B-Cell Lymphoma

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

James N. Parker, M.D.
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 B-cell lymphoma 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 B-cell lymphoma, 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 B-cell lymphoma, 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 B-cell lymphoma. 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 B-cell lymphoma, 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 B-cell lymphoma.

The Editors

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

CHAPTER 1. STUDIES ON B-CELL LYMPHOMA

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on B-cell lymphoma.

Federally Funded Research on B-Cell Lymphoma

The U.S. Government supports a variety of research studies relating to B-cell lymphoma. 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 B-cell lymphoma.

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 B-cell lymphoma. The following is typical of the type of information found when searching the CRISP database for B-cell lymphoma:

- **Project Title: BIOMARKERS FOR LYMPHOMA IN A NEW TRANSGENIC MOUSE MODEL**

  Principal Investigator & Institution: Denis, Gerald V.; Assistant Professor; Medicine; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

  Timing: Fiscal Year 2004; Project Start 15-MAR-2004; Project End 28-FEB-2006

[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).

Summary: (provided by applicant): Biological and statistical arguments are presented for a screen for the molecular signature of a B cell lymphoma model. Transgenic mice that constitutively express in their B cell lineage a newly characterized oncogene called BRD2, which we have functionally linked to human hematologic malignancy, sporadically develop lymphoma at an annual rate of 10 percent. Inoculation of these mice with an amphotropic retrovirus that expresses oncogenic ras accelerates the time to B cell lymphoma to four weeks. This model system has the potential to identify new, early, pre-malignant markers of lymphoma. Human models of cancer do not share these advantages, because individual variation often makes interpretation difficult. Furthermore, expensive family genetic studies are often the only way to acquire systematic data, and development of cancer in humans requires many years. We performed a genome-wide microarray experiment to detect altered patterns of gene expression in this B cell lymphoma and came to the preliminary conclusion that it possesses a molecular signature that closely resembles human large-B-cell lymphoma, in agreement with preliminary histology, as expected. The signature does not resemble other types of B cell malignancy or in vitro transformed B cell signatures, suggesting that the data obtained will indeed be comparable to existing databases of lymphoma signatures and could have clinical relevance in the search for new biomarkers for human cancers. The Application justifies a request for funds to perform the replicates necessary to draw reliable conclusions from the datasets and to obtain data on tumor progression. This well-controlled approach will permit the early detection of statistically significant, pre-malignant changes in the molecular signature of B cells, which will provide new potential markers for human lymphomagenesis and risk assessment.

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

- **Project Title: CORE--HEMATOPATHOLOGY**

  Principal Investigator & Institution: Aster, Jon C.; Associate Professor; Dana-Farber Cancer Institute 44 Binney St Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 22-JUL-2002; Project End 30-JUN-2003

  Summary: (Provided by Applicant) To support the specific aims of the Projects in this application, the Hematopathology Core will: 1. Provide the infrastructure for the procurement, evaluation, and banking of human germinal center **B-cell lymphoma** specimens. 2. Build a database for banked tumor specimens that includes pathologic, immunophenotypic, molecular genetic, and cytogenetic data. 3. Develop immunohistochemical methods for staining the protein products of genes identified by expression profiling of germinal center B-cell lymphomas. 4. Construct tissue arrays to study the protein products of prognostic markers and/or over-expressed genes in germinal center B-cell lymphomas. 5. Provide histology and immunohistology services for the evaluation of human germinal center B-cell lymphomas and their murine models. 6. Perform cytogenetic analyses to detect chromosomal translocations involving BCL2 and BCL6 in human B-cell lymphomas.

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

- **Project Title: DESIGN AND EFFICACY OF ANTI LYMPHOMA DNA VACCINE**

  Principal Investigator & Institution: Ghosh, Swapan K.; Life Sciences; Indiana State University 217 N 6Th St Terre Haute, in 47809

