing the vaccine. The method comprises: a) obtaining a nucleic acid sequence encoding a **herpes virus** antigen; b) introducing the nucleic acid sequence into cereal plant tissue competent to form seeds; c) permitting said cereal plant tissue to develop; and, d) directing preferential expression of the antigen encoded by the nucleic acid sequence in seeds formed by the cereal plant tissue. Herpes viruses antigens of particular interest include all or antigenic portions of gB (from human cytomegalovirus ("HCMV")), gH (from HCMV), and gD (from herpes simplex virus 1 or 2), as well as antigens from Epstein Barr virus and varicello-zoster virus-8. Envelope glycoproteins from herpes viruses are antigens of interest. Cereal crops of particular interest include rice, wheat, oats, barley, and corn. Vaccines produced according to the invention are very stable and may be administered by a variety of routes, including injection and contact with mucosal membranes, such as by oral administration in purified or unpurified form.

  Excerpt(s): Human cytomegalovirus ("HCMV") is a widely distributed member of the **herpes virus** family that is transmitted by blood and other body secretions. In immunocompromised individuals such as AIDS patients, organ transplant recipients and low weight pre-term infants, the virus can cause severe and/or lethal disease, while congenital infection may result in damage to the central nervous system. The HCMV encoded glycoprotein B complex ("gB") is a transmembrane protein of 907 amino acids (for the prototype Towne strain) which is initially synthesized in infected cells as a 105 kDa non-glycosylated polypeptide. In normal infected mammalian host cells, the gB polypeptide undergoes post-translational glycosylation, cleavage of the N-terminal 24 amino acid signal peptide, oligomerization and folding which take place in the endoplasmic reticulum of the cell, where it is transiently associated with a membrane-bound chaperonin. This results in transport of a 150 kDa gB precursor to the Golgi

complex where further carbohydrate modifications occur and the polypeptide is proteolytically cleaved to yield products of 116 kDa and 58 kDa which are disulfide linked. Both species are targets for neutralizing and non-neutralizing antibodies, each representing both continuous and discontinuous epitopes. A phosphorylation site is located in the cytoplasmic tail and may be important for correct intracellular trafficking. The sequence of gB (Towne) is reported in Spaete et al., Virology 167(1), 207 (1988), Pub. Med. Acc. No. M22343. Mammalian immune responses are highly specific and sensitive to even minor differences between potential antigenic sites. Thus, changes to the post-translational modification of an antigen such as gB will have the potential to render it unsuitable for use as a vaccine against infection by the native organism. Plant seeds are an ideal organ for the targeted synthesis of heterologous proteins. However, where the proteins of interest are of non-plant origin, numerous technical challenges arise in the production and recovery of useful transgenic proteins. In particular, differences in post-translational modification and transport may render plant-produced proteins unsuitable for some uses in mammals.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Rapid production of autologous tumor vaccines**

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  Patent Application Number: 20040047837

  Date filed: June 16, 2003

  Abstract: An autologous vaccine to tumor cells is produced by transducing the tumor cells with a **herpes virus** amplicon containing the gene for an immunomodulatory protein to provide transient expression of the immunomodulatory protein by the cells. The tumor cells may transduced with the herpes simplex amplicons ex vivo or in vivo. Suitable immunomodulatory proteins include cytokines, for example, interleukins, interferons, and chemokines such as RANTES, intercellular adhesion molecules, for example ICAM-1 and costimulatory factors such as B7.1. The tumor cells may also be transduced with one or more species of amplicon containing genes for two or more different immunomodulatory proteins.

  Excerpt(s): This application is a regular application filed under 35 USC.sctn. 111(a), claiming priority from U.S. Provisional Application No. 60/044,005 filed Mar. 21, 1997. Cytokine gene transfer to tumor cells has been used to increase local production of these immune modulating proteins, with the aim of enhancing tumor immunogenicity and consequent host recognition and elimination of tumor (Dranoff et al. 1993; Gansbacher et al. 1992). Production of irradiated, non-dividing tumor cells secreting cytokines such as Interleukin-2 (IL-2), gamma-interferon (.gamma.-IFN), or granulocyte macrophage-colony stimulating factor (GM-CSF) represents a potential therapeutic strategy for treatment of malignant disease (Saito et al. 1994; Dranoff et al. 1993; Gansbacher et al. 1992), and one that is currently being evaluated in clinical trials (Lotze et al. 1994; Seigler et al. 1994; Rosenberg et al. 1992). Many methods have been examined for gene transfer (Davidson et al. 1993; Drazan et al. 1994; Yang et al. 1995; Paquereau & Le Cam, 1992; Jarnagin et al. 1992); the most successful have been those using retroviral vectors (Dranoff et al. 1993; Gansbacher et al. 1992). An impediment to the production of autologous tumor vaccines has been logistic problems surrounding gene transfer to freshly harvested tumors. The most widely utilized approach for gene transfer to tumors

relies on retroviral vectors, which are relatively inefficient and require replicating cells for gene expression (Wilson et al. 1988). The production of an autologous vaccine using retroviral vectors requires placing harvested tumor in tissue culture before in vitro transduction, selection, and isolation of the minority of cells in which gene transfer was successful. Such a process is therefore lengthy, expensive, and fraught with technical problems of establishing and maintaining primary cell culture. These difficulties have forced investigators to examine as alternative vaccine strategies the administration of established allogeneic cytokine secreting tumor cell lines (Patel et al. 1994), use of other vectors for gene transfer such as adenoviral vectors (Drazan et al. 1994; Yang et al. 1995), or the administration of cytokine-producing fibroblast cell lines along with the autologous tumor cells (Lotze et al. 1994).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Recombinant canine herpesviruses**

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  Patent Application Number: 20030049844

  Date filed: May 28, 2002

  Abstract: The present invention includes novel recombinant canine **herpes virus** (CHV) and novel recombinant CHV genomes, and particularly to those CHV and CHV genomes that contain heterologous nucleic acid molecules. The present invention also relates to the use of such genomes and viruses in a variety of applications, including as therapeutic compositions to protect animals from disease. The present invention also relates to novel isolated CHV nucleic acid molecules, to CHV proteins encoded by such nucleic acid molecules, and to antibodies raised against such CHV proteins as well as to the use of such CHV nucleic acid molecules, proteins and antibodies as therapeutic compositions to protect an animal from CHV. The present invention also includes constructs comprising CHV nucleic acid molecules that include heterologous nucleic acid molecules, to recombinant vectors including such constructs, and to the use of such constructs and vectors in the production of recombinant CHV and recombinant CHV genomes.

  Excerpt(s): The present application is a continuation-in-part of pending U.S. patent application Ser. No. 08/602,010, entitled "Recombinant Canine Herpesviruses", filed Feb. 15, 1996, and which is incorporated by reference herein in its entirety. The present invention relates to canine herpesvirus (CHV), and particularly to novel recombinant CHV and recombinant CHV genomes, including those that contain heterologous nucleic acid molecules. The present invention also relates to the use of such genomes and viruses in a variety of applications, including as therapeutic compositions to protect animals from disease. The present invention also relates to novel isolated CHV nucleic acid molecules, to proteins encoded by such nucleic acid molecules, and to use of such CHV nucleic acid molecules to insert heterologous nucleic acid molecules into CHV genomes. Dogs and other canids are affected by a number of diseases against which it would be desirable to develop protective vaccines. Live vaccines, and particularly live viral vector vaccines, are attractive vaccine vector candidates as they appear to be associated with longer-lasting immunity than inactivated virus vaccines or subunit vaccines. One disadvantage of live vaccines, however, has been that attenuated virus strains often revert to virulence. Another disadvantage has been the host range of a

number of viral vaccines. In an attempt to deliver genes to an animal, several viral and bacterial systems, such as poxviruses, adenoviruses, Salmonella, and BCG (Bacillus Calmette-Guerin), have been genetically manipulated to generate vectors containing heterologous antigen genes in order to immunize a host with a vaccine in which the antigens are presented in a "live" configuration. See, for example, the following two review articles: Esposito et al., pp. 195-247, 1989, Advances in Veterinary Science and Comparative Medicine, Vol. 33; Dougan et al., pp. 271-300, 1989, Advances in Veterinary Science and Comparative Medicine, Vol. 33.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Replication competent herpes virus strains**

  Inventor(s): Coffin, Robert Stuart; (London, GB)

  Correspondence: Nixon & Vanderhye; 8th Floor; 1100 North Glebe Road; Arlington; VA; 22201-4714; US

  Patent Application Number: 20020192802

  Date filed: July 19, 2002

  Abstract: The present invention provides a **herpes virus** strain capable of replicating in permissive cells which comprises a mutation which results in enhanced ICP0 expression compared to the parental virus without said mutation for use in a method of treatment of the human or animal body by therapy.

  Excerpt(s): The present invention relates to **herpes virus** mutants with enhanced expression of ICP0. Such expression may be useful in (i) increasing expression of an inserted heterologous gene in target cells when an HSV strain is used as a vector and/or (ii) increasing the replicative ability of replication competent HSV strains in for example the oncolytic treatment of cancer. Viruses have been suggested or demonstrated to have utility in a variety of applications in biotechnology and medicine on many occasions. Each is due to the unique ability of viruses to enter cells at high efficiency. This is followed in such applications by either virus gene expression and replication and/or expression of an inserted heterologous gene. Thus viruses can either deliver and express genes in cells (either viral or other genes) which may be useful in for example gene therapy or the development of vaccines, or they may be useful in selectively killing cells by lytic replication or the action of a delivered gene in for example cancer. Herpes simplex virus (HSV) has been suggested to be of use both as a gene delivery vector in the nervous system and elsewhere and for the oncolytic treatment of cancer. In both applications the virus must however be disabled such that it is no longer pathogenic but such that it can still enter cells and perform the desired function. Thus for non-toxic gene delivery to target cells using HSV it has become apparent that in most cases immediate early gene expression must be prevented/minimised from the virus (Krisky et al 1998, Samaniego et al 1998). For the oncolytic treatment of cancer, which may also include the delivery of gene(s) enhancing the therapeutic effect, a number of mutations to HSV have been identified which still allow the virus to replicate in culture or in actively dividing cells in vivo (e.g. in tumors), but which prevent significant replication in normal tissue. Such mutations include disruption of the genes encoding ICP34.5, ICP6, and thymidine kinase. Of these, viruses with mutations to ICP34.5, or ICP34.5 together with mutation of e.g. ICP6 have so far shown the most favourable safety profile (see Andreansky et al 1996, Hunter et al 1999). Viruses deleted for only ICP34.5 have been shown to replicate in many tumor cell types in vitro and to selectively replicate in artificially induced brain tumors in mice while sparing surrounding tissue (e.g. see

McKie et al 1996, Randazzo et al 1997). Early stage clinical trials have also shown their safety in man. However, such viruses may not show the maximum replicative potential in tumors of which HSV is capable. Thus viruses which still retain the safety of ICP34.5 mutated viruses, in that they do not replicate effectively in most non-tumor tissue in vivo, but which show enhanced oncolytic capabilties may improve the liklihood of success of HSV-based approaches to the oncolytic treatment of cancer.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Replication incompetent herpes virus vectors**

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  Patent Application Number: 20030040500

  Date filed: September 11, 2002

  Abstract: Use replication incompetent **herpes virus** comprising a heterologous gene in the manufacture of a medicament for use in treating or preventing a peripheral nervous system disorder by administering said medicament to a peripheral nerve, in a method of determining whether a gene has an effect on a phenotype associated with a peripheral nervous system disorder and in a method of treatment of a disorder of the peripheral nervous system.

  Excerpt(s): The present invention relates to replication incompetent herpes simplex viruses capable of efficiently transferring genes to cells of the peripheral nervous system. It also relates to the use of such viruses in the study and treatment of diseases and conditions of the nervous system. Herpes simplex viruses 1 and 2 are large DNA viruses the lifecycles of which are characterised by the ability to enter a lifelong latent state in the sensory ganglia of an infected individual from which reactivation of the virus can occur intermittently. During latency the HSV genome, which remains extra-chromosomal, is largely quiescent although the fact that a small part of the genome encoding the latency associated transcripts (LATs) is transcribed during latency (Stevens, 1987) shows that the development of gene delivery vectors allowing transgene expression during this time should be possible. During latency HSV is not naturally cleared by the immune system and infected cells remain undamaged, further showing the potential for a long-term therapeutic benefit using HSV as a vector (reviewed by Coffin and Latchman 1995, Fink 1996). HSV also has the unique ability among viruses currently under development as vectors to infect axonal nerve terminals followed by efficient retrograde axonal transport of the virus to the cell body in the spinal ganglia. Thus HSV vectors might be developed allowing peripheral vector inoculation to give gene delivery to the spinal ganglia following such retrograde transport. There are a number of potential applications for vectors capable of axonal transport in the peripheral nervous system, including the stimulation of regrowth of damaged nerves, the study/treatment of various pain states, the protection of neurons from further degeneration in e.g. motor neuron disease, the study/treatment of various neuropathies, the study of neuronal development, and the screening of the relevance of genes implicated as being important in any of these processes by a gene delivery approach. Previous work has shown that HSV vectors can deliver genes to spinal ganglia by such routes, but this in each case has used vectors retaining at least same replication competence as this has been thought necessary for effective gene delivery. Here various mutant viruses have been used variously mutated for the non-essential genes encoding

ICP6 (Goldstein and Weller 1988), ICP0 (Leib et al. 1989), TK (Palella et al. 1988, Ho and Mokarski 1988), gC (Lokensgard et al. 1994; Dobson et al. 1995; Goins et al. 1994), vmw65 (Ecob prince et al. 1995), un-disabled (Margolis et al. 1993, Lachman et al. 1996, Lachmann and Efstathiou, 1997), or deleted for ICP34.5 or ICP34.5 and vmw65 (Coffin et al. 1996). Each of these viruses is attenuated compared to wild type virus even though the mutated genes are non-essential, and each have shown reasonable levels of at least short term gene delivery and/or the ability to enter latency following inoculation of animals by the footpad or ear pinna routes. As discussed however, all retain at least same degree of replication competence in vivo and in culture as no essential genes have been inactivated. Therefore, while replication incompetent HSV vectors have been available for some time, none have been used in the peripheral nervous system as it has so far been assumed that viruses incapable of replication in any cell (i.e. mutated for an essential gene/genes) would not allow gene delivery to spinal ganglia following inoculation by peripheral routes.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Replication incompetent herpes viruses for use in gene therapy**

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  Patent Application Number: 20030082142

  Date filed: September 18, 2002

  Abstract: Use of a replication incompetent **herpes virus** capable of delivering a gene to multiple connected sites within the nervous system, which virus comprises: (a) a mutation which prevents or reduces the expression of at least two immediate early genes; and (b) a heterologous gene operably linked to a promoter active during **herpes virus** latency; in the manufacture of a medicament for the treatment of a central nervous system disorder, a method of determining whether a gene has an effect on a phenotype associated with a central nervous system disorder and in a method of treatment of a disorder of the central nervous system are described.

  Excerpt(s): The present invention relates to replication incompetent herpes simplex viruses capable of efficiently transferring genes to multiple sites within the nervous system. It also relates to the use of such viruses in the study and treatment of diseases and conditions of the nervous system. Herpes simplex viruses (HSV) 1 and 2 have often been suggested as a vector for gene delivery to the nervous system and also other cell types (for reviews see Coffin and Latchman 1995, Fink et al. 1996). As a vector HSV has a number of potential advantages in that it naturally enters latency in neurons, providing the possibility of long term gene expression, does not integrate into the host genome, preventing insertional mutagenesis (for example the activation of oncogenes or inactivation of tumour suppressor genes), can accept very large DNA insertions allowing the delivery of multiple genes, is easy to propagate, and can infect a wide variety of other cell types as well as neurons. HSV also has the unique ability among viruses currently under development as vectors in that it can be efficiently transported along nerves to the cell body (usually in the spine) by retrograde axonal transport following an initial peripheral infection. However, while this property of retrograde axonal transport of HSV vectors has been observed with replication competent vectors in the peripheral nervous system (PNS), it has not previously been exploited in vectors used in the central nervous system (CNS), probably due to limitations in the vectors

which have previously been available. While HSVI is highly prevalent in the human population, in the vast majority of cases giving no obvious signs of disease, for use as a vector the virus must be disabled for safety and so as to minimise toxicity to target cells. Various strategies for disablement have been reported including the removal of genes which are unnecessary for growth in vitro but necessary for pathogenesis in vivo. Such genes include those encoding thymidine kinase (TK; Ho and Mokarski 1988), ribonucleotide reductase (Goldstein and Weller 1988) and ICP34.5 (Coffin et al. 1995). However for minimal toxicity it has become apparent that expression of the regulatory immediate early genes ICPO, ICP4, ICP22 and ICP27, which are themselves cytotoxic, must be minimised (Johnson et al. 1994, Johnson et al. 1992, Wu et al. 1996, Samaniego et al. 1998, Krisky et al. 1998). Such reductions in IE gene expression minimise transcription from the vast majority of the 80 or so other genes in the HSV genome. Removal of ICP4 or ICP27 completely prevents virus growth and so such deletions must be complemented in the cells used for virus propagation (e.g. Deluca et al. 1985). Deletion of ICP22 and/or ICPO, while these genes are not absolutely essential for virus growth (Sacks and Shaffer 1987, Stow and Stow 1986, Post and Roizman 1981, Sears et al. 1985), reduces virus titre. Thus for the growth of HSV mutants with multiple IE gene deficiencies, cell lines must be produced which effectively complement deletions from the virus, and for effective growth of viruses with deletions in ICP4, ICP27, ICP22 and ICPO, all these deficiencies would optimally need to be complemented. However as the IE proteins are highly cytotoxic (Johnson et al. 1994), IE gene expression in cell lines must be tightly regulated. This is usually achieved by the use of the homologous IE gene promoters which are relatively inactive in the absence of virus infection (e.g. E5 cells [ICP4], B130/2 cells [ICP27], E26 cells [ICP4+ICP27], F06 cells [ICP4+ICP27+ICPO]; Deluca and Schaffer 1987, Howard et al. 1998, Samaniego et al. 1995, Samaniego et al. 1997). This reduces the problem of IE protein cytotoxicity but still leaves an inherent problem in the generation of cells which are highly effective at complementing multiple IE gene deficiencies.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Treatment of tumors with genetically engineered herpes virus**

  Inventor(s): Roizman, Bernard; (Chicago, IL), Weichselbaum, Ralph; (Chicago, IL), Whitley, Richard J.; (Birmingham, AL)

  Correspondence: Marshall, O'toole, Gerstein, Murray & Borun; 6300 Sears Tower; 233 South Wacker Drive; Chicago; IL; 60606-6402; US

  Patent Application Number: 20020019362

  Date filed: September 26, 2001

  Abstract: Disclosed are methods for treating cancer by administering an effective amount of a modified Herpes simplex virus.

  Excerpt(s): The present invention relates generally to use of modified Herpes simplex viruses as therapeutic treatment for tumors. The development of viruses as anticancer agents has been an intriguing yet elusive strategy. The goal of anticancer viral therapy is to inoculate a small percentage of tumor cells with replication competent viruses resulting in viral replication in the targeted tumor cells followed by cellular lysis (oncolysis) and infection of surrounding tumor cells. A key to viral oncolysis is genetic modification of the virus such that replication occurs principally in tumor cells and not in the surrounding normal tissue. Many strategies have focused on the use of genetically engineered viruses for oncolysis. For example, in one approach, attenuated retroviruses,

modified to encode herpes simplex virus (HSV) thymidine kinase, were created to target dividing tumor cells [Culver, et al., Science 256:1550-1552 (1992); Ram, et al. Nat. Med. 3:1354-1361 (1997)]. In this technique, however, viral infection of tumor cells was limited since only 10 to 15% of tumor cells were actively progressing through the cell cycle. In another approach, conditional replication-competent adenoviruses (E1b deleted) were designed to replicate only in tumor cells lacking p53, however only 50% of tumors are estimated to contain nonfunctional p53 [Bischoff, et al., Science 274:373-376 (1996); Heise, et al. Nat. Med. 3:639-645 (1997); Hollstein, et al., Science 253:49-53 (1991)]. The success of these strategies, therefore has been limited experimentally only to small tumor xenografts. Recently, genetically engineered replication-competent HSV has been proposed to treat malignant gliomas [Martuza, et al., Science 252:854-856 (1991)]. In anti-glioma therapy, HSV-1 mutants were constructed to preferentially replicate in proliferating tumor cells thereby eliminating the risk of widespread dissemination of the virus in the central nervous system, which is observed in rare cases of HSV encephalitis in human. Initial strategies focused on deletion of viral genes encoding enzymes required for viral DNA synthesis (e.g., thymidine kinase, ribonucleotide reductase [Martuza, et al, Science 252:854-856 (1991); Mineta, et al., Cancer Res. 54:3963-3966 (1994)]. More recent studies centered on the use of HSV mutants that lack a newly identified.gamma.sub.134.5 gene involved in neurovirulence [Chou, et al., Science 250:1262-1266 (1990); Chou, et al., Proc. Natl. Acad. Sci. (USA) 89:3266-3270 (1992); Chou, et al., Proc. Natl. Acad. Sci. (USA) 92:10516-10520 (1995); Andreansky, et al. Cancer Res. 57:1502-1509 (1997)]. The combination of previous results suggested that a decrease in viral proliferative potential required for safe intracranial HSV inoculation, however, correlates with a decrease in the oncolytic potential of the virus [Advani, et al. Gene Ther. 5:160-165 (1998)]. The potential therapeutic effects of a genetically engineered HSV, having more potent antitumor efficacy than is possible for intracranial inoculation, has not been studied in models of common human tumors.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Tricyclic compounds and method of treating herpes virus**

  Inventor(s): Booth, Richard John; (Ann Arbor, MI), Josyula, Vara Prasad Venkata Nagendra; (Ann Arbor, MI), Meyer, Annette Lynn; (Brighton, MI), Steinbaugh, Bruce Allan; (Chelsea, MI)

  Correspondence: Elizabeth M Anderson; Warner Lambert Company; 2800 Plymouth Road; Ann Arbor; MI; 48105; US

  Patent Application Number: 20030229073

  Date filed: July 5, 2002

  Abstract: The present invention provides a compound of the formula (I) and pharmaceutically acceptable salts having useful antiviral activity against viruses of the herpes family. In said formula, X=O, (CH.sub.2).sub.m, S, SO, SO.sub.2, NH, NR.sub.8 or a chemical bond; Y=O, (CH.sub.2).sub.m, S, SO, SO.sub.2, NH, NR.sub.8; Z=NH, O, NR.sub.8, S, SO, SO.sub.2. The remaining substituents are described in the specification.

  Excerpt(s): The present invention relates to compounds possessing antiviral activity against viruses of the herpes family, or a composition containing them. These compounds provide a method for treating herpes viral infections, including condition caused by herpes simplex I such as cold sores, herpes simplex II such as genital herpes, as well as shingles caused by herpes zoster and infections caused by cytomegalovirus, Epstein Barr Virus. Various subfamilies of herpes viruses (Herpes viridae) exist:.alpha.-

herpesvirinae,.beta.-herpesvirinae,.gamma.-herpesvirinae and cercopithecing **Herpes virus** I (B virus); some specific viruses are: Herpes simplex virus-1 (HSV-1), Herpes simplex virus-2 (HSV-2), Cytomegalovirus (CMV), Varicella Zoster virus (VZV), Epstein-Barr virus (EBV), human herpes virus-6 (HHV-6), human herpes virus-7 (HHV-7), human herpes virus-8 (HHV) as well as others which may not yet be defined. The incidence of infections by Herpes simplex virus is very high throughout the world. Serological studies showed that herpes viral infections affect a substantial percentage of the population. Reactivation of **herpes virus** infections may lead to recurrent infections. The risk of severe diseases increases with decreasing immunocompetence of the host. There is a pressing need for improved therapy for treating this disease. Currently, exclusive of vaccines, treatment involves primarily nucleoside drugs such as acyclovir, which target thymidine kinase and suffer from development of resistance.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Unit dosage forms for the treatment of herpes simplex**

  Inventor(s): Pearson, Don C.; (Lakewood, WA), Richardson, Kenneth T.; (Anchorage, AK)

  Correspondence: Townsend And Townsend And Crew; Two Embarcadero Center; Eighth Floor; San Francisco; CA; 94111-3834; US

  Patent Application Number: 20010031737

  Date filed: April 5, 2001

  Abstract: The components of this invention are chosen because of their complementarity for the prevention or treatment of diseases caused by the herpes simplex virus. L-Lysine favorably increases the physiologic immunomodulation necessary for defense against this virus. Zinc improves and maintains a normal immune response. 2-Deoxy-2-D-glucose and heparin sodium alter the surface interaction between the **herpes virus** and the cell, preventing fusion and infectivity. N-Acetyl-L-cysteine increases glutathione levels thereby creating a thiol redox barrier to the virus at the cell membrane. Quercetin reduces intracellular replication of the **herpes virus** and viral infectivity. Ascorbate, in concert with copper and D-.alpha.-tocopherol, provides an antioxidant defense against the **herpes virus,** which tends to lose latency during period of oxidative, free radical excess. Selenium and quercetin also participate in reducing various oxidative stresses. Together the components of this invention provide the potential for improved resistance to, improved recovery from, and a decreased frequency of recurrence of herpes simplex virus infection.

  Excerpt(s): This application is related to U.S. Provisional Patent Application No. 60/101,308, filed Sep. 21, 1998, and claims all benefits legally available therefrom. Provisional Patent Application No. 60/101,308 is hereby incorporated by reference for all purposes capable of being served thereby. This invention is in the field of pharmacology, and relates specifically to the pharmacological treatment of conditions associated with herpes simplex virus infections. No human virus is considered normal flora; although some viruses may be more or less symptomatic, unlike bacteria none can be considered non-pathogenic. And because the viral life cycle is played out within a host cell, the membrane and molecular function of the target eukaryocyte and the biological life cycle of the invasive virion are inextricably entwined.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Vaccination against host cell-associated herpes viruses**

  Inventor(s): Fehler, Frank; (Cuxhaven, DE), Osterrieder, Klaus; (Insel Riems, DE)

  Correspondence: Trask Britt; P.O. Box 2550; Salt Lake City; UT; 84110; US

  Patent Application Number: 20030165537

  Date filed: January 30, 2003

  Abstract: The invention relates to the field of so-called "host cell-associated herpes viruses," such as Marek's disease-like virus (MDV) of poultry and Varicella Zoster virus (VZV) of man, and to vaccination against disease caused by these viruses. The invention provides a vaccine directed against an infection caused by a **herpes virus** that is essentially host cell-associated comprising a recombinant viral genome derived from the **herpes virus,** the genome allowing recombination essentially free of the host cell.

  Excerpt(s): This application is a continuation of PCT International Patent Application No. PCT/EP/01/08893, filed on Aug. 1, 2001, designating the United States of America, and published, in English, as PCT International Publication No. WO 02/12288 A3 on Feb. 14, 2002, the contents of the entirety of which is incorporated herein by this reference. The invention relates to the field of vaccination against so-called host cell-associated herpes viruses such as Marek's disease virus (MDV) of poultry and Varicella Zoster Virus (VZV, causing chickenpox and zoster after reactivation from latency) of man and to vaccination against disease caused by these viruses, and, in particular, relates to poultry disease, in particular to the field of vaccination against Marek's disease. In particular, Marek's disease has been a problem of the poultry industry from the beginning of intensive production of poultry meat. It is a herpes viral disease that is causing a large variety of clinical signs starting from immunosuppression, neurological disorders, anemia and unspecified apathies and ending with severe lymphatic cancers at later stages of infection. In the beginning of the history of Marek's disease, there were no treatments and no preventive measures. Then an apathogenic-related (Serotype 3) virus was isolated from turkeys (HVT) and was initially used for vaccination.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Viral nucleotide sequences**

  Inventor(s): Binns, Matthew McKinley; (Huntingdon, GB), Griffin, Annette Mary; (Huntingdon, GB), Ross, Louis Joseph Norman; (Huntingdon, GB), Scott, Simon David; (Huntingdon, GB)

  Correspondence: Larson & Taylor, Plc; 1199 North Fairfax Street; Suite 900; Alexandria; VA; 22314; US

  Patent Application Number: 20010024817

  Date filed: December 26, 2000

  Abstract: Various genes of **herpes virus** of turkeys (HVT), Marek's disease virus (MDV) and infectious laryngotracheitis virus (ILTV) have been identified as non-essential regions (and candidates for insertion sites for foreign genes) and/or as antigen-encoding regions. The former include the HVT homologue of the HSV (herpes simplex virus) gC gene, the TK (thymidine kinase) region of MDV or ILTV, ORF3 of ILTV (as defined herein), the ribonucleotide reductase (large subunit) gene of ILTV, MDV or HVT and the ribonucleotide reductase (small subunit) gene of MDV. The antigen-encoding regions include the HVT homologues of the HSV gB, gC and gH genes, the ILTV homologue of

HSV gB, ORF2 of ILTV, and the HVT homologue of the HSV-1 immediate early genes IE-175 and IE-68.Manipulation of these genes allows vaccines to be prepared comprising attenuated virus or virus carrying heterologous antigen-encoding sequences.

Excerpt(s): The present invention relates to viral nucleotide sequences which may be manipulated to provide vaccines against disease. Herpesviruses are large double stranded DNA viruses consisting of an icosahedral capsid surrounded by an envelope. The group has been classified as alpha, beta and gammaherpesviruses on the basis of genome structure and biological properties [Roizman, B et al (1981) Inter-virology 16, 201-217]. Avian herpes viruses include Marek's Disease Virus (MDV) (a gammaherpesvirus) which causes a lymphomatous disease of considerable economic importance in chickens [reviewed in Payne, L. N. (ed) Marek's Disease (1985), Martinus Nijhoff Publishing, Boston] and Infectious Laryngotracheitis Virus (ILTV) (an alphaherpesvirus) which causes an acute upper respiratory tract infection in chickens resulting in mortality and loss of egg production. A recent unexpected finding in out laboratory is that there is sufficient amino acid homology between MDV, ILTV and mammalian herpesviruses, particularly varicella zoster (VZV) and Herpes Simplex virus (HSV) to allow identification of numerous conserved genes. These include the MDV and Herpesvirus of Turkeys (HVT) homologues of glycoproteins gB, gC and gH of HSV; the ILTV, MDV and HVT homologues of TK and ribonucleotide reductase genes and the ILTV homologue of COB and genes 34 and 35 of VZV [Buckmaster, A et al, (1988) J. gen. Virol, 69, 2033-2042.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Viral vectors**

Inventor(s): Efstathiou, Stacey; (Cambridge, GB), Lachmann, Robin H.; (Cambridge, GB)

Correspondence: Klarquist Sparkman Campbell Leigh & Whinston, Llp; One World Trade Center, Suite 1600; 121 S.W. Salmon Street; Portland; OR; 97204; US

Patent Application Number: 20010012516

Date filed: January 19, 2001

Abstract: Constructs for delivery of sequences of interest to cells include a **herpes virus** latency active promoter (LAP) of the latency associated transcript (LAT) region. An internal ribosome entry site (IRES) is located downstream of the LAP, with a nucleotide sequence of interest downstream of the IRES. Stable, long-term expression, including export of mRNA to the cytoplasm and translation of the encoded polypeptide, is found in neuronal and non-neuronal cells.

Excerpt(s): The present invention relates to constructs for delivery of sequences of interest to cells of an individual, for instance using recombinant viruses. This can have a therapeutic aim: and examples of the constructs and cells containing them can be useful also, for example, in production of a polypeptide which can then be used as desired (e.g. as an immunogen). By employing a latency active promoter of a latency associated transcript (LAT) region of a herpes simplex virus, long-term, high-level expression of a reporter sequence can be achieved. It is often desirable to deliver exogenous DNA to cells in order to provide a missing gene or to help correct abnormal cellular behaviour. The present invention is not generally concerned with any difficulties that may be associated with delivery of nucleic acid to cells. Many viruses have evolved to deliver nucleic acid into the nucleus of the cell, where it can be expressed. Certain viruses have been genetically engineered to carry a gene to be delivered, and can deliver it to host

cells such as those the virus normally infects. Gene delivery vectors have also been based on attenuated or genetically disabled virus.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Virus coat protein/receptor chimeras and methods of use**

  Inventor(s): Devico, Anthony Louis; (Alexandria, VA), Fouts, Timothy R.; (Columbia, MD), Tuskan, Robert G.; (Baltimore, MD)

  Correspondence: Steven J. Hultquist; P.O. Box 14329; Research Triangle Park; NC; 27709; US

  Patent Application Number: 20020155121

  Date filed: August 21, 2001

  Abstract: The invention relates to chimeric molecules comprising a virus coat sequence and a receptor sequence that can inter-act with each other to form a complex that is capable of binding a co-receptor. Such chimeric molecules therefore exhibit functional properties characteristic of a receptor-coat protein complex and are useful as agents that inhibit virus infection of cells due to occupancy of a co-receptor present on the cell. In particular aspects, the chimeric polypeptide includes an immunodeficiency virus envelope polypeptide, such as that of HIV, SIV, FIV, FeLV, FPV and **herpes virus.** Receptor sequences suitable for use in a chimeric polypeptide include, for example, CD4 D1D2 and CD4M9 sequences.

  Excerpt(s): This application is related to co-pending application U.S. Ser. No. 09/684,026 filed on Oct. 6, 2000 that claims priority from United States Provisional application 60/158,321 filed on Oct. 8, 1999. This invention relates generally to receptor ligand interactions, and more specifically to chimeric polypeptides having virus coat polypeptide and cell receptor polypeptide sequences that bind to each other and mimic the structural, functional and immunogenic properties that naturally occur when the virus protein and receptor interact in vivo. Humoral immunity arising after primary infection with HIV-1 may not prevent progression to AIDS (R. A. Koup et al., Nature, 370:416 (1994); R. A. Koup et al.,.J Virol. 68:4650-5 (1994)). However, it is likely that Humoral immunity can prevent infection if an individual has high-titered neutralizing antibodies prior to exposure to the virus. This concept is largely supported by passive immunization studies in which chimps were transfused with neutralizing anti-V3 monoclonal antibodies or pooled, high-titered neutralizing antisera around the time of challenge with cell-free virus (E. A. Emini et al., Nature:355:728-30 (1992); R. Shibata et al., Nat. Med., 5:204-10 (1999)).

  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 herpes virus, 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 "herpes virus" (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 herpes virus.

You can also use this procedure to view pending patent applications concerning herpes virus. 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 5. BOOKS ON HERPES VIRUS

Overview

This chapter provides bibliographic book references relating to herpes virus. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on herpes virus 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 "herpes virus" (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 herpes virus:

- **50 Things You Should Know About the Chronic Fatigue Syndrome Epidemic**

  Contact: TNM, Incorporated, PO Box 1475, New York, NY, 10008, (212) 627-2120.

  Summary: The author of this book discusses Chronic Fatigue Syndrome (CFS), which he views as an AIDS-like illness that is of epidemic, and even pandemic, proportions. CFS is an illness of immune dysfunction that is contagious and has been overlooked by health authorities, says the author. He discusses symptoms that can develop in CFS, including blindness, skin problems, brain lesions, and loss of fingerprints. He says that CFS shares many characteristics with AIDS, such as immune dysfunction, nervous system problems, and high antibodies against cytomegalovirus (CMV), Epstein-Barr Virus, and Human **Herpes Virus** 6 (HHV-6). The author urges people to write their Congressional representatives to voice their concerns about this growing public health problem.

- **Infection Control for the Dental Team**

  Contact: Mosby - Year Book, 11830 Westline Industrial Dr, St. Louis, MO, 63146. American Federation of State County and Municipal Employees, District Council 47 (Philadelphia), 1606 Walnut St, Philadelphia, PA, 19103-5482, (215) 546-9880, http://www.dc47afscme.org.

  Summary: This monograph outlines infection-control guidelines for dental-care workers. It says that dental workers are obligated to treat anyone who seeks care, but that they also have an obligation to control cross-infection in the dental practice. The monograph explains infection-control procedures and disease prevention in general, looking at the spread of microorganisms, patient evaluation, universal precautions, and principles of sterilization and disinfection. Chapters deal specifically with instrument sterilization, surface and equipment disinfection, the laboratory, and office design. Groups which are perceived to be at high risk for Human immunodeficiency virus (HIV) infection are listed. One chapter focuses on several infectious diseases that it says are of special concern to dental workers; these include viral hepatitis, **herpes virus,** rubella, bacterial infections, and HIV.

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 "herpes virus" at online booksellers' Web sites, you may discover non-medical books that use the generic term "herpes virus" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "herpes virus" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **Acyclovir Therapy for Herpes Virus Infections** by David A. Baker (Editor); ISBN: 0824780914; http://www.amazon.com/exec/obidos/ASIN/0824780914/icongroupinterna
- **Epstein-Barr Virus and Kaposi's Sarcoma Herpesvirus/Human Herpes Virus 8 (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans)**; ISBN: 9283212703; http://www.amazon.com/exec/obidos/ASIN/9283212703/icongroupinterna
- **Herpes Simplex/the Self-Help Guide to Managing the Herpes Virus (Thorsons Health)** by Philippa Harknett; ISBN: 0722529821; http://www.amazon.com/exec/obidos/ASIN/0722529821/icongroupinterna
- **Herpes virus : epidemiology, molecular events, oncogenicity, and therapy : based on a series of lectures presented at the Given Institute of Pathology [i.e. Pathobiology] of the University of Colorado in Aspen, Colorado, July 1975**; ISBN: 0913258407; http://www.amazon.com/exec/obidos/ASIN/0913258407/icongroupinterna
- **Herpes Virus Infections** by Ann. Arvin; ISBN: 0702021733; http://www.amazon.com/exec/obidos/ASIN/0702021733/icongroupinterna
- **Herpes Viruses and Virus Chemotherapy: Pharmacological and Clinical Approaches (International Congress Series, No 667)** by R. Kono, A. Nakajima (Editor); ISBN:

0444806806;
http://www.amazon.com/exec/obidos/ASIN/0444806806/icongroupinterna

- **Human Herpes Virus Infections, Clinical Aspects** by Ronald Glaser; ISBN: 0824715365; http://www.amazon.com/exec/obidos/ASIN/0824715365/icongroupinterna
- **Human Herpes Virus Infections: Pathogenesis, Diagnosis, and Treatment/Order No, 1694** by Carlos Lopez, Bernard Roizman (Editor); ISBN: 0881672351; http://www.amazon.com/exec/obidos/ASIN/0881672351/icongroupinterna
- **Latent Herpes Virus Infection in Veterinary Medicine** by G. Wittmann (Editor); ISBN: 0898386225; http://www.amazon.com/exec/obidos/ASIN/0898386225/icongroupinterna
- **Living With Herpes: The Comprehensive and Authoritative Guide to the Causes, Symptoms and Treatment of Herpes Virus Illnesses** by Deborah, Dr. Langston; ISBN: 0385184107; http://www.amazon.com/exec/obidos/ASIN/0385184107/icongroupinterna
- **XVIIth International Congress on Herpes Virus of Man and Animal: Standardization of Immunological Procedures : proceedings of a symposium**; ISBN: 3805536364; http://www.amazon.com/exec/obidos/ASIN/3805536364/icongroupinterna

Chapters on Herpes Virus

In order to find chapters that specifically relate to herpes virus, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and herpes virus 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 "herpes virus" (or synonyms) into the "For these words:" box. The following is a typical result when searching for book chapters on herpes virus:

- **AIDS and Related Conditions**

  Source: in Little, J.W., et al. Dental Management of the Medically Compromised Patient. 5th ed. St. Louis, MO: Mosby, Inc. 1997. p. 325-356.