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

  Summary: The overall objective is to understand mechanisms of action of scFv plasmid DNA vaccines that encode the idiotype (Id) ,i.e., the variable regions of heavy (VH) and

light chains (VL) of the clonotypic immunoglobulin (Ig) of a murine **B-cell lymphoma** 2C3, and evaluate efficacy in terms of protection against the 2C3 tumor and the nature of immune responses evoked. Vaccination with Ig protein or scFv plasmid DNA usually induces humoral responses with limited prophylactic efficacy. With the 2C3 tumor, repeated immunizations using irradiated cells evoke both CTLs (cytotoxic T lymphocytes) and protective immunity. In contrast, similar immunization with purified secreted Ig is less effective, and results in indolent tumors. Furthermore, 2C3-Id- specific CTLs also occur at the early stages, but decline at late stages of tumor growth. The scFv plasmids are expected to overcome problems associated with protein immunogens by consistently producing only Id determinants of an Ig and thereby provoking memory immune cells. The question is whether scFv plasmids, to be effective, express cytosolic, secreted or membrane forms of the idiotype. To facilitate this study, we developed: (1) a prototype scFv construct encoding cytosolic VH- VL of 2C3 Ig based on the nucleotide sequences of both heavy and light chains; (2) a permanent transfectant P815A4, that expresses both intact scFv as well as CTL-recognized idiopeptides; (3) PCR, ELISA and cellular methodologies; (4) Id-specific CTL lines; and (5) anti-Id antibody reagents. With these tools, we will address the following: Design and construct a series of scFv producing plasmids that express distinct variants of the 2C3 idiotype. These variants will differ in the structure of the scFv itself, as well as in the subcellular localization of the scFv molecule (cytoplasmic, membrane-bound, or secreted); (2) Characterize the expression and mechanism of presentation of the above scFv variants after in vitro transfection into two different antigen-presenting cells: P815, and A20; and (3) Determine the in vivo effects of these scFv variants on the nature, magnitude and specificity of humoral and cellular (CTL) immune responses and on host survival rates against tumor challenge. We expect that these studies will provide understanding of molecular features of immunoglobulin idiotype that can be successfully exploited to design CTL- inducing antitumor responses.

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

- **Project Title: EBV VECTORS FOR TARGETED GENE THERAPY OF B-LYMPHOMAS**

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

  Timing: Fiscal Year 2002; Project Start 10-SEP-2000; Project End 31-AUG-2004

  Summary: (Applicant's Abstract): The goal of this application is to effectively and selectively eliminate B-cell derived lymphoma and leukemia cells in cancer patients using a naturally targeted viral vector system. To achieve this goal, the applicant proposes to develop a novel combinatorial gene therapy approach as applied to Burkett B lymphoma based on i) a minimal "gene-less" B lymphotropic Epstein-Barr virus (miniEBV) vector, and ii) a genetically enhanced "hyper-suicide" HSV1 thymidine kinase (super-TK). Specifically, the following studies will be undertaken: Aim 1) To test the efficacy of B lymphotropic miniEBV vectors to deliver and express a suicide gene into human B-cell lymphomas following oncotropic and oncolytic strategies. This approach is based on the transfer of the viral thymidine kinase (TK) gene into B-cell derived lymphomas rendering them sensitive to the prodrug ganciclovir (GCV). For this endeavor miniEBV/sTK will be used to infect B-lymphoma cells in vitro and the transiently infected cells implanted in an animal model to analyze prodrug mediated eradication of the lymphoma using ex vivo protocol. Aim 2) Development of an in vitro cultured packaging cell system to produce helper-free infectious miniEBV. This will involve cloning the genome of EBV in a BAC based vector to delete the packaging

sequence by homologous recombination. In addition, EBV negative cell lines will be evaluated for their permissivity to miniEBV replication and packaging into infectious virions. Aim 3) Use the results obtained in Aims 1-2 to test the miniEBV system for its efficiency and safety in a SCID-Human lymphoma/leukemia animal model using an in vivo protocol. Pre-established human B-lymphoma in vivo by intravenous (i.v.) injection with this system will be also evaluated in order to eliminate the disseminated B-lymphoma from various organs of the animal.

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

- **Project Title: IMMUNOGENETICS OF NON-HODGKIN LYMPHOMA SURVIVAL**

  Principal Investigator & Institution: Cerhan, James R.; Associate Professor; Mayo Clinic Coll of Medicine, Rochester 200 1St St Sw Rochester, Mn 55905