  Contact: Available from Harcourt Health Sciences. 11830 Westline Industrial Drive, St. Louis, MO 63146. (800) 325-4177. Fax (800) 874-6418. Website: www.harcourthealth.com. PRICE: $48.00 plus shipping and handling. ISBN: 0815156340.

  Summary: A working knowledge of the multitude of compromised health states is essential for dental professionals, as the majority of medically compromised patients need or want oral health care. This chapter on AIDS and related conditions is from a text that provides the dental practitioner with an up to date reference work describing the dental management of patients with selected medical problems. After an introductory section that covers definitions, morbidity and mortality statistics, and geographic factors, the authors discuss incidence and prevalence, etiology, pathophysiology and complications, signs and symptoms (clinical presentation and laboratory findings), the medical management of patients with AIDS, managing opportunistic infections (cytomegalovirus, herpes viruses, Epstein Barr virus, human papillomavirus), and the dental management of this population. Dental considerations include the prevention of medical complications, patient evaluation, treatment planning considerations, and

common oral complications in patients with AIDS, including candidiasis, Kaposi's sarcoma, hairy leukoplakia, aphthous lesions (canker sores), HIV periodontal disease, salivary gland disease, and lymphadenopathy. 18 figures. 16 tables. 108 references.

- **Infections**

  Source: in Kwon, P.H. and Laskin, D.M. Clinician's Manual of Oral and Maxillofacial Surgery. Chicago, IL: Quintessence Publishing Co, Inc. 2001. p. 348-365.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $58.00 plus shipping and handling. ISBN: 0867153962.

  Summary: This chapter on infections is from a spiral-bound handbook that offers quick reference information to the oral and maxillofacial surgeon. The outline and chart-based format is designed to offer quick access to information that may be needed in situations that do not allow time for a leisurely perusal of textbooks and journals. The introduction of the chapter stresses that infections should be treated promptly and aggressively to avoid the following complications: spread to potential fascial (connective tissue) and airway compromise, orbital and intracranial spread, spread into the neck with large vessel complications, septic shock from gram-negative organisms, loss of bone and teeth, and scarring and sinus tracts of fistulae with facial disfigurement. The chapter then covers the initial evaluation, the diagnostic workup, culture and antibiotic sensitivity testing, principles of infection management, surgical management, principles of incision and drainage, infectious clinical syndromes, special orofacial infections (actinomycosis, mycotic infections, Lyme disease, tuberculosis, syphilis, **herpes virus** infections), and considerations in the pregnant or lactating patient with infections. 3 tables.

- **Mouth and Dental Problems**

  Source: in Mettler, M. and Kemper, D.W. Healthwise for Life: Medical Self Care for Healthy Aging. Boise, ID: Healthwise, Incorporated. 1996. p. 201-210.

  Contact: Available from Healthwise, Incorporated. P.O. Box 1989, Boise, ID 82701. (800) 706-9646 or (208) 345-1161. Fax (208) 345-1897. E-mail: moreinfo@healthwise.org. Website: www.healthwise.com. PRICE: $14.35. ISBN: 2877930385.

  Summary: This chapter on mouth and dental problems is from a manual of self care for health aging. The authors outline the aspects of aging that may impact the mouth and teeth, including a dryer mouth, receding gums, and loss of teeth. The authors also discuss a variety of specific problems, focusing on prevention and self-care strategies for coping with those problems. Topics include canker sores, cold sores (herpes virus), plaque and tooth decay, plaque and gum (periodontal) disease, dry mouth, oral cancer, and temporomandibular joint (TMJ) problems. For each topic, the authors note when to consult with a health care professional. Sidebars offer strategies for adapting toothbrushes for easier handling, denture care, and managing taste changes. The book is printed in large print for ease of use and written in non-technical language. 3 figures.

- **Oral Infections and Related Conditions**

  Source: in Griffiths, J. and Boyle, S. Colour Guide to Holistic Oral Care: A Practical Approach. Mosby-Year Book Europe. 1993. p. 194-204.

Contact: Available from Mosby-Year Book Europe. Lynton House, 7-12 Tavistock Square, London WC1H 9LB, England. Telephone 0171-391 4471. Fax 0171-391 6598. ISBN: 0723417792.

Summary: This chapter, from a textbook that outlines the role of the nurse in oral health care, discusses oral infections and related conditions. The chapter's topics include candidiasis, **herpes virus** infection, Epstein-Barr virus, hepatitis virus, human immunodeficiency virus (HIV), transmission of HIV, oral conditions associated with HIV infections, a summary of HIV-related conditions, oral health care for people with HIV infection, cross infection control in oral care for people with HIV infection, and good practice guidelines for oral care. 4 tables. 14 references.

CHAPTER 6. MULTIMEDIA ON HERPES VIRUS

Overview

In this chapter, we show you how to keep current on multimedia sources of information on herpes virus. 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.

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 "herpes virus" (or synonyms) into the "For these words:" box. The following is a typical result when searching for sound recordings on herpes virus:

- **Herpesvirus Infection in the Immunocompromised Host: 15th National Lesbian & Gay Health Conference & 11th Annual AIDS/HIV Forum; Houston, TX, July 20-25, 1993**

  Contact: Encore Cassettes, PO Box 231340, San Diego, CA, 92194, (619) 596-8402.

  Summary: This sound recording contains a presentation on the family of herpes viruses, their manifestations, and available treatments. It informs the listener that some of the herpes viruses may be cofactors in the progression of HIV disease. While the primary infection is the most severe, reactivations can occur; the mechanism of reactivation is not understood although stress is thought to be a factor. The family of viruses consists of: Herpes simplex I (oral herpes); herpes simplex II (genital herpes); varicella (chicken pox and shingles); Epstein-Barr (mononucleosis and hairy leukoplakia); herpes VI (believed to be cofactor of HIV); and herpes VII (recently discovered, role unknown). Each type of virus is briefly discussed, both singly and in combination, in both immunocompromised and control hosts. The presentation emphasizes the seriousness of disseminated **herpes virus** infection.

CHAPTER 7. PERIODICALS AND NEWS ON HERPES VIRUS

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover herpes virus.

News Services and Press Releases

One of the simplest ways of tracking press releases on herpes virus 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 "herpes virus" (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 herpes virus. 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 "herpes virus" (or synonyms). The following was recently listed in this archive for herpes virus:

- **Non-ulcerative genital herpes virus shedding may increase HIV-1 transmission**
  Source: Reuters Medical News
  Date: January 01, 2003
- **Maternal herpes virus infection raises risk of psychosis in offspring**
  Source: Reuters Medical News
  Date: November 13, 2001

- **Infection from genital herpes virus soars in US**
  Source: Reuters Health eLine
  Date: May 23, 2001
- **Mutant herpes virus causes cell death in metastatic melanoma**
  Source: Reuters Industry Breifing
  Date: February 16, 2001
- **Herpes virus may help treat skin cancer**
  Source: Reuters Health eLine
  Date: February 16, 2001
- **Rare Kaposi's sarcoma-associated herpes virus genotypes found in South Texas**
  Source: Reuters Medical News
  Date: January 26, 2001
- **Researchers zoom in on herpes virus**
  Source: Reuters Health eLine
  Date: May 04, 2000
- **Herpes virus targets, destroys cancer cells in mice**
  Source: Reuters Health eLine
  Date: April 17, 2000
- **Herb extract fights herpes virus**
  Source: Reuters Health eLine
  Date: September 29, 1998
- **Herpes Virus May Trigger Multiple Sclerosis**
  Source: Reuters Health eLine
  Date: November 25, 1997
- **Herpes Virus 6: Possible Etiologic Trigger In Multiple Sclerosis**
  Source: Reuters Medical News
  Date: November 25, 1997
- **Herpes Virus Protein Combats HIV?**
  Source: Reuters Health eLine
  Date: September 11, 1997
- **Herpes Virus Linked to Cancer**
  Source: Reuters Health eLine
  Date: June 19, 1997
- **Human Herpes Virus 6 Linked To Disease Progression In AIDS Patients**
  Source: Reuters Medical News
  Date: April 01, 1996
- **Researchers Offer First Glimpse Of The Kaposi Sarcoma Herpes Viruslt;P**
  Source: Reuters Medical News
  Date: March 01, 1996
- **Kaposi Sarcoma Herpes Virus Found In Semen**
  Source: Reuters Medical News
  Date: December 15, 1995

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 "herpes virus" (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 "herpes virus" (or synonyms). If you know the name of a company that is relevant to herpes virus, 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 "herpes virus" (or synonyms).

Academic Periodicals covering Herpes Virus

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to herpes virus. In addition to

these sources, you can search for articles covering herpes virus 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 8. 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 herpes virus. 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 herpes virus. 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 herpes virus:

Acyclovir

- **Systemic - U.S. Brands:** Zovirax
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202008.html

Famciclovir

- **Systemic - U.S. Brands:** Famvir
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202723.html

Valacyclovir

- **Systemic - U.S. Brands:** Valtrex
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202790.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.

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[11]:

- 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/**

[11] 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.[12] 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:[13]

- **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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[12] 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**).

[13] 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 NLM Gateway[14]

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.[15] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "herpes virus" (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.

Results Summary

Category	Items Found
Journal Articles	29083
Books / Periodicals / Audio Visual	232
Consumer Health	808
Meeting Abstracts	462
Other Collections	64
Total	30649

HSTAT[16]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[17] 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.[18] Simply search by "herpes virus" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

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[14] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[15] 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).

[16] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[17] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[18] 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.

Coffee Break: Tutorials for Biologists[19]

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.[20] 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.[21] 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/**.

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/**.

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[19] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[20] 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.

[21] 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.

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 herpes virus 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 herpes virus. 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 herpes virus. 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 "herpes virus":

- Other guides

  Herpes Simplex
  http://www.nlm.nih.gov/medlineplus/herpessimplex.html

  Infections and Pregnancy
  http://www.nlm.nih.gov/medlineplus/infectionsandpregnancy.html

  Sexually Transmitted Diseases
  http://www.nlm.nih.gov/medlineplus/sexuallytransmitteddiseases.html

  Shingles
  http://www.nlm.nih.gov/medlineplus/shingles.html

  Viral Infections
  http://www.nlm.nih.gov/medlineplus/viralinfections.html

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 herpes virus. 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:

- **What Is Herpes?**

  Contact: American College Health Association, PO Box 28937, Baltimore, MD, 21223-8937, (410) 859-1500.

  Summary: This brochure explains what herpes simplex is. Two strains of the virus are discussed, herpes simplex virus Type 1 and Type 2. The body's response to the **herpes virus** is described, as well as the parts of the body that are susceptible to it. Recurrences of the disease are explained as well as its transmission. Recommended courses of action for those who think they have herpes are presented. Methods of easing the physical discomfort and emotional pain associated with this disease are included. Additional reading materials are listed.

- **VD and the Homosexual Male**

  Contact: SEARCH, Venereal Disease Clinic for Gays, 1068 Davie St, Vancouver, (604) 689-1039.

  Summary: This brochure presents information about the transmission and prevention of the more common Sexually transmitted diseases (STD's), which include Human

immunodeficiency virus (HIV) and Acquired immunodeficiency syndrome (AIDS). It describes the symptoms, diagnosis, and treatment of gonorrhea, nongonococcal urethritis,the **herpes virus** group, syphilis, pubic lice, scabies, venereal warts, hepatitis, and bacterial and parasitic enteric infections.

- **STD Facts. Translated title**

  Contact: AIDS Project New Haven, 1302 Chapel St, New Haven, CT, 06511, (203) 624-0947.

  Summary: This brochure presents parents with information about Sexually transmitted diseases (STD's), including Acquired immunodeficiency syndrome (AIDS) and Human immunodeficiency virus (HIV) infection. In a chart format, it lists eight common STD's, their symptoms in both men and women, modes of transmission, and severity of diseases if not treated. In addition to AIDS, the other STD's include chlamydia, genital warts, gonorrhea, **herpes virus** group, nongonococcal urethritis, syphilis, and vaginitis. It also lists risk-reduction measures in sexual behaviors to prevent their transmission. This brochure is part of an information package AD0007681, which in turn is part of a teaching aid AD0007680.

- **Kaposi's Sarcoma (KS): New Developments in Kaposi's Sarcoma**

  Source: GMHC's Treatment Issues: Vol. 9, Number 7/8: August, 1995.

  Contact: Project Inform, HIV Treatment Hotline, 205 13th St Ste 2001, San Francisco, CA, 94103, (415) 558-8669, http://www.projectinform.org.

  Summary: This fact sheet discusses Karposi's sarcoma (KS) as an opportunistic infection associated with the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS). The fact sheet examines the clinical features of KS and the potential treatment therapies. It explains the controversy concerning whether KS is a member of the **herpes virus** group or a cancer. It provides information about possible KS treatment, if KS is a member of the **herpes virus** group. The fact sheet also reviews a study that shows the effects and the implications for treatment of KS in pregnant women, and the effectiveness of two new therapies that have been approved to treat the disease.

- **Pityriasis Rosea**

  Source: American Osteopathic College of Dermatology. 2001. 2 p.

  Contact: Available from American Osteopathic College of Dermatology. (800) 449-2623. Fax: (660) 627-2623. Website: www.aocd.org/skin. Email: info@aocd.org.

  Summary: This fact sheet for patients discusses pityriasis rosea, a mild, but common, skin condition characterized by scaly, pink, inflamed skin. This condition can last from a couple of weeks to a couple of months, but usually leaves no lasting marks. The cause of this condition is unknown although there is some evidence that it may be a relapse of **Herpes Virus** Type 7, a virus that many children are infected with but to which they develop immunity. Pityriasis rosea usually starts with a pink or tan round or oval area (called the herald patch) on the chest or back and is usually followed (after a couple of weeks) by smaller pink or tan patches elsewhere on the body. Often the herald patch is mistaken for eczema or ringworm. The patches resemble an evergreen tree with drooping branches. The condition heals after 2 to 4 weeks and is usually gone by 6 to 14 weeks. In some patients, the disease causes a more serious skin reaction. The patient experiences severe itching when overheated as well as tiredness and aching. The rash will fade after 6 or more weeks but can sometimes reappear after physical activity or

bathing in hot water. Blood tests and skin scrapings are often necessary to diagnose this condition. Antiviral and antibiotic drugs are used to treat the condition along with anti-itching medications. In more severe cases oral anti-inflammatory medications are prescribed.

- **Erythema Multiforme**

  Source: Kirksville, MO: American Osteopathic College of Dermatology (AOCD). 2001. 2 p.

  Contact: Available online from American Osteopathic College of Dermatology. 1501 East Illinois Street, P.O. Box 7525, Kirksville, MO 63501. (800) 449-2623 or (660) 665-2184. Fax (660) 627-2623. E-mail: info@aocd.org. Website: www.aocd.org/skin/dermatologic_diseases/ index.html.

  Summary: This fact sheet provides people who have erythema multiforme (EM) with information on the etiology, symptoms, and treatment of this acute, self limiting, inflammatory skin eruption. EM appears in multiple forms, and because of this variation EM has been divided into the overlapping subgroups EM minor and Stevens-Johnson syndrome (SJS). EM minor is usually caused by the **herpes virus.** Additional causes are other bacterial or viral infections or reactions to medications. EM minor is characterized by a rash that may be accompanied by minor burning or itch. Round bulls eye target shaped rings are usually present on the palms. SJS causes a greater degree of damage than EM minor. SJS is characterized by large blood blisters accompanied by a red rash. A skin biopsy is needed to confirm the diagnosis. Treatment of EM begins with the identification and removal of the trigger factor if possible. EM minor usually needs no treatment because the lesions will resolve themselves within 2 to 4 weeks. Recurrent EM caused by the **herpes virus** can be prevented with a continuous low dose of Zovirax or Valtrex. SJS, if identified in the early stages, can be treated with intravenous Cytoxan, pooled gamma globulin, or oral cyclosporine. Oral steroids are useful in some cases. 2 figures.

- **Genital Herpes**

  Contact: Washington State Department of Health Office of STD Services, PO Box 47842, Olympia, WA, 98504-7842, http://www.doh.wa.gov/cfh/STD/default.htm.

  Summary: This fact sheet, written for the general public, discusses the sexually transmitted disease (STD), herpes type 2 (genital herpes). The genital **herpes virus** is spread through skin-to-skin contact during sexual intercourse. Genital herpes can be asymptomatic, although some individuals may have fluid-filled sores that may itch, burn, or tingle as well as flu-like symptoms. After the sores heal, the virus becomes dormant, and more outbreaks may occur later and be less severe and painful. Women with herpes should notify their partners and should take special precautions during pregnancy. A test can determine if individuals have herpes by testing the sores themselves for the virus. There is no cure for herpes, but medicine can help sores to be less painful and to heal faster. Because herpes sores can facilitate the transmission of the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) from one person to another, individuals with herpes should never have sex during an outbreak. The fact sheet provides contact information for services from which individuals can learn more about STDs.

- **STD Fast Facts: Herpes**

  Contact: Education Training and Research Associates, PO Box 1830, Santa Cruz, CA, 95061-1830, (800) 321-4407, http://www.etr.org.

  Summary: This pamphlet discusses herpes, a sexually transmitted disease caused by the **herpes virus.** There is no cure for this disease, which can cause painful sores and blisters on or around the mouth or genitals. The pamphlet explains its transmission, effects, recurrences, the lack of symptoms in some people who have the **herpes virus,** what an individual should do who thinks he/she has herpes, treatment, and prevention. The best prevention is abstinence. Other methods include proper use of latex condoms, monogamy, and avoiding risky behavior.

- **AIDS/STDs: The Sexually Transmissible Diseases**

  Contact: University of Nebraska Lincoln, Cooperative Extension Services, 211 Agriculture Hall, Lincoln, NE, 68583-0703, (402) 472-2966.

  Summary: This paper presents information about the transmission and prevention of Sexually transmitted diseases (STD's), with a focus on Acquired immunodeficiency syndrome (AIDS) and Human immunodeficiency virus (HIV) infection. It also describes the symptoms, treatment, and prevention of chlamydia, **herpes virus** group, venereal warts, vaginitis, gonorrhea, and syphilis.

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 "herpes virus" (or synonyms). The following was recently posted:

- **2001 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1999 August (updated 2001 November 28); 64 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3080&nbr=2306&string=herpes+AND+virus

- **2002 national guideline for the management of anogenital warts**

  Source: Association for Genitourinary Medicine - Medical Specialty Society; 1999 August (revised 2002); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3046&nbr=2272&string=herpes+AND+virus

- **2002 national guideline for the management of chancroid**

  Source: Association for Genitourinary Medicine - Medical Specialty Society; 1999 August (revised 2002); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3040&nbr=2266&string=herpes+AND+virus

- **2002 national guideline for the management of genital herpes**

  Source: Association for Genitourinary Medicine - Medical Specialty Society; 1999 August (revised 2002); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3035&nbr=2261&string=herpes+AND+virus

- **2002 national guideline for the management of lymphogranuloma venereum**

  Source: Association for Genitourinary Medicine - Medical Specialty Society; 1999 August (revised 2002); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3039&nbr=2265&string=herpes+AND+virus

- **2002 national guideline on the management of balanitis**

  Source: Association for Genitourinary Medicine - Medical Specialty Society; 1999 August (revised 2002); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3051&nbr=2277&string=herpes+AND+virus

- **2002 national guidelines on the management of early syphilis**

  Source: Association for Genitourinary Medicine - Medical Specialty Society; 1999 August (revised 2002); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3036&nbr=2262&string=herpes+AND+virus

- **ACR Appropriateness Criteria for imaging evaluation of patients with acute abdominal pain and fever**

  Source: American College of Radiology - Medical Specialty Society; 1998 (revised 2001); 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3258&nbr=2484&string=herpes+AND+virus

- **ACR Appropriateness Criteria for imaging recommendations for patients with dysphagia**

  Source: American College of Radiology - Medical Specialty Society; 1998 (revised 2001); 6 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3259&nbr=2485&string=herpes+AND+virus

- **ACR Appropriateness Criteria for imaging of intracranial infections**

  Source: American College of Radiology - Medical Specialty Society; 1996 (revised 1999); 11 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2446&nbr=1672&string=herpes+AND+virus

- **ASHP therapeutic guidelines for nonsurgical antimicrobial prophylaxis**

  Source: American Society of Health-System Pharmacists - Professional Association; 1999 June 15; 50 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=1959&nbr=1185&string=herpes+AND+virus

- **Care of the contact lens patient**

  Source: American Optometric Association - Professional Association; 2000; 77 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2603&nbr=1829&string=herpes+AND+virus

- **Chemotherapy and biotherapy: guidelines and recommendations for practice**

  Source: Oncology Nursing Society - Professional Association; 2001; 226 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3209&nbr=2435&string=herpes+AND+virus

- **Childhood immunizations**

  Source: American College of Preventive Medicine - Medical Specialty Society; 1997 (revised 2003 Aug); 7 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=4119&nbr=3164&string=herpes+AND+virus

- **Clinical prevention guidelines. Sexually transmitted diseases treatment guidelines 2002**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1993 (revised 2002 May 10); 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3230&nbr=2456&string=herpes+AND+virus

- **Clinical standards for the screening and management of acquired syphilis in HIV-positive adults**

  Source: Medical Society for the Study of Venereal Diseases - Disease Specific Society; 2002 February; 9 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3440&nbr=2666&string=herpes+AND+virus

- **Common gynecologic problems: a guide to diagnosis and treatment**

  Source: Brigham and Women's Hospital (Boston) - Hospital/Medical Center; 2002; 11 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3486&nbr=2712&string=herpes+AND+virus

- **Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2001 July; 24 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2874&nbr=2100&string=herpes+AND+virus

- **Diseases characterized by genital ulcers. Sexually transmitted diseases treatment guidelines 2002**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1993 (revised 2002 May 10); 25 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3233&nbr=2459&string=herpes+AND+virus

- **Diseases characterized by urethritis and cervicitis. Sexually transmitted diseases treatment guidelines 2002**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1993 (revised 2002 May 10); 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3236&nbr=2462&string=herpes+AND+virus

- **Evaluation of surgery for Parkinson's disease. A report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. The Task Force on Surgery for Parkinson's Disease**

  Source: American Academy of Neurology - Medical Specialty Society; 1999 December; 12 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2830&nbr=2056&string=herpes+AND+virus

- **General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP)**

  Source: American Academy of Family Physicians - Medical Specialty Society; 2002 February 8; 36 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3180&nbr=2406&string=herpes+AND+virus

- **Global initiative for asthma. Global strategy for asthma management and prevention**

  Source: National Heart, Lung, and Blood Institute (U.S.) - Federal Government Agency [U.S.]; 1995 January (revised 2002); 176 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3203&nbr=2429&string=herpes+AND+virus

- **Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients**

  Source: American Society for Blood and Marrow Transplantation - Professional Association; 2000 October 20; 126 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2573&nbr=1799&string=herpes+AND+virus

- **Guidelines for quality standards for immunization**

  Source: Infectious Diseases Society of America - Medical Specialty Society; 1997 (revised 2002); 9 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3412&nbr=2638&string=herpes+AND+virus

- **Guidelines for referral to pediatric surgical specialists**

  Source: American Academy of Pediatrics - Medical Specialty Society; 2002 July; 5 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3420&nbr=2646&string=herpes+AND+virus

- **Hearing assessment in infants and children: recommendations beyond neonatal screening**

  Source: American Academy of Pediatrics - Medical Specialty Society; 2003 February; 5 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3614&nbr=2840&string=herpes+AND+virus

- **HIV disease management**

  Source: University of Texas Medical Branch Correctional Managed Care - Academic Institution; 1996 September (revised 2002 Jul); 7 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3477&nbr=2703&string=herpes+AND+virus

- **Immunizations**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1994 May (revised 2002 Jun); 49 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3353&nbr=2579&string=herpes+AND+virus

- **Incorporating HIV prevention into the medical care of persons living with HIV. Recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2003 July 18; 24 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3866&nbr=3076&string=herpes+AND+virus

- **Indications for and techniques of red cell transfusion**

  Source: Finnish Medical Society Duodecim - Professional Association; 2000 March 30; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3402&nbr=2628&string=herpes+AND+virus

- **Infection control in physicians' offices**

  Source: American Academy of Pediatrics - Medical Specialty Society; 2000 June; 9 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2769&nbr=1995&string=herpes+AND+virus

- **Management of sore throat and indications for tonsillectomy. A national clinical guideline**

  Source: Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]; 1999 January; 23 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=1841&nbr=1067&string=herpes+AND+virus

- **Newborn hearing screening: recommendations and rationale**

  Source: United States Preventive Services Task Force - Independent Expert Panel; 1996 (revised 2001 Dec); 9 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2979&nbr=2205&string=herpes+AND+virus

- **Pediatric eye and vision examination**

  Source: American Optometric Association - Professional Association; 1994 (revised 2002); 57 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3548&nbr=2774&string=herpes+AND+virus

- **Prevention of varicella: updated recommendations of the Advisory Committee on Immunization Practices (ACIP)**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1999 May; 6 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=1980&nbr=1206&string=herpes+AND+virus

- **Proctitis, proctocolitis, and enteritis. Sexually transmitted diseases treatment guidelines 2002**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1993 (revised 2002 May 10); 2 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3244&nbr=2470&string=herpes+AND+virus

- **Recommendations for using smallpox vaccine in a pre-event smallpox vaccination program. Supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Healthcare Infection Control Practices Advisory Committee (HICPAC).**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2003 February 26; 17 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3623&nbr=2849&string=herpes+AND+virus

- **Recommended childhood and adolescent immunization schedule-United States, January-June 2004**

  Source: American Academy of Family Physicians - Medical Specialty Society; 2004 January 16; 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=4763&nbr=3444&string=herpes+AND+virus

- **Revised guidelines for HIV counseling, testing, and referral**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2001 November 9; 59 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3052&nbr=2278&string=herpes+AND+virus

- **Sexual assault and STDs. Sexually transmitted diseases treatment guidelines 2002**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1993 (revised 2002 May 10); 6 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3246&nbr=2472&string=herpes+AND+virus

- **Smallpox vaccination and adverse reactions. Guidance for clinicians**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2003 January 24; 29 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3597&nbr=2823&string=herpes+AND+virus

- **Special populations. 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=3231&nbr=2457&string=herpes+AND+virus

- **Summary of policy recommendations for periodic health examinations**

  Source: American Academy of Family Physicians - Medical Specialty Society; 1996 November (revised 2003 Aug); 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=4183&nbr=3208&string=herpes+AND+virus

- **Syphilis**

  Source: Finnish Medical Society Duodecim - Professional Association; 2001 November 22; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3396&nbr=2622&string=herpes+AND+virus

- **The use of electronic fetal monitoring. The use and interpretation of cardiotocography in intrapartum fetal surveillance**

  Source: Royal College of Obstetricians and Gynaecologists - Medical Specialty Society; 2001 May; 136 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2952&nbr=2178&string=herpes+AND+virus

- **U.S. Public Health Service guideline on infectious disease issues in xenotransplantation**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2001 August 24; 56 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2931&nbr=2157&string=herpes+AND+virus

- **Vaccine preventable STDs. Sexually transmitted diseases treatment guidelines 2002**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1993 (revised 2002 May 10); 6 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3242&nbr=2468&string=herpes+AND+virus

- **Vaccine-preventable diseases: improving vaccination coverage in children, adolescents and adults.**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2000 January; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=2107&nbr=1333&string=herpes+AND+virus

- **Vaccinia (smallpox) vaccine**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2001 June; 43 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2850&nbr=2076&string=herpes+AND+virus

- **Varicella vaccination. Recommendation statement from the Canadian Task Force on Preventive Health Care.**

  Source: Canadian Task Force on Preventive Health Care - National Government Agency [Non-U.S.]; 2001 June; 2 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2859&nbr=2085&string=herpes+AND+virus

- **Varicella vaccine update**

  Source: American Academy of Pediatrics - Medical Specialty Society; 2000 January; 6 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2766&nbr=1992&string=herpes+AND+virus

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 herpes virus. 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**

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to herpes virus. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with herpes virus.

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 herpes virus. 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 "herpes virus" (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 "herpes virus". 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 "herpes virus" (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 "herpes virus" (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.[22]

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

[22] 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)[23]:

- **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/**

[23] 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**).

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**

HERPES VIRUS DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

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]

Abdominal Pain: Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

Aberrant: Wandering or deviating from the usual or normal course. [EU]

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]

Acetaminophen: Analgesic antipyretic derivative of acetanilide. It has weak anti-inflammatory properties and is used as a common analgesic, but may cause liver, blood cell, and kidney damage. [NIH]

Acoustic: Having to do with sound or hearing. [NIH]

Acquired Immunodeficiency Syndrome: An acquired defect of cellular immunity associated with infection by the human immunodeficiency virus (HIV), a CD4-positive T-lymphocyte count under 200 cells/microliter or less than 14% of total lymphocytes, and increased susceptibility to opportunistic infections and malignant neoplasms. Clinical manifestations also include emaciation (wasting) and dementia. These elements reflect criteria for AIDS as defined by the CDC in 1993. [NIH]

Actinomycosis: Infections with bacteria of the genus Actinomyces. [NIH]

Acyclovir: Functional analog of the nucleoside guanosine. It acts as an antimetabolite, especially in viruses. It is used as an antiviral agent, especially in herpes infections. [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]

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]

Adjustment: The dynamic process wherein the thoughts, feelings, behavior, and biophysiological mechanisms of the individual continually change to adjust to the environment. [NIH]

Adoptive Transfer: Form of passive immunization where previously sensitized immunologic agents (cells or serum) are transferred to non-immune recipients. When transfer of cells is used as a therapy for the treatment of neoplasms, it is called adoptive immunotherapy (immunotherapy, adoptive). [NIH]

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]

Aequorin: A photoprotein isolated from the bioluminescent jellyfish Aequorea. It emits visible light by an intramolecular reaction when a trace amount of calcium ion is added. The light-emitting moiety in the bioluminescence reaction is believed to be 2-amino-3-benzyl-5-(p-hydroxyphenyl)pyrazine (AF-350). [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]

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]

Airway: A device for securing unobstructed passage of air into and out of the lungs during general anesthesia. [NIH]

Alanine: A non-essential amino acid that occurs in high levels in its free state in plasma. It is produced from pyruvate by transamination. It is involved in sugar and acid metabolism, increases immunity, and provides energy for muscle tissue, brain, and the central nervous system. [NIH]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [NIH]

Alimentary: Pertaining to food or nutritive material, or to the organs of digestion. [EU]

Alkaline: Having the reactions of an alkali. [EU]

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]

Allogeneic: Taken from different individuals of the same species. [NIH]

Allografts: A graft of tissue obtained from the body of another animal of the same species but with genotype differing from that of the recipient; tissue graft from a donor of one genotype to a host of another genotype with host and donor being members of the same species. [NIH]

Allopurinol: A xanthine oxidase inhibitor that decreases uric acid production. [NIH]

Alopecia: Absence of hair from areas where it is normally present. [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]

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]

Amber: A yellowish fossil resin, the gum of several species of coniferous trees, found in the alluvial deposits of northeastern Germany. It is used in molecular biology in the analysis of organic matter fossilized in amber. [NIH]

Ameloblastoma: An epithelial tumor of the jaw originating from the epithelial rests of Malassez or from other epithelial remnants of the developing period of the enamel. [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]

Amphetamines: Analogs or derivatives of amphetamine. Many are sympathomimetics and central nervous system stimulators causing excitation, vasopression, bronchodilation, and to varying degrees, anorexia, analepsis, nasal decongestion, and some smooth muscle relaxation. [NIH]

Amplification: The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

Amygdala: Almond-shaped group of basal nuclei anterior to the inferior horn of the lateral ventricle of the brain, within the temporal lobe. The amygdala is part of the limbic system. [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]

Analytes: A component of a test sample the presence of which has to be demonstrated. The term "analyte" includes where appropriate formed from the analyte during the analyses. [NIH]

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]

Androgens: A class of sex hormones associated with the development and maintenance of the secondary male sex characteristics, sperm induction, and sexual differentiation. In addition to increasing virility and libido, they also increase nitrogen and water retention and stimulate skeletal growth. [NIH]

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]

Antiallergic: Counteracting allergy or allergic conditions. [EU]

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]

Anticonvulsant: An agent that prevents or relieves convulsions. [EU]

Antifungal: Destructive to fungi, or suppressing their reproduction or growth; effective against fungal infections. [EU]

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]

Antimicrobial: Killing microorganisms, or suppressing their multiplication or growth. [EU]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

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]

Antipruritic: Relieving or preventing itching. [EU]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Antiviral Agents: Agents used in the prophylaxis or therapy of virus diseases. Some of the ways they may act include preventing viral replication by inhibiting viral DNA polymerase; binding to specific cell-surface receptors and inhibiting viral penetration or uncoating; inhibiting viral protein synthesis; or blocking late stages of virus assembly. [NIH]

Anus: The opening of the rectum to the outside of the body. [NIH]

Anxiety: Persistent feeling of dread, apprehension, and impending disaster. [NIH]

Anxiolytic: An anxiolytic or antianxiety agent. [EU]

Apolipoproteins: The protein components of lipoproteins which remain after the lipids to which the proteins are bound have been removed. They play an important role in lipid transport and metabolism. [NIH]

Aponeurosis: Tendinous expansion consisting of a fibrous or membranous sheath which serves as a fascia to enclose or bind a group of muscles. [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]

Aqueous: Having to do with water. [NIH]

Arenavirus: The only genus in the family Arenaviridae. It contains two groups LCM-Lassa complex viruses and Tacaribe complex viruses, which are distinguished by antigenic relationships and geographic distribution. [NIH]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arteritis: Inflammation of an artery. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Astrocytes: The largest and most numerous neuroglial cells in the brain and spinal cord. Astrocytes (from "star" cells) are irregularly shaped with many long processes, including those with "end feet" which form the glial (limiting) membrane and directly and indirectly contribute to the blood brain barrier. They regulate the extracellular ionic and chemical environment, and "reactive astrocytes" (along with microglia) respond to injury. Astrocytes have high- affinity transmitter uptake systems, voltage-dependent and transmitter-gated ion channels, and can release transmitter, but their role in signaling (as in many other functions) is not well understood. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [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]

Attenuated: Strain with weakened or reduced virulence. [NIH]

Attenuation: Reduction of transmitted sound energy or its electrical equivalent. [NIH]

Atypical: Irregular; not conformable to the type; in microbiology, applied specifically to strains of unusual type. [EU]

Auditory: Pertaining to the sense of hearing. [EU]

Auditory Cortex: Area of the temporal lobe concerned with hearing. [NIH]

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

Autologous: Taken from an individual's own tissues, cells, or DNA. [NIH]

Autologous tumor cells: Cancer cells from an individual's own tumor. [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]

Avian: A plasmodial infection in birds. [NIH]

Axonal: Condition associated with metabolic derangement of the entire neuron and is manifest by degeneration of the distal portion of the nerve fiber. [NIH]

Axons: Nerve fibers that are capable of rapidly conducting impulses away from the neuron cell body. [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]

Bacterial Infections: Infections by bacteria, general or unspecified. [NIH]

Bacterial Physiology: Physiological processes and activities of bacteria. [NIH]

Bacterial toxin: A toxic substance, made by bacteria, that can be modified to kill specific tumor cells without harming normal cells. [NIH]

Bactericidal: Substance lethal to bacteria; substance capable of killing bacteria. [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]

Balanitis: Inflammation of the glans penis. [NIH]

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [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]

Basilar Membrane: A membrane that stretches from the spiral lamina to the basilar crest consisting of an inner and an outer part. The inner part supports the spiral organ of Corti. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Benign tumor: A noncancerous growth that does not invade nearby tissue or spread to other parts of the body. [NIH]

Benzamides: Benzoic acid amides. [NIH]

Benzodiazepines: A two-ring heterocyclic compound consisting of a benzene ring fused to a diazepine ring. Permitted is any degree of hydrogenation, any substituents and any H-isomer. [NIH]

Beta-Thalassemia: A disorder characterized by reduced synthesis of the beta chains of hemoglobin. There is retardation of hemoglobin A synthesis in the heterozygous form (thalassemia minor), which is asymptomatic, while in the homozygous form (thalassemia major, Cooley's anemia, Mediterranean anemia, erythroblastic anemia), which can result in severe complications and even death, hemoglobin A synthesis is absent. [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]

Binding Sites: The reactive parts of a macromolecule that directly participate in its specific combination with another molecule. [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]

Bioluminescence: The emission of light by living organisms such as the firefly, certain mollusks, beetles, fish, bacteria, fungi and protozoa. [NIH]

Biomolecular: A scientific field at the interface between advanced computing and biotechnology. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

Biosynthesis: The building up of a chemical compound in the physiologic processes of a living organism. [EU]

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]

Bioterrorism: The use of biological agents in terrorism. This includes the malevolent use of bacteria, viruses, or toxins against people, animals, or plants. [NIH]