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

  Summary: (provided by applicant): Non-Hodgkin Lymphoma (NHL) incidence and mortality have been increasing over the past 50 years, and these trends are largely unexplained. The five-year survival rates are 50% overall, and appear to have changed little over the last several decades. For NHL, a compelling hypothesis is that survival may be related to the host immune status, which is in part influenced by functional polymorphisms in genes encoding cytokines and chemokines central to immune function and regulation. The role for host immunogenetic susceptibility in overall survival from NHL is largely unexplored. We propose to systematically test the hypothesis that genes with functional, common variant polymorphisms involved in immune function and regulation are associated with overall survival from NHL. Our specific aims are: 1) to evaluate the association of polymorphisms in selected immune-related genes from four key pathways on NHL survival that include genes encoding inflammatory and regulatory cytokines (IL-1A IL-1B IL-1RN TNFalpha), Th1/Th2 cytokines (LTA, INFgamma IL-4, IL-4RA IL-6 iL-JO, IL-13), innate immunity (MPO, ICAM-1) and chemokines (IL-8, SDF-1, CCR2, CCR5); 2) to evaluate whether any effects are independent of other NHIL prognostic factors (e.g., age, stage, ECOG performance status, extranodal site involvement, and serum LDH), and treatment modality; and 3) to evaluate whether any effects are specific for diffuse large **B-cell lymphoma** or the combination of follicular and small lymphocytic lymphoma. To achieve these aims, we will develop a prognostic cohort using 364 HIV-negative NHL patients who participated in a population-based case-control study in Iowa. The patients were aged 20-74 years when first diagnosed from 1998-2000. We will abstract treatment and other clinical/laboratory prognostic data from the medical record. We will follow all of these patients by both passive and active means through mid-2006 (a minimum of 6.5 years) in order to identify all deaths (including cause of death) and disease recurrences. Genotyping will be conducted in conjunction with the investigators at the National Cancer Institute. The association of genotype frequencies with NEIL survival will be evaluated using standard survival analysis approaches, and we have sufficient statistical power to detect clinically meaningful hazard ratios. In summary, we will evaluate innovative translational hypotheses regarding the immunogenetic determinants of NEIL survival in order to better understand disease pathogenesis, treatment response, and disease prognosis among patients from the community.

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

- **Project Title: MOLECULAR CLASSIFICATION OF B-CELL LYMPHOMA**

  Principal Investigator & Institution: Chan, Wing C.; Professor of Pathology; Pathology and Microbiology; University of Nebraska Medical Center Omaha, Ne 681987835

Timing: Fiscal Year 2002; Project Start 30-SEP-1999; Project End 31-MAR-2004

Summary: Tumors derived from the same cell type and having similar morphology may nevertheless have a distinctly different clinical behavior and response to therapy. Differences in the genetic lesions in these tumors, as reflected by their gene expression profiles, will provide insight into the mechanisms underlying the divergent clinical spectrum that is observed. Comparative genomic hybridization (CGH) and spectral karyotyping (SKY) are highly complementary novel techniques that examine the entire genome for genetic abnormalities and can supplement and extend conventional cytogenetic studies. In addition, the recently - developed high-density cDNA microarray technology is a very promising method for displaying the pattern of gene expression in tumor tissues. These powerful technologies with their associated informatic systems are now available for translational research. In order to evaluate the information generated by these technologies, an adequate number of well-characterized tumors with detailed clinical data must be available. We propose a multi-institutional, comprehensive molecular analysis of a large series of B-cell non-Hodgkin's lymphoma (NHL). The molecular data obtained will be correlated with the clinical and pathologic information in the extensive databases kept at our institutions to identify clinically and biologically distinct subsets of B- NHL. When unique molecular profiles of clinical and biological significance are identified, we will then define which components within each profile are essential determinants of the clinical features and outcome. Specific confirmatory assays for the expression of key genes, and the cytogenetic abnormalities involving these genes, will be performed. Our longer term goal is to use this information to design a simpler and less expensive microarray for diagnostic use. This "diagnostic chip" could provide rapid molecular characterization of every B-NHL at presentation for optimal treatment decisions and prognostication. We also anticipate the identification of new and significant genetic alterations that will contribute to our understanding of the key events in neoplastic transformation and tumor progression. The insights gained from this project may also identify novel targets for preventive and therapeutic interventions.