Bladder: The organ that stores urine. [NIH]

Blasts: Immature blood cells. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [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]

Blotting, Western: Identification of proteins or peptides that have been electrophoretically separated by blotting and transferred to strips of nitrocellulose paper. The blots are then detected by radiolabeled antibody probes. [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]

Bone Marrow Transplantation: The transference of bone marrow from one human or animal to another. [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]

Brain Stem: The part of the brain that connects the cerebral hemispheres with the spinal cord. It consists of the mesencephalon, pons, and medulla oblongata. [NIH]

Branch: Most commonly used for branches of nerves, but applied also to other structures. [NIH]

Breakdown: A physical, metal, or nervous collapse. [NIH]

Breeding: The science or art of changing the constitution of a population of plants or animals through sexual reproduction. [NIH]

Bronchoalveolar Lavage: Washing out of the lungs with saline or mucolytic agents for diagnostic or therapeutic purposes. It is very useful in the diagnosis of diffuse pulmonary infiltrates in immunosuppressed patients. [NIH]

Bronchoalveolar Lavage Fluid: Fluid obtained by washout of the alveolar compartment of the lung. It is used to assess biochemical and inflammatory changes in and effects of therapy on the interstitial lung tissue. [NIH]

Buspirone: An anxiolytic agent and a serotonin receptor agonist belonging to the azaspirodecanedione class of compounds. Its structure is unrelated to those of the benzodiazepines, but it has an efficacy comparable to diazepam. [NIH]

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]

Calicivirus: A genus in the family Caliciviridae containing many species including feline calicivirus , vesicular exanthema of swine virus, and San Miguel sea lion viruses. [NIH]

Camphor: A bicyclic monoterpene ketone found widely in plant (primarily the camphor tree, Cinnamomum camphora). Natural camphor is used topically as a skin antipruritic and as an anti-infective agent. [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]

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]

Capsid: The outer protein protective shell of a virus, which protects the viral nucleic acid. [NIH]

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

Carbamazepine: An anticonvulsant used to control grand mal and psychomotor or focal seizures. Its mode of action is not fully understood, but some of its actions resemble those of phenytoin; although there is little chemical resemblance between the two compounds, their three-dimensional structure is similar. [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]

Carcinogenic: Producing carcinoma. [EU]

Carcinogens: Substances that increase the risk of neoplasms in humans or animals. Both genotoxic chemicals, which affect DNA directly, and nongenotoxic chemicals, which induce neoplasms by other mechanism, are included. [NIH]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

Cardiac: Having to do with the heart. [NIH]

Cardiological: Relating to the study of the heart. [EU]

Cardiotocography: Monitoring of fetal heart frequency before birth in order to assess impending prematurity in relation to the pattern or intensity of antepartum uterine contraction. [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]

Carrier Proteins: Transport proteins that carry specific substances in the blood or across cell membranes. [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]

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [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 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 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 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]

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]

Central Nervous System Diseases: Diseases of any component of the brain (including the cerebral hemispheres, diencephalon, brain stem, and cerebellum) or the spinal cord. [NIH]

Cerebellum: Part of the metencephalon that lies in the posterior cranial fossa behind the brain stem. It is concerned with the coordination of movement. [NIH]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebral hemispheres: The two halves of the cerebrum, the part of the brain that controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. The right hemisphere controls muscle movement on the left side of the body, and the left hemisphere controls muscle movement on the right side of the body. [NIH]

Cerebrospinal: Pertaining to the brain and spinal cord. [EU]

Cerebrospinal fluid: CSF. The fluid flowing around the brain and spinal cord. Cerebrospinal fluid is produced in the ventricles in the brain. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

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]

Cervix: The lower, narrow end of the uterus that forms a canal between the uterus and vagina. [NIH]

Chancroid: Acute, localized autoinoculable infectious disease usually acquired through sexual contact. Caused by Haemophilus ducreyi, it occurs endemically almost worldwide, especially in tropical and subtropical countries and more commonly in seaports and urban areas than in rural areas. [NIH]

Character: In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

Chemokines: Class of pro-inflammatory cytokines that have the ability to attract and activate leukocytes. They can be divided into at least three structural branches: C (chemokines, C), CC (chemokines, CC), and CXC (chemokines, CXC), according to variations in a shared cysteine motif. [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]

Chest cavity: Space in body surrounding the lungs. [NIH]

Chickenpox: A mild, highly contagious virus characterized by itchy blisters all over the body. [NIH]

Chimeras: Organism that contains a mixture of genetically different cells. [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]

Chlorides: Inorganic compounds derived from hydrochloric acid that contain the Cl- ion. [NIH]

Chlorine: A greenish-yellow, diatomic gas that is a member of the halogen family of elements. It has the atomic symbol Cl, atomic number 17, and atomic weight 70.906. It is a powerful irritant that can cause fatal pulmonary edema. Chlorine is used in manufacturing, as a reagent in synthetic chemistry, for water purification, and in the production of chlorinated lime, which is used in fabric bleaching. [NIH]

Chlorophyll: Porphyrin derivatives containing magnesium that act to convert light energy in photosynthetic organisms. [NIH]

Cholera: An acute diarrheal disease endemic in India and Southeast Asia whose causative agent is vibrio cholerae. This condition can lead to severe dehydration in a matter of hours unless quickly treated. [NIH]

Cholesterol: The principal sterol of all higher animals, distributed in body tissues, especially the brain and spinal cord, and in animal fats and oils. [NIH]

Cholesterol Esters: Fatty acid esters of cholesterol which constitute about two-thirds of the cholesterol in the plasma. The accumulation of cholesterol esters in the arterial intima is a characteristic feature of atherosclerosis. [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]

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 Fatigue Syndrome: Fatigue caused by the combined effects of different types of prolonged fatigue. [NIH]

Chylomicrons: A class of lipoproteins that carry dietary cholesterol and triglycerides from the small intestines to the tissues. [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]

Clear cell carcinoma: A rare type of tumor of the female genital tract in which the inside of the cells looks clear when viewed under a microscope. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [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]

Coca: Any of several South American shrubs of the Erythroxylon genus (and family) that yield cocaine; the leaves are chewed with alum for CNS stimulation. [NIH]

Cocaine: An alkaloid ester extracted from the leaves of plants including coca. It is a local anesthetic and vasoconstrictor and is clinically used for that purpose, particularly in the eye, ear, nose, and throat. It also has powerful central nervous system effects similar to the amphetamines and is a drug of abuse. Cocaine, like amphetamines, acts by multiple mechanisms on brain catecholaminergic neurons; the mechanism of its reinforcing effects is thought to involve inhibition of dopamine uptake. [NIH]

Cochlear: Of or pertaining to the cochlea. [EU]

Cochlear Nerve: The cochlear part of the 8th cranial nerve (vestibulocochlear nerve). The cochlear nerve fibers originate from neurons of the spiral ganglion and project peripherally to cochlear hair cells and centrally to the cochlear nuclei (cochlear nucleus) of the brain stem. They mediate the sense of hearing. [NIH]

Codons: Any triplet of nucleotides (coding unit) in DNA or RNA (if RNA is the carrier of primary genetic information as in some viruses) that codes for particular amino acid or signals the beginning or end of the message. [NIH]

Cofactor: A substance, microorganism or environmental factor that activates or enhances the action of another entity such as a disease-causing agent. [NIH]

Coliphages: Viruses whose host is Escherichia coli. [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]

Colloidal: Of the nature of a colloid. [EU]

Colloids: Two-phase systems in which one is uniformly dispersed in another as particles small enough so they cannot be filtered or will not settle out. The dispersing or continuous phase or medium envelops the particles of the discontinuous phase. All three states of matter can form colloids among each other. [NIH]

Common Variable Immunodeficiency: Heterogeneous group of immunodeficiency syndromes characterized by hypogammaglobulinemia of most isotypes, variable B-cell defects, and the presence of recurrent bacterial infections. [NIH]

Communicable disease: A disease that can be transmitted by contact between persons. [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]

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]

Condoms: A sheath that is worn over the penis during sexual behavior in order to prevent pregnancy or spread of sexually transmitted disease. [NIH]

Condyloma: C. acuminatum; a papilloma with a central core of connective tissue in a treelike structure covered with epithelium, usually occurring on the mucous membrane or skin of the external genitals or in the perianal region. [EU]

Congestion: Excessive or abnormal accumulation of blood in a part. [EU]

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]

Connective Tissue Cells: A group of cells that includes fibroblasts, cartilage cells, adipocytes, smooth muscle cells, and bone cells. [NIH]

Constriction: The act of constricting. [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]

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]

Convulsions: A general term referring to sudden and often violent motor activity of cerebral or brainstem origin. Convulsions may also occur in the absence of an electrical cerebral discharge (e.g., in response to hypotension). [NIH]

Coordination: Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [NIH]

Cornea: The transparent part of the eye that covers the iris and the pupil and allows light to enter the inside. [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]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Cortical: Pertaining to or of the nature of a cortex or bark. [EU]

Corticosteroid: Any of the steroids elaborated by the adrenal cortex (excluding the sex hormones of adrenal origin) in response to the release of corticotrophin (adrenocorticotropic hormone) by the pituitary gland, to any of the synthetic equivalents of these steroids, or to angiotensin II. They are divided, according to their predominant biological activity, into three major groups: glucocorticoids, chiefly influencing carbohydrate, fat, and protein metabolism; mineralocorticoids, affecting the regulation of electrolyte and water balance; and C19 androgens. Some corticosteroids exhibit both types of activity in varying degrees, and others exert only one type of effect. The corticosteroids are used clinically for hormonal replacement therapy, for suppression of ACTH secretion by the anterior pituitary, as antineoplastic, antiallergic, and anti-inflammatory agents, and to suppress the immune response. Called also adrenocortical hormone and corticoid. [EU]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Cross Infection: Any infection which a patient contracts in a healthcare institution. [NIH]

Crossing-over: The exchange of corresponding segments between chromatids of homologous chromosomes during meiosia, forming a chiasma. [NIH]

Cryotherapy: Any method that uses cold temperature to treat disease. [NIH]

Cultured cells: Animal or human cells that are grown in the laboratory. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Cutaneous: Having to do with the skin. [NIH]

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]

Cyst: A sac or capsule filled with fluid. [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]

Cytogenetics: A branch of genetics which deals with the cytological and molecular behavior of genes and chromosomes during cell division. [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]

Cytomegalovirus Infections: Infection with Cytomegalovirus, characterized by enlarged cells bearing intranuclear inclusions. Infection may be in almost any organ, but the salivary glands are the most common site in children, as are the lungs in adults. [NIH]

Cytomegalovirus Retinitis: Infection of the retina by cytomegalovirus characterized by retinal necrosis, hemorrhage, vessel sheathing, and retinal edema. Cytomegalovirus retinitis is a major opportunistic infection in AIDS patients and can cause blindness. [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]

Cytotoxic: Cell-killing. [NIH]

Cytotoxicity: Quality of being capable of producing a specific toxic action upon cells of special organs. [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]

Decarboxylation: The removal of a carboxyl group, usually in the form of carbon dioxide, from a chemical compound. [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]

Delusions: A false belief regarding the self or persons or objects outside the self that persists despite the facts, and is not considered tenable by one's associates. [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]

Dentigerous Cyst: Most common follicular odontogenic cyst. Occurs in relation to a partially erupted or unerupted tooth with at least the crown of the tooth to which the cyst is attached protruding into the cystic cavity. May give rise to an ameloblastoma and, in rare instances, undergo malignant transformation. [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]

Dermal: Pertaining to or coming from the skin. [NIH]

Dermatitis: Any inflammation of the skin. [NIH]

DES: Diethylstilbestrol. A synthetic hormone that was prescribed from the early 1940s until 1971 to help women with complications of pregnancy. DES has been linked to an increased risk of clear cell carcinoma of the vagina in daughters of women who used DES. DES may also increase the risk of breast cancer in women who used DES. [NIH]

Deuterium: Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

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]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Diaphragm: The musculofibrous partition that separates the thoracic cavity from the abdominal cavity. Contraction of the diaphragm increases the volume of the thoracic cavity aiding inspiration. [NIH]

Diencephalon: The paired caudal parts of the prosencephalon from which the thalamus, hypothalamus, epithalamus, and subthalamus are derived. [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]

Dihydrotestosterone: Anabolic agent. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

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]

Disinfectant: An agent that disinfects; applied particularly to agents used on inanimate objects. [EU]

Disinfection: Rendering pathogens harmless through the use of heat, antiseptics, antibacterial agents, etc. [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]

Dizziness: An imprecise term which may refer to a sense of spatial disorientation, motion of the environment, or lightheadedness. [NIH]

Domesticated: Species in which the evolutionary process has been influenced by humans to meet their needs. [NIH]

Dopamine: An endogenous catecholamine and prominent neurotransmitter in several systems of the brain. In the synthesis of catecholamines from tyrosine, it is the immediate precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain, and important in regulating movement. A family of dopaminergic receptor subtypes mediate its action. Dopamine is used pharmacologically for its direct (beta adrenergic agonist) and indirect (adrenergic releasing) sympathomimetic effects including its actions as an inotropic agent and as a renal vasodilator. [NIH]

Dorsal: 1. Pertaining to the back or to any dorsum. 2. Denoting a position more toward the back surface than some other object of reference; same as posterior in human anatomy; superior in the anatomy of quadrupeds. [EU]

Dorsum: A plate of bone which forms the posterior boundary of the sella turcica. [NIH]

Dosage Forms: Completed forms of the pharmaceutical preparation in which prescribed doses of medication are included. They are designed to resist action by gastric fluids, prevent vomiting and nausea, reduce or alleviate the undesirable taste and smells associated with oral administration, achieve a high concentration of drug at target site, or produce a delayed or long-acting drug effect. They include capsules, liniments, ointments, pharmaceutical solutions, powders, tablets, etc. [NIH]

Dose-dependent: Refers to the effects of treatment with a drug. If the effects change when the dose of the drug is changed, the effects are said to be dose dependent. [NIH]

Drive: A state of internal activity of an organism that is a necessary condition before a given

stimulus will elicit a class of responses; e.g., a certain level of hunger (drive) must be present before food will elicit an eating response. [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 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]

Duct: A tube through which body fluids pass. [NIH]

Dysphagia: Difficulty in swallowing. [EU]

Dysplasia: Cells that look abnormal under a microscope but are not cancer. [NIH]

Eczema: A pruritic papulovesicular dermatitis occurring as a reaction to many endogenous and exogenous agents (Dorland, 27th ed). [NIH]

Edema: Excessive amount of watery fluid accumulated in the intercellular spaces, most commonly present in subcutaneous tissue. [NIH]

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [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]

Effusion: The escape of fluid into a part or tissue, as an exudation or a transudation. [EU]

Ejaculation: The release of semen through the penis during orgasm. [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]

Emaciation: Clinical manifestation of excessive leanness usually caused by disease or a lack of nutrition. [NIH]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Emollient: Softening or soothing; called also malactic. [EU]

Encapsulated: Confined to a specific, localized area and surrounded by a thin layer of tissue. [NIH]

Encephalitis: Inflammation of the brain due to infection, autoimmune processes, toxins, and other conditions. Viral infections (see encephalitis, viral) are a relatively frequent cause of this condition. [NIH]

Encephalitis, Viral: Inflammation of brain parenchymal tissue as a result of viral infection. Encephalitis may occur as primary or secondary manifestation of Togaviridae infections; Herpesviridae infections; Adenoviridae infections; Flaviviridae infections; Bunyaviridae infections; Picornaviridae infections; Paramyxoviridae infections; Orthomyxoviridae infections; Retroviridae infections; and Arenaviridae infections. [NIH]

Encephalomyelitis: A general term indicating inflammation of the brain and spinal cord, often used to indicate an infectious process, but also applicable to a variety of autoimmune and toxic-metabolic conditions. There is significant overlap regarding the usage of this term and encephalitis in the literature. [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]

Endocrinology: A subspecialty of internal medicine concerned with the metabolism, physiology, and disorders of the endocrine system. [NIH]

Endocytosis: Cellular uptake of extracellular materials within membrane-limited vacuoles or microvesicles. Endosomes play a central role in endocytosis. [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]

Endonucleases: Enzymes that catalyze the hydrolysis of the internal bonds and thereby the formation of polynucleotides or oligonucleotides from ribo- or deoxyribonucleotide chains. EC 3.1.-. [NIH]

Endothelial cell: The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart. [NIH]

Endotoxic: Of, relating to, or acting as an endotoxin (= a heat-stable toxin, associated with the outer membranes of certain gram-negative bacteria. Endotoxins are not secreted and are released only when the cells are disrupted). [EU]

Endotoxin: Toxin from cell walls of bacteria. [NIH]

Enkephalin: A natural opiate painkiller, in the hypothalamus. [NIH]

Enteritis: Inflammation of the intestine, applied chiefly to inflammation of the small intestine; see also enterocolitis. [EU]

Enterocolitis: Inflammation of the intestinal mucosa of the small and large bowel. [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]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epidemiology, Molecular: The application of molecular biology to the answering of epidemiological questions. The examination of patterns of changes in DNA to implicate particular carcinogens and the use of molecular markers to predict which individuals are at highest risk for a disease are common examples. [NIH]

Epidermal: Pertaining to or resembling epidermis. Called also epidermic or epidermoid. [EU]

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]

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]

Epithelial: Refers to the cells that line the internal and external surfaces of the body. [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]

Epstein: Failure of the upper eyelid to move downward on downward movement of the eye, occurring in premature and nervous infants. [NIH]

Erythema: Redness of the skin produced by congestion of the capillaries. This condition may result from a variety of causes. [NIH]

Erythema Multiforme: A skin and mucous membrane disease characterized by an eruption of macules, papules, nodules, vesicles, and/or bullae with characteristic "bull's-eye" lesions usually occurring on the dorsal aspect of the hands and forearms. [NIH]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Exanthema: Diseases in which skin eruptions or rashes are a prominent manifestation. Classically, six such diseases were described with similar rashes; they were numbered in the

order in which they were reported. Only the fourth (Duke's disease), fifth (erythema infectiosum), and sixth (exanthema subitum) numeric designations survive as occasional synonyms in current terminology. [NIH]

Exhaustion: The feeling of weariness of mind and body. [NIH]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

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 Space: Interstitial space between cells, occupied by fluid as well as amorphous and fibrous substances. [NIH]

Extravasation: A discharge or escape, as of blood, from a vessel into the tissues. [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]

Facial: Of or pertaining to the face. [EU]

Facial Paralysis: Severe or complete loss of facial muscle motor function. This condition may result from central or peripheral lesions. Damage to CNS motor pathways from the cerebral cortex to the facial nuclei in the pons leads to facial weakness that generally spares the forehead muscles. Facial nerve diseases generally results in generalized hemifacial weakness. Neuromuscular junction diseases and muscular diseases may also cause facial paralysis or paresis. [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]

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]

Febrile: Pertaining to or characterized by fever. [EU]

Feline Infectious Peritonitis: Common coronavirus infection of cats caused by the feline infectious peritonitis virus. The disease is characterized by a long incubation period, fever, depression, loss of appetite, wasting, and progressive abdominal enlargement. Infection of cells of the monocyte-macrophage lineage appears to be essential in FIP pathogenesis. [NIH]