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

- **Project Title: MOLECULAR GENETIC BASIS OF MOUSE B CELL LYMPHOMA**

  Principal Investigator & Institution: Justice, Monica; Assistant Professor; Molecular and Human Genetics; Baylor College of Medicine 1 Baylor Plaza Houston, Tx 77030

  Timing: Fiscal Year 2002; Project Start 01-JAN-1995; Project End 28-FEB-2006

  Summary: (Adapted from the investigator's abstract) The primary goal of the proposed research is to understand the molecular genetic basis for the development of B-cell leukemias and lymphomas. Murine leukemia retroviruses (MuLVs) cause leukemia and lymphoma in susceptible strains of mice by insertional mutation of cellular proto-oncogenes or tumor suppressor genes. Some AKXD recombinant inbred strains of mice have a high incidence of B-cell lymphomas caused by MuLV insertion, making them valuable resources for identifying new proto-oncogenes using the retrovirus as a molecular tag. Viral insertion site amplification (VISA) can quickly identify proviral flanking sequences in the AKXD somatic tumors by obtaining a viral sequence tag (VST). An analysis of four AKXD strains 35 genes well as many unknown VSTs altered by retroviral insertion. We will extend this study to obtain VSTs for the remaining five AKXD strains that develop primarily B-cell lymphomas. Insertions at one locus called lymphoid viral insertion site 1 (Lvisl) account for 23 percent of the proviral insertion mutations in the AKXID B-lineage tumors, suggesting that genes at Lvis1 play a primary role in the development of hematopoietic disease. Two genes proximal to Lvisl are misexpressed: the hematopoietic homeobox gene, Hex, and a kinesin-related spindle

protein, Eg5. Either of these genes could play a role in leukemogenesis, and we will examine this hypothesis by 1) overexpressing the genes in transgenic mice, and 2) transducing the genes into hematopoietic cells using retroviral gene transfer. These genes may act singly or together to potentiate leukemogenesis. Further, we propose to examine the role of Hex in hematopoeisis by eliminating function by a tissue-specific targeted gene disruption. The VSTs represent the majority of genes that contribute to disease onset and progression within the hematopoietic lineages of the AKXD strains. To make the data publicly accessible, we will develop a database describing VSTs and tumor phenotypes. Through collaborations, we will examine the potential involvement of some genes in human leukemias and lymphomas. These data can be integrated with both genomic and gene expression profiles from human cancers to uncover the pathways involved in the development of leukemia and lymphoma in both mouse and human.

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

- **Project Title: MOLECULAR TARGETS OF GERMINAL CENTER B CELL LYMPHOMAS**

  Principal Investigator & Institution: Shipp, Margaret A.; Associate Professor; Dana-Farber Cancer Institute 44 Binney St Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 02-AUG-2001; Project End 30-JUN-2006

  Summary: (provided by applicant) We have assembled a complementary team of basic B-cell scientists, lymphoma biologists, immunologists, hematopathologists, genomics and bioinformatics specialists, clinical investigators and biostatisticians to delineate the critical events in the pathogenesis and pathophysiology of the most common adult lymphoid malignancies and germinal center (GC) B-cell lymphomas, follicular lymphoma (FL) and diffuse large B-cell lymphomas (DLBCL). Although the treatment options for these diseases have expanded in recent years, FL is still incurable and DLBCL is cured in less than 50 percent of patients. It is our belief that the proposed studies will identify rational targets for more effective and specific treatment of these diseases in the funding period. This new P01 application is based upon the following hypothesis: 1) errors in immunoglobulin gene rearrangement predispose to the development of GC B-cell lymphomas; 2) dysregulated expression of genes controlling apoptosis (bcl-2) or normal GC development (bcl-6) also contribute to the pathogenesis of these diseases; 3) biologically-discrete subsets of GC B-cell lymphomas with unique natural histories remain to be defined; and 4) host immune responses influence outcome in GC B-cell lymphomas. Drs. F. Alt and K. Rajewsky will evaluate molecular mechanisms of translocations in GC B-cell lymphomas (Project 1). Dr. S. Korsmeyer will assess apoptosis as a molecular target in the genesis and maintenance of **B-cell lymphoma** (Project 2) and Dr. Dalla-Favera will evaluate the role of bcl-6 in GC formation and lymphomagenesis (Project 3). Dr. M. Shipp will delineate molecular signatures of outcome in GC B-cell lymphomas (Project 4) and Drs. L. Nadler, A. Freedman, and J. Schultze will analyze T-cell immunity in GC B-cell lymphomas. Cores which support the proposed studies include: DNA Microarray/Bioinformatics (T. Golub); Hematopathology (J. Aster); Clinical Trials (J. Gribben); Biostatistics (D. Neuberg); and Administration (M. Shipp).