Fetal Heart: The heart of the fetus of any viviparous animal. It refers to the heart in the postembryonic period and is differentiated from the embryonic heart (heart/embryology) only on the basis of time. [NIH]

Fetal Monitoring: Physiologic or biochemical monitoring of the fetus. It is usually done during labor and may be performed in conjunction with the monitoring of uterine activity. It may also be performed prenatally as when the mother is undergoing surgery. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibroblasts: Connective tissue cells which secrete an extracellular matrix rich in collagen and other macromolecules. [NIH]

Fibroma: A benign tumor of fibrous or fully developed connective tissue. [NIH]

Fibronectin: An adhesive glycoprotein. One form circulates in plasma, acting as an opsonin; another is a cell-surface protein which mediates cellular adhesive interactions. [NIH]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Flexor: Muscles which flex a joint. [NIH]

Flounder: Common name for two families of fish belonging to the order Pleuronectiformes and described as left-eye flounders and right-eye flounders. The latter is more commonly used in research. [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]

Follicles: Shafts through which hair grows. [NIH]

Fractionation: Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days. [NIH]

Fulminant Hepatic Failure: Liver failure that occurs suddenly in a previously healthy person. The most common causes of FHF are acute hepatitis, acetaminophen overdose, and liver damage from prescription drugs. [NIH]

Fungi: A kingdom of eukaryotic, heterotrophic organisms that live as saprobes or parasites, including mushrooms, yeasts, smuts, molds, etc. They reproduce either sexually or asexually, and have life cycles that range from simple to complex. Filamentous fungi refer to those that grow as multicelluar colonies (mushrooms and molds). [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]

Gadolinium: An element of the rare earth family of metals. It has the atomic symbol Gd, atomic number 64, and atomic weight 157.25. Its oxide is used in the control rods of some nuclear reactors. [NIH]

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]

Gammaherpesvirinae: A subfamily of Herpesviridae characterized by variable reproductive cycles. There are two official genera, Lymphocryptovirus and Rhadinovirus, and possibly a third, as yet unnamed, which includes Marek's Disease Herpesvirus 1 (gallid herpesvirus 2). [NIH]

Gamma-interferon: Interferon produced by T-lymphocytes in response to various mitogens and antigens. Gamma interferon appears to have potent antineoplastic, immunoregulatory and antiviral activity. [NIH]

Ganciclovir: Acyclovir analog that is a potent inhibitor of the Herpesvirus family including cytomegalovirus. Ganciclovir is used to treat complications from AIDS-associated cytomegalovirus infections. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Ganglion: 1. A knot, or knotlike mass. 2. A general term for a group of nerve cell bodies located outside the central nervous system; occasionally applied to certain nuclear groups within the brain or spinal cord, e.g. basal ganglia. 3. A benign cystic tumour occurring on a aponeurosis or tendon, as in the wrist or dorsum of the foot; it consists of a thin fibrous capsule enclosing a clear mucinous fluid. [EU]

Gangrenous: A circumscribed, deep-seated, suppurative inflammation of the subcutaneous tissue of the eyelid discharging pus from several points. [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]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

Gelatin: A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [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]

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 Deletion: A genetic rearrangement through loss of segments of DNA or RNA, bringing sequences which are normally separated into close proximity. This deletion may be detected using cytogenetic techniques and can also be inferred from the phenotype, indicating a deletion at one specific locus. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [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 testing: Analyzing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder. [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]

Glioma: A cancer of the brain that comes from glial, or supportive, cells. [NIH]

Glucocorticoid: A compound that belongs to the family of compounds called corticosteroids (steroids). Glucocorticoids affect metabolism and have anti-inflammatory and immunosuppressive effects. They may be naturally produced (hormones) or synthetic (drugs). [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]

Glycine: A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [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]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosaminoglycan: A type of long, unbranched polysaccharide molecule. Glycosaminoglycans are major structural components of cartilage and are also found in the cornea of the eye. [NIH]

Glycosidic: Formed by elimination of water between the anomeric hydroxyl of one sugar and a hydroxyl of another sugar molecule. [NIH]

Glycosylation: The chemical or biochemical addition of carbohydrate or glycosyl groups to other chemicals, especially peptides or proteins. Glycosyl transferases are used in this biochemical reaction. [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]

Gp120: 120-kD HIV envelope glycoprotein which is involved in the binding of the virus to its membrane receptor, the CD4 molecule, found on the surface of certain cells in the body. [NIH]

GP41: 41-kD HIV transmembrane envelope glycoprotein which mediates the fusion of the viral membrane with the membrane of the target cell. [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]

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]

Gram-positive: Retaining the stain or resisting decolorization by alcohol in Gram's method of staining, a primary characteristic of bacteria whose cell wall is composed of a thick layer of peptidologlycan with attached teichoic acids. [EU]

Granule: A small pill made from sucrose. [EU]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Granuloma: A relatively small nodular inflammatory lesion containing grouped mononuclear phagocytes, caused by infectious and noninfectious agents. [NIH]

Granuloma Inguinale: Anogenital ulcers caused by Calymmatobacterium granulomatis as distinguished from lymphogranuloma inguinale (see lymphogranuloma venereum) caused by Chlamydia trachomatis. Diagnosis is made by demonstration of typical intracellular Donovan bodies in crushed-tissue smears. [NIH]

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]

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]

Habitual: Of the nature of a habit; according to habit; established by or repeated by force of habit, customary. [EU]

Haemopoietic: Haematopoietic; pertaining to or effecting the formation of blood cells. [EU]

Hair Cells: Mechanoreceptors located in the organ of Corti that are sensitive to auditory stimuli and in the vestibular apparatus that are sensitive to movement of the head. In each case the accessory sensory structures are arranged so that appropriate stimuli cause movement of the hair-like projections (stereocilia and kinocilia) which relay the information centrally in the nervous system. [NIH]

Hair follicles: Shafts or openings on the surface of the skin through which hair grows. [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 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]

Hematologic Diseases: Disorders of the blood and blood forming tissues. [NIH]

Hematoma: An extravasation of blood localized in an organ, space, or tissue. [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]

Hemolytic: A disease that affects the blood and blood vessels. It destroys red blood cells, cells that cause the blood to clot, and the lining of blood vessels. HUS is often caused by the Escherichia coli bacterium in contaminated food. People with HUS may develop acute renal failure. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Heparan Sulfate Proteoglycan: A substance released by astrocytes, which is critical in stopping nervous fibers in their tracks. [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]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatitis Viruses: Any of the viruses that cause inflammation of the liver. They include both DNA and RNA viruses as well viruses from humans and animals. [NIH]

Hepatocyte: A liver cell. [NIH]

Hepatomegaly: Enlargement of the liver. [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]

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]

Herpesvirus 6, Human: The type species of Roseolovirus isolated from patients with AIDS and other lymphoproliferative disorders. It infects and replicates in fresh and established lines of hematopoietic cells and cells of neural origin. It also appears to alter NK cell activity. HHV-6 (HBLV) antibodies are elevated in patients with AIDS, Sjogren's syndrome, sarcoidosis, chronic fatigue syndrome, and certain malignancies. HHV-6 is the cause of exanthema subitum and has been implicated in encephalitis. [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]

Histiocytosis: General term for the abnormal appearance of histiocytes in the blood. Based on the pathological features of the cells involved rather than on clinical findings, the histiocytic diseases are subdivided into three groups: Langerhans cell histiocytosis, non-Langerhans cell histiocytosis, and malignant histiocytic disorders. [NIH]

Histology: The study of tissues and cells under a microscope. [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]

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]

Hybridomas: Cells artificially created by fusion of activated lymphocytes with neoplastic cells. The resulting hybrid cells are cloned and produce pure or "monoclonal" antibodies or T-cell products, identical to those produced by the immunologically competent parent, and continually grow and divide as the neoplastic parent. [NIH]

Hydration: Combining with water. [NIH]

Hydrochloric Acid: A strong corrosive acid that is commonly used as a laboratory reagent. It is formed by dissolving hydrogen chloride in water. Gastric acid is the hydrochloric acid component of gastric juice. [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]

Hydrophobic: Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

Hyperplasia: An increase in the number of cells in a tissue or organ, not due to tumor formation. It differs from hypertrophy, which is an increase in bulk without an increase in the number of cells. [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]

Hypesthesia: Absent or reduced sensitivity to cutaneous stimulation. [NIH]

Hypogammaglobulinemia: The most common primary immunodeficiency in which antibody production is deficient. [NIH]

Hypotension: Abnormally low blood pressure. [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]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Illusion: A false interpretation of a genuine percept. [NIH]

Immortal: Stage when the mother cell and its descendants will multiply indefinitely. [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]

Immunization Schedule: Schedule giving optimum times usually for primary and/or secondary immunization. [NIH]

Immunoassay: Immunochemical assay or detection of a substance by serologic or immunologic methods. Usually the substance being studied serves as antigen both in antibody production and in measurement of antibody by the test substance. [NIH]

Immunoblotting: Immunologic methods for isolating and quantitatively measuring immunoreactive substances. When used with immune reagents such as monoclonal antibodies, the process is known generically as western blot analysis (blotting, western). [NIH]

Immunocompetence: The ability of lymphoid cells to mount a humoral or cellular immune response when challenged by antigen. [NIH]

Immunocompromised: Having a weakened immune system caused by certain diseases or treatments. [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]

Immunodeficiency Virus, Feline: A species of lentivirus, subgenus feline lentiviruses isolated from cats with a chronic wasting syndrome, presumed to be immune deficiency. There is no antigenic relationship between FIV and HIV, nor does FIV grow in human T-cells. [NIH]

Immunofluorescence: A technique for identifying molecules present on the surfaces of cells or in tissues using a highly fluorescent substance coupled to a specific antibody. [NIH]

Immunogen: A substance that is capable of causing antibody formation. [NIH]

Immunogenic: Producing immunity; evoking an immune response. [EU]

Immunoglobulin: A protein that acts as an antibody. [NIH]

Immunohistochemistry: Histochemical localization of immunoreactive substances using labeled antibodies as reagents. [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]

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Immunosuppressive Agents: Agents that suppress immune function by one of several mechanisms of action. Classical cytotoxic immunosuppressants act by inhibiting DNA synthesis. Others may act through activation of suppressor T-cell populations or by inhibiting the activation of helper cells. While immunosuppression has been brought about in the past primarily to prevent rejection of transplanted organs, new applications involving mediation of the effects of interleukins and other cytokines are emerging. [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]

Impetigo: A common superficial bacterial infection caused by staphylococcus aureus or group A beta-hemolytic streptococci. Characteristics include pustular lesions that rupture and discharge a thin, amber-colored fluid that dries and forms a crust. This condition is commonly located on the face, especially about the mouth and nose. [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]

Incubated: Grown in the laboratory under controlled conditions. (For instance, white blood cells can be grown in special conditions so that they attack specific cancer cells when returned to the body.) [NIH]

Incubation: The development of an infectious disease from the entrance of the pathogen to the appearance of clinical symptoms. [EU]

Incubation period: The period of time likely to elapse between exposure to the agent of the

disease and the onset of clinical symptoms. [NIH]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

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]

Infancy: The period of complete dependency prior to the acquisition of competence in walking, talking, and self-feeding. [NIH]

Infantile: Pertaining to an infant or to infancy. [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]

Infectious Mononucleosis: A common, acute infection usually caused by the Epstein-Barr virus (Human herpesvirus 4). There is an increase in mononuclear white blood cells and other atypical lymphocytes, generalized lymphadenopathy, splenomegaly, and occasionally hepatomegaly with hepatitis. [NIH]

Infectious Peritonitis Virus, Feline: A species of coronavirus infecting cats of all ages and commonly found in catteries and zoos. Cats are often found carrying the virus but only a small proportion develop disease. [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]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Inguinal: Pertaining to the inguen, or groin. [EU]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Inlay: In dentistry, a filling first made to correspond with the form of a dental cavity and then cemented into the cavity. [NIH]

Inorganic: Pertaining to substances not of organic origin. [EU]

Insertional: A technique in which foreign DNA is cloned into a restriction site which occupies a position within the coding sequence of a gene in the cloning vector molecule. Insertion interrupts the gene's sequence such that its original function is no longer

expressed. [NIH]

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]

Insulator: Material covering the metal conductor of the lead. It is usually polyurethane or silicone. [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-1: A soluble factor produced by monocytes, macrophages, and other cells which activates T-lymphocytes and potentiates their response to mitogens or antigens. IL-1 consists of two distinct forms, IL-1 alpha and IL-1 beta which perform the same functions but are distinct proteins. The biological effects of IL-1 include the ability to replace macrophage requirements for T-cell activation. The factor is distinct from interleukin-2. [NIH]

Interleukin-18: Cytokine which resembles IL-1 structurally and IL-12 functionally. It enhances the cytotoxic activity of NK cells and CTLs, and appears to play a role both as neuroimmunomodulator and in the induction of mucosal immunity. [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]

Interleukin-6: Factor that stimulates the growth and differentiation of human B-cells and is also a growth factor for hybridomas and plasmacytomas. It is produced by many different cells including T-cells, monocytes, and fibroblasts. [NIH]

Interleukins: Soluble factors which stimulate growth-related activities of leukocytes as well as other cell types. They enhance cell proliferation and differentiation, DNA synthesis, secretion of other biologically active molecules and responses to immune and inflammatory stimuli. [NIH]

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]

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]

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intramuscular: IM. Within or into muscle. [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]

Involuntary: Reaction occurring without intention or volition. [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]

Iris: The most anterior portion of the uveal layer, separating the anterior chamber from the posterior. It consists of two layers - the stroma and the pigmented epithelium. Color of the iris depends on the amount of melanin in the stroma on reflection from the pigmented epithelium. [NIH]

Jellyfish: Free swimming marine cnidarians. Most of the large jellyfish are in the class Scyphozoa; the small jellyfish are in the class Hydrozoa (hydra). [NIH]

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]

Keratitis: Inflammation of the cornea. [NIH]

Ketoconazole: Broad spectrum antifungal agent used for long periods at high doses, especially in immunosuppressed patients. [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]

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]

Latency: The period of apparent inactivity between the time when a stimulus is presented and the moment a response occurs. [NIH]

Latent: Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

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]

Lens: The transparent, double convex (outward curve on both sides) structure suspended between the aqueous and vitreous; helps to focus light on the retina. [NIH]

Lentivirus: A genus of the family Retroviridae consisting of non-oncogenic retroviruses that produce multi-organ diseases characterized by long incubation periods and persistent infection. Lentiviruses are unique in that they contain open reading frames (ORFs) between the pol and env genes and in the 3' env region. Five serogroups are recognized, reflecting the mammalian hosts with which they are associated. HIV-1 is the type species. [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]

Leucocyte: All the white cells of the blood and their precursors (myeloid cell series, lymphoid cell series) but commonly used to indicate granulocytes exclusive of lymphocytes. [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]

Leukopenia: A condition in which the number of leukocytes (white blood cells) in the blood is reduced. [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]

Lice: A general name for small, wingless, parasitic insects, previously of the order Phthiraptera. Though exact taxonomy is still controversial, they can be grouped in the orders Anoplura (sucking lice), Mallophaga (biting lice), and Rhynchophthirina (elephant lice). [NIH]

Lichen Planus: An inflammatory, pruritic disease of the skin and mucous membranes, which can be either generalized or localized. It is characterized by distinctive purplish, flat-topped papules having a predilection for the trunk and flexor surfaces. The lesions may be discrete or coalesce to form plaques. Histologically, there is a "saw-tooth" pattern of epidermal hyperplasia and vacuolar alteration of the basal layer of the epidermis along with an intense upper dermal inflammatory infiltrate composed predominantly of T-cells. Etiology is unknown. [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]

Ligands: A RNA simulation method developed by the MIT. [NIH]

Limbic: Pertaining to a limbus, or margin; forming a border around. [EU]

Limbic System: A set of forebrain structures common to all mammals that is defined functionally and anatomically. It is implicated in the higher integration of visceral, olfactory, and somatic information as well as homeostatic responses including fundamental survival behaviors (feeding, mating, emotion). For most authors, it includes the amygdala, epithalamus, gyrus cinguli, hippocampal formation (see hippocampus), hypothalamus,

parahippocampal gyrus, septal nuclei, anterior nuclear group of thalamus, and portions of the basal ganglia. (Parent, Carpenter's Human Neuroanatomy, 9th ed, p744; NeuroNames, http://rprcsgi.rprc.washington.edu/neuronames/index.html (September 2, 1998)). [NIH]

Linkages: 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]

Lipid A: Lipid A is the biologically active component of lipopolysaccharides. It shows strong endotoxic activity and exhibits immunogenic properties. [NIH]

Lipid Peroxidation: Peroxidase catalyzed oxidation of lipids using hydrogen peroxide as an electron acceptor. [NIH]

Lipopolysaccharide: Substance consisting of polysaccaride and lipid. [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]

Liposomes: Artificial, single or multilaminar vesicles (made from lecithins or other lipids) that are used for the delivery of a variety of biological molecules or molecular complexes to cells, for example, drug delivery and gene transfer. They are also used to study membranes and membrane proteins. [NIH]

Liquor: 1. A liquid, especially an aqueous solution containing a medicinal substance. 2. A general term used in anatomical nomenclature for certain fluids of the body. [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 metastases: Cancer that has spread from the original (primary) tumor to the liver. [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]

Low-density lipoprotein: Lipoprotein that contains most of the cholesterol in the blood. LDL carries cholesterol to the tissues of the body, including the arteries. A high level of LDL increases the risk of heart disease. LDL typically contains 60 to 70 percent of the total serum cholesterol and both are directly correlated with CHD risk. [NIH]

Lung Transplantation: The transference of either one or both of the lungs from one human or animal to another. [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]

Lymphadenopathy: Disease or swelling of the lymph nodes. [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]

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 Count: A count of the number of lymphocytes in the blood. [NIH]

Lymphogranuloma Venereum: Subacute inflammation of the inguinal lymph glands caused by certain immunotypes of Chlamydia trachomatis. It is a sexually transmitted disease in the U.S. but is more widespread in developing countries. It is distinguished from granuloma venereum (granuloma inguinale), which is caused by Calymmatobacterium granulomatis. [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]

Lymphoproliferative: Disorders characterized by proliferation of lymphoid tissue, general or unspecified. [NIH]

Lymphoproliferative Disorders: Disorders characterized by proliferation of lymphoid tissue, general or unspecified. [NIH]

Lysine: An essential amino acid. It is often added to animal feed. [NIH]

Lysosome: A sac-like compartment inside a cell that has enzymes that can break down cellular components that need to be destroyed. [NIH]

Lytic: 1. Pertaining to lysis or to a lysin. 2. Producing lysis. [EU]

Macrophage: A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. [NIH]

Maculopapular: Both macular and papular, as an eruption consisting of both macules and papules; sometimes erroneously used to designate a papule that is only slightly elevated. [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]

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 tumor: A tumor capable of metastasizing. [NIH]

Manic: Affected with mania. [EU]

Manic-depressive psychosis: One of a group of psychotic reactions, fundamentally marked by severe mood swings and a tendency to remission and recurrence. [NIH]

Manifest: Being the part or aspect of a phenomenon that is directly observable : concretely expressed in behaviour. [EU]