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

- **Project Title: NOVEL HUMAN ANTI-CD19 ANTIBODIES FOR LYMPHOMA THERAPY**

  Principal Investigator & Institution: Ma, Dangshe; Progenics Pharmaceuticals, Inc. 777 Old Saw Mill River Rd Tarrytown, Ny 10591

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

  Summary: (provided by applicant): Non-Hodgkin's lymphoma (NHL) is the fifth most common type of cancer in the United States. Approximately 300,000 people are currently living with NHL in the U.S. and an estimated 53,900 new cases will occur in 2002. The 5% annual increase in incidence is the fastest for any human cancer. The therapeutic utility of unmodified monoclonal antibodies (mAbs) and radiolabeled mAbs against the B-cell antigen CD20 is demonstrated by the recent FDA approvals of these agents for the treatment of relapse and refractory B-cell NHL. Although response rates are high, complete cures are rare and the median duration of response is only 1-2 years. Consequently, there is an urgent need for new therapies to prevent or combat disease relapse. CD19 is a 95-kD membrane glycoprotein found on nearly all of B-cell lymphomas, chronic lymphocytic leukemias (CLL), and acute lymphoblastic leukemias (ALL). CD19 is not expressed on mature plasma cells, hematopoietic stem cells, or normal tissues outside the B-lineage. The CDI9 protein is not shed into the circulation and is maintained on tumors despite loss of CD20 expression following anti-CD20 therapy. Taken together, the expression profile of CD19 makes it a highly attractive target for immunotherapy of B-cell neoplasms. Our recent studies in mouse models of human lymphoma demonstrated that CD19 offers clear advantages over CD20 as a target for radioimmunotherapies that employ both traditional and highly innovative radionuclides. The profound anti-tumor effects observed in these studies provide compelling proof-of-principle for CD19-directed therapies. However, our studies employed murine CD19 mAbs that have foreseeable limitations for use in humans. A fully human mAb that recognizes CD19 with high affinity and specificity would be an ideal candidate for therapy. We propose development of novel, fully-human anti-CD19 mAbs using mice that are transgenic for the human immunoglobulin gene locus. The mAbs will be evaluated for specificity and anti-tumor properties in vitro in both unlabeled form and when labeled with novel alpha- and beta-emitting therapeutic isotopes. The most promising immunotherapeutic agents will be critically evaluated for their therapeutic potential using the best available animal models of human lymphoma. Success in the project would provide strong impetus to rapidly advance the most promising agents into development for human clinical testing.

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

- **Project Title: NOVEL NF KAPPA B ACTIVATING GENE INVOLVED IN CANCER**

  Principal Investigator & Institution: Nunez, Gabriel; Professor; Pathology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2002; Project Start 01-AUG-2000; Project End 31-JUL-2005

  Summary: (Adapted from the investigator's abstract) Deregulation of the apoptotic pathway plays a critical role in the development of cancer. The identification and characterization of apoptotic genes involved in the deregulation of apoptosis is critical for the development of novel therapeutic approaches. He has identified CIPER, a gene that regulates both apoptosis and NF-kB activation. CIPER (also called bc110) has been found to be located at the breakpoint regions of t(1;14) (p22;q32), a recurrent chromosomal location associated with mucosa-associated lymphoid tissue (MALT) **B-cell lymphoma.** Importantly, the CIPER/bc110 product is frequently mutated in

lymphomas of various histological types. Sequence analysis revealed that CIPER encodes a protein containing a caspase-recruitment domain (CARD) in its amino terminus and a C-terminal region rich in serine and threonine residues. Muational analysis revealed that two regions of CIPER, the CARD and a region just outside the CARD, are critical for NF-kB-inducing activity. N-terminal region of CIPER containing the CARD was sufficient and necessary for NF-kB-inducing activity. Point mutations in highly conserved residues in the CARD of CIPER disrupted the ability of CIPER to activate NF-kB and form homodimers, indicating that the CARD is essential for NF-kB activation and dimerization. He has evidence that CIPER interacts with IKKy(also called Nemo), the regulatory subunit of the IkB kinase (IKK) complex. Their hypothesis is that CIPER/bc110 promotes tumor development via a NF-kB activation pathway that is deregulated in cancer. The focus of this grant application is the molecular and functional characterization of CIPER. He is proposing a series of Aims to further define the mechanism by which CIPER promotes apoptosis and NF-kB activation. The experiments outlined in this application should provide important insight into the physiological role of CIPER in cellular processes and the mechanism by which it promotes cancer development.