Mannans: Polysaccharides consisting of mannose units. [NIH]

Masseter Muscle: A masticatory muscle whose action is closing the jaws. [NIH]

Mastication: The act and process of chewing and grinding food in the mouth. [NIH]

Mastitis: Inflammatory disease of the breast, or mammary gland. [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]

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]

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]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Membrane Fusion: The adherence of cell membranes, intracellular membranes, or artifical membrane models of either to each other or to viruses, parasites, or interstitial particles through a variety of chemical and physical processes. [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]

Meninges: The three membranes that cover and protect the brain and spinal cord. [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]

Mental Processes: Conceptual functions or thinking in all its forms. [NIH]

Mesothelial: It lines the peritonealla and pleural cavities. [NIH]

Metabolic disorder: A condition in which normal metabolic processes are disrupted, usually because of a missing enzyme. [NIH]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

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]

Methionine: A sulfur containing essential amino acid that is important in many body functions. It is a chelating agent for heavy metals. [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]

Mice Minute Virus: The type species of parvovirus prevalent in mouse colonies and found as a contaminant of many transplanted tumors or leukemias. [NIH]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbicide: Any substance (gels, creams, suppositories, etc.) that can reduce transmission of sexually transmitted infections. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [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]

Micro-organism: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [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]

Mineralocorticoids: A group of corticosteroids primarily associated with the regulation of water and electrolyte balance. This is accomplished through the effect on ion transport in renal tubules, resulting in retention of sodium and loss of potassium. Mineralocorticoid secretion is itself regulated by plasma volume, serum potassium, and angiotensin II. [NIH]

Mitochondria: Parts of a cell where aerobic production (also known as cell respiration) takes place. [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]

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]

Mobility: Capability of movement, of being moved, or of flowing freely. [EU]

Mode of Transmission: Hepatitis A [NIH]

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]

Monocyte: A type of white blood cell. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Mononucleosis: The presence of an abnormally large number of mononuclear leucocytes (monocytes) in the blood. The term is often used alone to refer to infectious mononucleosis. [EU]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Motility: The ability to move spontaneously. [EU]

Motor Activity: The physical activity of an organism as a behavioral phenomenon. [NIH]

Mucinous: Containing or resembling mucin, the main compound in mucus. [NIH]

Mucins: A secretion containing mucopolysaccharides and protein that is the chief constituent of mucus. [NIH]

Mucocutaneous: Pertaining to or affecting the mucous membrane and the skin. [EU]

Mucolytic: Destroying or dissolving mucin; an agent that so acts : a mucopolysaccharide or glycoprotein, the chief constituent of mucus. [EU]

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]

Multiple sclerosis: A disorder of the central nervous system marked by weakness, numbness, a loss of muscle coordination, and problems with vision, speech, and bladder control. Multiple sclerosis is thought to be an autoimmune disease in which the body's immune system destroys myelin. Myelin is a substance that contains both protein and fat (lipid) and serves as a nerve insulator and helps in the transmission of nerve signals. [NIH]

Muscular Diseases: Acquired, familial, and congenital disorders of skeletal muscle and smooth muscle. [NIH]

Mutagenesis: Process of generating genetic mutations. It may occur spontaneously or be induced by mutagens. [NIH]

Mutagens: Chemical agents that increase the rate of genetic mutation by interfering with the function of nucleic acids. A clastogen is a specific mutagen that causes breaks in chromosomes. [NIH]

Myalgia: Pain in a muscle or muscles. [EU]

Mycobacterial disease: Any disease caused by Mycobacterium other than M. tuberculosis, M. bovis, and M. avium. [NIH]

Mycosis: Any disease caused by a fungus. [EU]

Mycotic: Pertaining to a mycosis; caused by fungi. [EU]

Myelin: The fatty substance that covers and protects nerves. [NIH]

Myeloma: Cancer that arises in plasma cells, a type of white blood cell. [NIH]

Myocarditis: Inflammation of the myocardium; inflammation of the muscular walls of the heart. [EU]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myopathy: Any disease of a muscle. [EU]

Naloxone: A specific opiate antagonist that has no agonist activity. It is a competitive antagonist at mu, delta, and kappa opioid receptors. [NIH]

Nasal Mucosa: The mucous membrane lining the nasal cavity. [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]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Neonatal Screening: The identification of selected parameters in newborn infants by various tests, examinations, or other procedures. Screening may be performed by clinical or laboratory measures. A screening test is designed to sort out healthy neonates from those not well, but the screening test is not intended as a diagnostic device, rather instead as epidemiologic. [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]

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]

Neural: 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

Neuraminidase: An enzyme that catalyzes the hydrolysis of alpha-2,3, alpha-2,6-, and alpha-2,8-glycosidic linkages (at a decreasing rate, respectively) of terminal sialic residues in

oligosaccharides, glycoproteins, glycolipids, colominic acid, and synthetic substrate. (From Enzyme Nomenclature, 1992) EC 3.2.1.18. [NIH]

Neuritis: A general term indicating inflammation of a peripheral or cranial nerve. Clinical manifestation may include pain; paresthesias; paresis; or hypesthesia. [NIH]

Neuroblastoma: Cancer that arises in immature nerve cells and affects mostly infants and children. [NIH]

Neurodegenerative Diseases: Hereditary and sporadic conditions which are characterized by progressive nervous system dysfunction. These disorders are often associated with atrophy of the affected central or peripheral nervous system structures. [NIH]

Neurologic: Having to do with nerves or the nervous system. [NIH]

Neurology: A medical specialty concerned with the study of the structures, functions, and diseases of the nervous system. [NIH]

Neuronal: Pertaining to a neuron or neurons (= conducting cells of the nervous system). [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]

Neuropathy: A problem in any part of the nervous system except the brain and spinal cord. Neuropathies can be caused by infection, toxic substances, or disease. [NIH]

Neuropeptide: A member of a class of protein-like molecules made in the brain. Neuropeptides consist of short chains of amino acids, with some functioning as neurotransmitters and some functioning as hormones. [NIH]

Neurotransmitters: Endogenous signaling molecules that alter the behavior of neurons or effector cells. Neurotransmitter is used here in its most general sense, including not only messengers that act directly to regulate ion channels, but also those that act through second messenger systems, and those that act at a distance from their site of release. Included are neuromodulators, neuroregulators, neuromediators, and neurohumors, whether or not acting at synapses. [NIH]

Neutralization: An act or process of neutralizing. [EU]

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]

Neutropenia: An abnormal decrease in the number of neutrophils, a type of white blood cell. [NIH]

Neutrophils: Granular leukocytes having a nucleus with three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine inconspicuous granules and stainable by neutral dyes. [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]

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]

Nucleocapsid: A protein-nucleic acid complex which forms part or all of a virion. It consists of a capsid plus enclosed nucleic acid. Depending on the virus, the nucleocapsid may correspond to a naked core or be surrounded by a membranous envelope. [NIH]

Nucleolus: A small dense body (sub organelle) within the nucleus of eukaryotic cells, visible by phase contrast and interference microscopy in live cells throughout interphase. Contains RNA and protein and is the site of synthesis of ribosomal RNA. [NIH]

Nucleoprotein: Chromosomes consist largely of nuclei acids and proteins, joined here as complexes called nucleoproteins. [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]

Ocular: 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

Odontogenic Cysts: Cysts found in the jaws and arising from epithelium involved in tooth formation. They include follicular cysts (e.g., primordial cyst, dentigerous cyst, multilocular cyst), lateral periodontal cysts, and radicular cysts. They may become keratinized (odontogenic keratocysts). Follicular cysts may give rise to ameloblastomas and, in rare cases, undergo malignant transformation. [NIH]

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]

Oligo: Chemical and mineral elements that exist in minimal (oligo) quantities in the body, in foods, in the air, in soil; name applied to any element observed as a microconstituent of plant or animal tissue and of beneficial, harmful, or even doubtful significance. [NIH]

Oligosaccharides: Carbohydrates consisting of between two and ten monosaccharides connected by either an alpha- or beta-glycosidic link. They are found throughout nature in both the free and bound form. [NIH]

Oncogenes: Genes which can potentially induce neoplastic transformation. They include genes for growth factors, growth factor receptors, protein kinases, signal transducers, nuclear phosphoproteins, and transcription factors. When these genes are constitutively expressed after structural and/or regulatory changes, uncontrolled cell proliferation may result. Viral oncogenes have prefix "v-" before the gene symbol; cellular oncogenes (proto-oncogenes) have the prefix "c-" before the gene symbol. [NIH]

Oncogenic: Chemical, viral, radioactive or other agent that causes cancer; carcinogenic. [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]

Open Reading Frames: Reading frames where successive nucleotide triplets can be read as codons specifying amino acids and where the sequence of these triplets is not interrupted by

stop codons. [NIH]

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]

Oral Health: The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

Oral Hygiene: The practice of personal hygiene of the mouth. It includes the maintenance of oral cleanliness, tissue tone, and general preservation of oral health. [NIH]

Oral Manifestations: Disorders of the mouth attendant upon non-oral disease or injury. [NIH]

Orbit: One of the two cavities in the skull which contains an eyeball. Each eye is located in a bony socket or orbit. [NIH]

Orbital: Pertaining to the orbit (= the bony cavity that contains the eyeball). [EU]

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]

Organ Transplantation: Transference of an organ between individuals of the same species or between individuals of different species. [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]

Ornithine: An amino acid produced in the urea cycle by the splitting off of urea from arginine. [NIH]

Ornithine Decarboxylase: A pyridoxal-phosphate protein, believed to be the rate-limiting compound in the biosynthesis of polyamines. It catalyzes the decarboxylation of ornithine to form putrescine, which is then linked to a propylamine moiety of decarboxylated S-adenosylmethionine to form spermidine. EC 4.1.1.17. [NIH]

Orofacial: Of or relating to the mouth and face. [EU]

Osteonecrosis: Death of a bone or part of a bone, either atraumatic or posttraumatic. [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]

Overdose: An accidental or deliberate dose of a medication or street drug that is in excess of what is normally used. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [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]

Oxidative Stress: A disturbance in the prooxidant-antioxidant balance in favor of the former, leading to potential damage. Indicators of oxidative stress include damaged DNA bases, protein oxidation products, and lipid peroxidation products (Sies, Oxidative Stress, 1991, pxv-xvi). [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Palsy: Disease of the peripheral nervous system occurring usually after many years of increased lead absorption. [NIH]

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]

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]

Paramyxovirus: A genus of the family Paramyxoviridae (subfamily Paramyxovirinae) where all the virions have both hemagglutinin and neuraminidase activities and encode a C protein. Human parainfluenza virus 1 is the type species. [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]

Parenteral: Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

Paresis: A general term referring to a mild to moderate degree of muscular weakness, occasionally used as a synonym for paralysis (severe or complete loss of motor function). In the older literature, paresis often referred specifically to paretic neurosyphilis. "General paresis" and "general paralysis" may still carry that connotation. Bilateral lower extremity paresis is referred to as paraparesis. [NIH]

Paresthesias: Abnormal touch sensations, such as burning or prickling, that occur without an outside stimulus. [NIH]

Parietal: 1. Of or pertaining to the walls of a cavity. 2. Pertaining to or located near the parietal bone, as the parietal lobe. [EU]

Particle: A tiny mass of material. [EU]

Parvovirus: A genus of the family Parvoviridae, subfamily Parvovirinae, infecting a variety of vertebrates including humans. Parvoviruses are responsible for a number of important diseases but also can be non-pathogenic in certain hosts. The type species is mice minute virus. [NIH]

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]

Pathology, Oral: A dental specialty concerned with pathology of the oral cavity. [NIH]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

Peer Review: An organized procedure carried out by a select committee of professionals in evaluating the performance of other professionals in meeting the standards of their specialty. Review by peers is used by editors in the evaluation of articles and other papers submitted for publication. Peer review is used also in the evaluation of grant applications. It is applied also in evaluating the quality of health care provided to patients. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

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]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Perianal: Located around the anus. [EU]

Periodontal Cyst: An epithelium-lined sac containing fluid; usually found at the apex of a pulp-involved tooth. The lateral type occurs less frequently along the side of the root. [NIH]

Periodontal disease: Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [NIH]

Periodontics: A dental specialty concerned with the histology, physiology, and pathology of the tissues that support, attach, and surround the teeth, and of the treatment and prevention of disease affecting these tissues. [NIH]

Periodontitis: Inflammation of the periodontal membrane; also called periodontitis simplex. [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 Nervous System: The nervous system outside of the brain and spinal cord. The peripheral nervous system has autonomic and somatic divisions. The autonomic nervous system includes the enteric, parasympathetic, and sympathetic subdivisions. The somatic nervous system includes the cranial and spinal nerves and their ganglia and the peripheral sensory receptors. [NIH]

Petroleum: Naturally occurring complex liquid hydrocarbons which, after distillation, yield combustible fuels, petrochemicals, and lubricants. [NIH]

Phagocytosis: The engulfing of microorganisms, other cells, and foreign particles by phagocytic cells. [NIH]

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]

Pharmaceutical Solutions: Homogeneous liquid preparations that contain one or more chemical substances dissolved, i.e., molecularly dispersed, in a suitable solvent or mixture of mutually miscible solvents. For reasons of their ingredients, method of preparation, or use, they do not fall into another group of products. [NIH]

Pharmacokinetics: Dynamic and kinetic mechanisms of exogenous chemical and drug absorption, biotransformation, distribution, release, transport, uptake, and elimination as a function of dosage, and extent and rate of metabolic processes. It includes toxicokinetics, the pharmacokinetic mechanism of the toxic effects of a substance. [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]

Phosphates: Inorganic salts of phosphoric acid. [NIH]

Phospholipases: A class of enzymes that catalyze the hydrolysis of phosphoglycerides or glycerophosphatidates. EC 3.1.-. [NIH]

Phospholipids: Lipids containing one or more phosphate groups, particularly those derived from either glycerol (phosphoglycerides; glycerophospholipids) or sphingosine (sphingolipids). They are polar lipids that are of great importance for the structure and function of cell membranes and are the most abundant of membrane lipids, although not stored in large amounts in the system. [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]

Phosphorylated: Attached to a phosphate group. [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]

Photodermatitis: Dermatitis caused or elicited by exposure to ultraviolet light, may be phototoxic or photoallergic. [NIH]

Phototherapy: Treatment of disease by exposure to light, especially by variously concentrated light rays or specific wavelengths. [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 study: The initial study examining a new method or treatment. [NIH]

Pituitary Gland: A small, unpaired gland situated in the sella turcica tissue. It is connected to the hypothalamus by a short stalk. [NIH]

Pityriasis: A name originally applied to a group of skin diseases characterized by the formation of fine, branny scales, but now used only with a modifier. [EU]

Pityriasis Rosea: A mild exanthematous inflammation of unknown etiology. It is characterized by the presence of salmon-colored maculopapular lesions. The most striking feature is the arrangement of the lesions such that the long axis is parallel to the lines of cleavage. The eruptions are usually generalized, affecting chiefly the trunk, and the course is often self-limiting. [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]

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]

Plastids: Self-replicating cytoplasmic organelles of plant and algal cells that contain pigments and may synthesize and accumulate various substances. Plastids are used in phylogenetic studies. [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]

Pleura: The thin serous membrane enveloping the lungs and lining the thoracic cavity. [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]

Pleural cavity: A space enclosed by the pleura (thin tissue covering the lungs and lining the interior wall of the chest cavity). It is bound by thin membranes. [NIH]

Pleural Effusion: Presence of fluid in the pleural cavity resulting from excessive transudation or exudation from the pleural surfaces. It is a sign of disease and not a diagnosis in itself. [NIH]

Pneumonitis: A disease caused by inhaling a wide variety of substances such as dusts and molds. Also called "farmer's disease". [NIH]

Pollen: The male fertilizing element of flowering plants analogous to sperm in animals. It is released from the anthers as yellow dust, to be carried by insect or other vectors, including wind, to the ovary (stigma) of other flowers to produce the embryo enclosed by the seed. The pollens of many plants are allergenic. [NIH]

Polyesters: Polymers of organic acids and alcohols, with ester linkages--usually

polyethylene terephthalate; can be cured into hard plastic, films or tapes, or fibers which can be woven into fabrics, meshes or velours. [NIH]

Polyethylene: A vinyl polymer made from ethylene. It can be branched or linear. Branched or low-density polyethylene is tough and pliable but not to the same degree as linear polyethylene. Linear or high-density polyethylene has a greater hardness and tensile strength. Polyethylene is used in a variety of products, including implants and prostheses. [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]

Polymers: Compounds formed by the joining of smaller, usually repeating, units linked by covalent bonds. These compounds often form large macromolecules (e.g., polypeptides, proteins, plastics). [NIH]

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]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Pons: The part of the central nervous system lying between the medulla oblongata and the mesencephalon, ventral to the cerebellum, and consisting of a pars dorsalis and a pars ventralis. [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]

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]

Potentiate: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

Potentiating: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [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]

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]

Precipitation: The act or process of precipitating. [EU]

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]

Premalignant: A term used to describe a condition that may (or is likely to) become cancer. Also called precancerous. [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 central nervous system lymphoma: Cancer that arises in the lymphoid tissue found in the central nervous system (CNS). The CNS includes the brain and spinal cord. [NIH]

Proctocolitis: Inflammation of the rectum and colon. [NIH]

Prodrug: A substance that gives rise to a pharmacologically active metabolite, although not itself active (i. e. an inactive precursor). [NIH]

Progeny: The offspring produced in any generation. [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]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [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]

Propylene Glycol: A clear, colorless, viscous organic solvent and diluent used in pharmaceutical preparations. [NIH]

Protein Binding: The process in which substances, either endogenous or exogenous, bind to proteins, peptides, enzymes, protein precursors, or allied compounds. Specific protein-binding measures are often used as assays in diagnostic assessments. [NIH]

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 Kinases: A family of enzymes that catalyze the conversion of ATP and a protein to ADP and a phosphoprotein. EC 2.7.1.37. [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]

Proteoglycans: Glycoproteins which have a very high polysaccharide content. [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-Oncogenes: Normal cellular genes homologous to viral oncogenes. The products of proto-oncogenes are important regulators of biological processes and appear to be involved in the events that serve to maintain the ordered procession through the cell cycle. Proto-oncogenes have names of the form c-onc. [NIH]

Pruritic: Pertaining to or characterized by pruritus. [EU]

Pseudorabies: A highly contagious herpesvirus infection affecting the central nervous system of swine, cattle, dogs, cats, rats, and other animals. [NIH]

Psychic: Pertaining to the psyche or to the mind; mental. [EU]

Psychology: The science dealing with the study of mental processes and behavior in man and animals. [NIH]

Psychomotor: Pertaining to motor effects of cerebral or psychic activity. [EU]

Psychosis: A mental disorder characterized by gross impairment in reality testing as evidenced by delusions, hallucinations, markedly incoherent speech, or disorganized and agitated behaviour without apparent awareness on the part of the patient of the incomprehensibility of his behaviour; the term is also used in a more general sense to refer to mental disorders in which mental functioning is sufficiently impaired as to interfere grossly with the patient's capacity to meet the ordinary demands of life. Historically, the term has been applied to many conditions, e.g. manic-depressive psychosis, that were first described in psychotic patients, although many patients with the disorder are not judged psychotic. [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]

Pulmonary: Relating to the lungs. [NIH]

Pulmonary Edema: An accumulation of an excessive amount of watery fluid in the lungs, may be caused by acute exposure to dangerous concentrations of irritant gasses. [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]

Pupil: The aperture in the iris through which light passes. [NIH]

Purifying: Respiratory equipment whose function is to remove contaminants from otherwise wholesome air. [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]

Putrescine: A toxic diamine formed by putrefaction from the decarboxylation of arginine and ornithine. [NIH]

Pyogenic: Producing pus; pyopoietic (= liquid inflammation product made up of cells and a thin fluid called liquor puris). [EU]

Pyridoxal: 3-Hydroxy-5-(hydroxymethyl)-2-methyl-4- pyridinecarboxaldehyde. [NIH]

Quercetin: Aglucon of quercetrin, rutin, and other glycosides. It is widely distributed in the plant kingdom, especially in rinds and barks, clover blossoms, and ragweed pollen. [NIH]

Quiescent: Marked by a state of inactivity or repose. [EU]

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 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]

Radicular: Having the character of or relating to a radicle or root. [NIH]

Radicular Cyst: Slow-growing fluid-filled epithelial sac at the apex of a tooth with a nonvital pulp or defective root canal filling. [NIH]

Radioactive: Giving off radiation. [NIH]

Radioimmunoassay: Classic quantitative assay for detection of antigen-antibody reactions using a radioactively labeled substance (radioligand) either directly or indirectly to measure the binding of the unlabeled substance to a specific antibody or other receptor system. Non-immunogenic substances (e.g., haptens) can be measured if coupled to larger carrier proteins (e.g., bovine gamma-globulin or human serum albumin) capable of inducing antibody formation. [NIH]

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]

Radiolabeled: Any compound that has been joined with a radioactive substance. [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]

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]

Reality Testing: The individual's objective evaluation of the external world and the ability to differentiate adequately between it and the internal world; considered to be a primary ego function. [NIH]

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]

Recombinant Proteins: Proteins prepared by recombinant DNA technology. [NIH]

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]

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]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [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]

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]

Relapse: The return of signs and symptoms of cancer after a period of improvement. [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]

Replicon: In order to be replicated, DNA molecules must contain an origin of duplication and in bacteria and viruses there is usually only one per genome. Such molecules are called replicons. [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]

Residual disease: Cancer cells that remain after attempts have been made to remove the cancer. [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]

Retina: The ten-layered nervous tissue membrane of the eye. It is continuous with the optic

nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [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]

Retinitis: Inflammation of the retina. It is rarely limited to the retina, but is commonly associated with diseases of the choroid (chorioretinitis) and of the optic nerve (neuroretinitis). The disease may be confined to one eye, but since it is generally dependent on a constitutional factor, it is almost always bilateral. It may be acute in course, but as a rule it lasts many weeks or even several months. [NIH]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

Retinoblastoma Protein: Product of the retinoblastoma tumor suppressor gene. It is a nuclear phosphoprotein hypothesized to normally act as an inhibitor of cell proliferation. Rb protein is absent in retinoblastoma cell lines. It also has been shown to form complexes with the adenovirus E1A protein, the SV40 T antigen, and the human papilloma virus E7 protein. [NIH]

Retrograde: 1. Moving backward or against the usual direction of flow. 2. Degenerating, deteriorating, or catabolic. [EU]

Retrospective: Looking back at events that have already taken place. [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]

Rhadinovirus: A genus of the family Herpesviridae, subfamily Gammaherpesvirinae, infecting New World primates. Herpesvirus 2, Ateline is the type species. [NIH]

Rheumatism: A group of disorders marked by inflammation or pain in the connective tissue structures of the body. These structures include bone, cartilage, and fat. [NIH]

Rheumatoid: Resembling rheumatism. [EU]

Rheumatoid arthritis: A form of arthritis, the cause of which is unknown, although infection, hypersensitivity, hormone imbalance and psychologic stress have been suggested as possible causes. [NIH]

Rhinitis: Inflammation of the mucous membrane of the nose. [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]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Rod: A reception for vision, located in the retina. [NIH]

Rubella: An acute, usually benign, infectious disease caused by a togavirus and most often

affecting children and nonimmune young adults, in which the virus enters the respiratory tract via droplet nuclei and spreads to the lymphatic system. It is characterized by a slight cold, sore throat, and fever, followed by enlargement of the postauricular, suboccipital, and cervical lymph nodes, and the appearances of a fine pink rash that begins on the head and spreads to become generalized. Called also German measles, roetln, röteln, and three-day measles, and rubeola in French and Spanish. [EU]

Rutin: 3-((6-O-(6-Deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl)oxy)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-1-benzopyran-4-one. Found in many plants, including buckwheat, tobacco, forsythia, hydrangea, pansies, etc. It has been used therapeutically to decrease capillary fragility. [NIH]

Saline: A solution of salt and water. [NIH]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Sarcoidosis: An idiopathic systemic inflammatory granulomatous disorder comprised of epithelioid and multinucleated giant cells with little necrosis. It usually invades the lungs with fibrosis and may also involve lymph nodes, skin, liver, spleen, eyes, phalangeal bones, and parotid glands. [NIH]

Sarcoma: A connective tissue neoplasm formed by proliferation of mesodermal cells; it is usually highly malignant. [NIH]

Satellite: Applied to a vein which closely accompanies an artery for some distance; in cytogenetics, a chromosomal agent separated by a secondary constriction from the main body of the chromosome. [NIH]

Scabies: A contagious cutaneous inflammation caused by the bite of the mite Sarcoptes scabiei. It is characterized by pruritic papular eruptions and burrows and affects primarily the axillae, elbows, wrists, and genitalia, although it can spread to cover the entire body. [NIH]

Schizoid: Having qualities resembling those found in greater degree in schizophrenics; a person of schizoid personality. [NIH]

Schizophrenia: A mental disorder characterized by a special type of disintegration of the personality. [NIH]

Schizotypal Personality Disorder: A personality disorder in which there are oddities of thought (magical thinking, paranoid ideation, suspiciousness), perception (illusions, depersonalization), speech (digressive, vague, overelaborate), and behavior (inappropriate affect in social interactions, frequently social isolation) that are not severe enough to characterize schizophrenia. [NIH]

Sclera: The tough white outer coat of the eyeball, covering approximately the posterior five-sixths of its surface, and continuous anteriorly with the cornea and posteriorly with the external sheath of the optic nerve. [EU]

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]

Sebaceous: Gland that secretes sebum. [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]

Sedative: 1. Allaying activity and excitement. 2. An agent that allays excitement. [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]

Self Care: Performance of activities or tasks traditionally performed by professional health care providers. The concept includes care of oneself or one's family and friends. [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]

Septic: Produced by or due to decomposition by microorganisms; putrefactive. [EU]

Septicaemia: A term originally used to denote a putrefactive process in the body, but now usually referring to infection with pyogenic micro-organisms; a genus of Diptera; the severe type of infection in which the blood stream is invaded by large numbers of the causal. [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]

Sequester: A portion of dead bone which has become detached from the healthy bone tissue, as occurs in necrosis. [NIH]

Seroconversion: The change of a serologic test from negative to positive, indicating the development of antibodies in response to infection or immunization. [EU]

Serologic: Analysis of a person's serum, especially specific immune or lytic serums. [NIH]

Serology: The study of serum, especially of antigen-antibody reactions in vitro. [NIH]

Serotonin: A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

Serotypes: A cause of haemorrhagic septicaemia (in cattle, sheep and pigs), fowl cholera of birds, pasteurellosis of rabbits, and gangrenous mastitis of ewes. It is also commonly found in atrophic rhinitis of pigs. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Serum Albumin: A major plasma protein that serves in maintaining the plasma colloidal osmotic pressure and transporting large organic anions. [NIH]

Sexual Partners: Married or single individuals who share sexual relations. [NIH]

Sexually Transmitted Diseases: Diseases due to or propagated by sexual contact. [NIH]

Shedding: Release of infectious particles (e. g., bacteria, viruses) into the environment, for example by sneezing, by fecal excretion, or from an open lesion. [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]

Shunt: A surgically created diversion of fluid (e.g., blood or cerebrospinal fluid) from one area of the body to another area of the body. [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]

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]

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]

Sneezing: Sudden, forceful, involuntary expulsion of air from the nose and mouth caused by irritation to the mucous membranes of the upper respiratory tract. [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]

Solvent: 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving; the component of a solution that is present in greater amount. [EU]

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]

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]

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]

Spermidine: A polyamine formed from putrescine. It is found in almost all tissues in association with nucleic acids. It is found as a cation at all pH values, and is thought to help stabilize some membranes and nucleic acid structures. It is a precursor of spermine. [NIH]

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]

Spinal Nerves: The 31 paired peripheral nerves formed by the union of the dorsal and ventral spinal roots from each spinal cord segment. The spinal nerve plexuses and the spinal roots are also included. [NIH]

Spinous: Like a spine or thorn in shape; having spines. [NIH]

Spiral Ganglion: The sensory ganglion of the cochlear nerve. The cells of the spiral ganglion send fibers peripherally to the cochlear hair cells and centrally to the cochlear nuclei of the brain stem. [NIH]

Spiral Lamina: The bony plate which extends outwards from the modiolus. It is part of the structure which divides trhe cochlea into sections. [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]

Splenomegaly: Enlargement of the spleen. [NIH]

Spondylitis: Inflammation of the vertebrae. [EU]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Squamous: Scaly, or platelike. [EU]

Staphylococcus: A genus of gram-positive, facultatively anaerobic, coccoid bacteria. Its organisms occur singly, in pairs, and in tetrads and characteristically divide in more than one plane to form irregular clusters. Natural populations of Staphylococcus are membranes of warm-blooded animals. Some species are opportunistic pathogens of humans and animals. [NIH]

Staphylococcus aureus: Potentially pathogenic bacteria found in nasal membranes, skin, hair follicles, and perineum of warm-blooded animals. They may cause a wide range of infections and intoxications. [NIH]

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]

Sterilization: The destroying of all forms of life, especially microorganisms, by heat, chemical, or other means. [NIH]

Steroids: Drugs used to relieve swelling and inflammation. [NIH]

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]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Streptococci: A genus of spherical Gram-positive bacteria occurring in chains or pairs. They are widely distributed in nature, being important pathogens but often found as normal commensals in the mouth, skin, and intestine of humans and other animals. [NIH]

Streptococcus: A genus of gram-positive, coccoid bacteria whose organisms occur in pairs or chains. No endospores are produced. Many species exist as commensals or parasites on man or animals with some being highly pathogenic. A few species are saprophytes and occur in the natural environment. [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]

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]

Subcutaneous: Beneath the skin. [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]

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]

Sulfur Compounds: Inorganic or organic compounds that contain sulfur as an integral part of the molecule. [NIH]

Suppositories: A small cone-shaped medicament having cocoa butter or gelatin at its basis and usually intended for the treatment of local conditions in the rectum. [NIH]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Surface Plasmon Resonance: A biosensing technique in which biomolecules capable of binding to specific analytes or ligands are first immobilized on one side of a metallic film. Light is then focused on the opposite side of the film to excite the surface plasmons, that is, the oscillations of free electrons propagating along the film's surface. The refractive index of light reflecting off this surface is measured. When the immobilized biomolecules are bound by their ligands, an alteration in surface plasmons on the opposite side of the film is created which is directly proportional to the change in bound, or adsorbed, mass. Binding is measured by changes in the refractive index. The technique is used to study biomolecular interactions, such as antigen-antibody binding. [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]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

Symptomatic treatment: Therapy that eases symptoms without addressing the cause of disease. [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]

Syphilis: A contagious venereal disease caused by the spirochete Treponema pallidum. [NIH]

Systemic: Affecting the entire body. [NIH]

Systemic disease: Disease that affects the whole body. [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]

Temporal Lobe: Lower lateral part of the cerebral hemisphere. [NIH]

Terminator: A DNA sequence sited at the end of a transcriptional unit that signals the end of transcription. [NIH]

Testosterone: A hormone that promotes the development and maintenance of male sex characteristics. [NIH]

Tetanus: A disease caused by tetanospasmin, a powerful protein toxin produced by Clostridium tetani. Tetanus usually occurs after an acute injury, such as a puncture wound or laceration. Generalized tetanus, the most common form, is characterized by tetanic muscular contractions and hyperreflexia. Localized tetanus presents itself as a mild condition with manifestations restricted to muscles near the wound. It may progress to the generalized form. [NIH]

Thalassemia: A group of hereditary hemolytic anemias in which there is decreased

synthesis of one or more hemoglobin polypeptide chains. There are several genetic types with clinical pictures ranging from barely detectable hematologic abnormality to severe and fatal anemia. [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]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombomodulin: A cell surface glycoprotein of endothelial cells that binds thrombin and serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [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]

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]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [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]

Titre: The quantity of a substance required to produce a reaction with a given volume of another substance, or the amount of one substance required to correspond with a given amount of another substance. [EU]

Tolerance: 1. The ability to endure unusually large doses of a drug or toxin. 2. Acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

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]

Tooth Loss: The failure to retain teeth as a result of disease or injury. [NIH]

Tooth Preparation: Procedures carried out with regard to the teeth or tooth structures preparatory to specified dental therapeutic and surgical measures. [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]

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]

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]

Transferases: Transferases are enzymes transferring a group, for example, the methyl group or a glycosyl group, from one compound (generally regarded as donor) to another compound (generally regarded as acceptor). The classification is based on the scheme "donor:acceptor group transferase". (Enzyme Nomenclature, 1992) EC 2. [NIH]

Transfusion: The infusion of components of blood or whole blood into the bloodstream. The blood may be donated from another person, or it may have been taken from the person earlier and stored until needed. [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]

Translocation: The movement of material in solution inside the body of the plant. [NIH]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [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]

Trigeminal: Cranial nerve V. It is sensory for the eyeball, the conjunctiva, the eyebrow, the skin of face and scalp, the teeth, the mucous membranes in the mouth and nose, and is motor to the muscles of mastication. [NIH]

Trismus: Spasmodic contraction of the masseter muscle resulting in forceful jaw closure. This may be seen with a variety of diseases, including tetanus, as a complication of radiation therapy, trauma, or in association with neoplastic conditions. [NIH]

Tropism: Directed movements and orientations found in plants, such as the turning of the

sunflower to face the sun. [NIH]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [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 infiltrating lymphocytes: White blood cells that have left the bloodstream and migrated into a tumor. [NIH]

Tumor Necrosis Factor: Serum glycoprotein produced by activated macrophages and other mammalian mononuclear leukocytes which has necrotizing activity against tumor cell lines and increases ability to reject tumor transplants. It mimics the action of endotoxin but differs from it. It has a molecular weight of less than 70,000 kDa. [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]

Ulcer: A localized necrotic lesion of the skin or a mucous surface. [NIH]

Ulceration: 1. The formation or development of an ulcer. 2. An ulcer. [EU]

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]

Uracil: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Urea: A compound (CO(NH2)2), formed in the liver from ammonia produced by the deamination of amino acids. It is the principal end product of protein catabolism and constitutes about one half of the total urinary solids. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Urethritis: Inflammation of the urethra. [EU]

Uric: A kidney stone that may result from a diet high in animal protein. When the body breaks down this protein, uric acid levels rise and can form stones. [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]

Uterine Contraction: Contraction of the uterine muscle. [NIH]

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]

Vacuoles: Any spaces or cavities within a cell. They may function in digestion, storage, secretion, or excretion. [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]

Vaginitis: Inflammation of the vagina characterized by pain and a purulent discharge. [NIH]

Varicella: Chicken pox. [EU]

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]

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]

Verruca: A circumscribed, cutaneous excrescence having a papilliferous surface; a small, circumscribed, epidermal tumor. [NIH]

Vertebrae: A bony unit of the segmented spinal column. [NIH]

Vertigo: An illusion of movement; a sensation as if the external world were revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

Vesicular: 1. Composed of or relating to small, saclike bodies. 2. Pertaining to or made up of vesicles on the skin. [EU]

Vesicular Exanthema of Swine: A calicivirus infection of swine characterized by hydropic degeneration of the oral and cutaneous epithelia. [NIH]

Vesicular Exanthema of Swine Virus: The type species of the genus Calicivirus, an RNA virus infecting pigs. The resulting infection is an acute febrile disease which is clinically indistinguishable from foot and mouth disease. Transmission is by contaminated food. [NIH]

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]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viral Hepatitis: Hepatitis caused by a virus. Five different viruses (A, B, C, D, and E) most commonly cause this form of hepatitis. Other rare viruses may also cause hepatitis. [NIH]

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 Vaccines: Suspensions of attenuated or killed viruses administered for the prevention or treatment of infectious viral disease. [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]

Viremia: The presence of viruses in the blood. [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]

Virus Diseases: A general term for diseases produced by viruses. [NIH]

Virus Latency: The ability of a pathogenic virus to lie dormant within a cell (latent infection). In eukaryotes, subsequent activation and viral replication is thought to be caused by extracellular stimulation of cellular transcription factors. Latency in bacteriophage is maintained by the expression of virally encoded repressors. [NIH]

Virus Replication: The process of intracellular viral multiplication, consisting of the synthesis of proteins, nucleic acids, and sometimes lipids, and their assembly into a new infectious particle. [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]

Vulgaris: An affection of the skin, especially of the face, the back and the chest, due to chronic inflammation of the sebaceous glands and the hair follicles. [NIH]

Warts: Benign epidermal proliferations or tumors; some are viral in origin. [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]

Withdrawal: 1. A pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) A substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

Xanthine: An urinary calculus. [NIH]

Xanthine Oxidase: An iron-molybdenum flavoprotein containing FAD that oxidizes hypoxanthine, some other purines and pterins, and aldehydes. Deficiency of the enzyme, an autosomal recessive trait, causes xanthinuria. EC 1.1.3.22. [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]

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]

Zidovudine: A dideoxynucleoside compound in which the 3'-hydroxy group on the sugar moiety has been replaced by an azido group. This modification prevents the formation of phosphodiester linkages which are needed for the completion of nucleic acid chains. The compound is a potent inhibitor of HIV replication, acting as a chain-terminator of viral DNA during reverse transcription. It improves immunologic function, partially reverses the HIV-induced neurological dysfunction, and improves certain other clinical abnormalities associated with AIDS. Its principal toxic effect is dose-dependent suppression of bone marrow, resulting in anemia and leukopenia. [NIH]

Zinc Fingers: Motifs in DNA- and RNA-binding proteins whose amino acids are folded into a single structural unit around a zinc atom. In the classic zinc finger, one zinc atom is bound to two cysteines and two histidines. In between the cysteines and histidines are 12 residues which form a DNA binding fingertip. By variations in the composition of the sequences in the fingertip and the number and spacing of tandem repeats of the motif, zinc fingers can form a large number of different sequence specific binding sites. [NIH]

Zoster: A virus infection of the Gasserian ganglion and its nerve branches, characterized by discrete areas of vesiculation of the epithelium of the forehead, the nose, the eyelids, and the cornea together with subepithelial infiltration. [NIH]

Zymogen: Inactive form of an enzyme which can then be converted to the active form, usually by excision of a polypeptide, e. g. trypsinogen is the zymogen of trypsin. [NIH]

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