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

- **Project Title: RADIOIMMUNOTHERAPY OF B CELL LYMPHOMA WITH ANTI CD74**

  Principal Investigator & Institution: Mattes, M Jules.; Garden St Cncr Ctr/Ctr Mol Med & Immunol for Molecular Med & Immunology Belleville, Nj 07109

  Timing: Fiscal Year 2002; Project Start 01-MAY-2000; Project End 30-APR-2004

  Summary: (Adapted from applicant's abstract) Recent results of cancer radioimmunotherapy (using radiolabeled antibodies) have been encouraging, especially for **B-cell lymphoma.** However, the selection of the optimal Ab and radionuclide remains uncertain. While high energy beta-emitters, which have been widely used, can kill large tumor masses, the radiation dose delivered is primarily due to the cross-fire from neighboring cells and such radiation is unable to efficiently and specially kill single cells in vitro. This of course represents a significant clinical problem, since it implies that single cells or small clusters of cells cannot be effectively targeted by RAIT. Radioisotopes emitting Auger and conversion electrons, which are very low energy electrons, are potentially able to kill single target cells if sufficient radioactivity is delivered intracellularly. The investigators have characterized an Ab, LL1, anti-MHC class II invariant chain (CD74), which reacts with B-cell lymphomas and is internalized by cells in large amounts, approximately 107 Ab molecules internalized per cell per day. The investigators have demonstrated that this Ab conjugated to 111 In or 99mTc, which are Auger electron-emitters, kills **B-cell lymphoma** cells specifically and efficiently. Conjugates with 125I are also effective, but only if a residualizing form of 125I is used (which is trapped in lysosomes after catabolism of the Ab to which it was attached). Conjugates with beta-particle emitters, 131 I and 90Y, are also able to kill cells specifically, although with a higher level of non-specific toxicity. The investigators propose herein to further test, in a more quantitative assay, the ability of these conjugates to kill tumor cells, in order to select the optimal isotope. In addition to in vitro studies, toxicity in vivo will also be evaluated, using nude or SCID mice bearing human tumor xenografts. Preliminary data shows effective therapy of systemic B cell lymphoma in SCID mice by 111In-LL1. Since the antigen recognized is also expressed on melanomas and carcinoma cells, after induction by interferon-gamma, these target cells will also be tested. They will also attempt to extend these experiments to other Abs,

particularly those that react with high-density antigens, labeled to a high specific activity. This study may lead to the development of more effective radio-conjugates for the therapy of cancer and other diseases. Also, it will provide basic information about the toxic effects of intracellular (really lysosomal) radionuclides.

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- **Project Title: ROLE OF EPSTEIN-BARR VIRUS IN BURKITT LYMPHOMA**

  Principal Investigator & Institution: Sample, Jeffery T.; Associate Professor; St. Jude Children's Research Hospital Memphis, Tn 381052794

  Timing: Fiscal Year 2003; Project Start 30-SEP-1996; Project End 31-MAR-2008

  Summary: (provided by applicant): The long-term objective of the work supported by this grant is to define the role of Epstein-Barr virus (EBV) in **Burkitt lymphoma** (BL), a B-cell tumor that occurs in geographically distinct regions, and which is also associated with immunosuppression as a consequence of HIV infection and AIDS. The underlying hypothesis of this grant is that EBV contributes directly to BL, despite lack of expression of the known viral transforming genes within the tumor cells. This is supported by the observation that the tumorigenic potential of the BL cell line Akata is dependent on EBV infection and at least two viral gene products the EBV small RNAs EBER-1 and EBER-2. The contribution of the EBER RNAs to tumorigenic potential, however, is partial relative to that conferred by EBV infection as a whole, indicating that additional viral genes expressed during infection of BL cells are important. The immediate goals of the proposed work are to define the mechanistic contributions of the EBER RNAs and other EBV gene products to the tumorigenic potential of BL cells and to lymphomagenesis itself. Three specific aims are proposed. Under Aim 1, we will identify the cellular targets of the EBER RNAs and define the mechanisms through which they are regulated. We will address two potential mechanisms of EBER function that are suggested by previous experimental observations. The first is that the EBER RNAs function in posttranscriptional gene silencing through direct RNA:RNA interactions with cellular gene RNAs. The second, based on known interactions of the EBERs with components of the cellular translational machinery, is that the EBERs regulate translation of specific cellular mRNAs. Under Aim 2, we will define the contributions of proteins encoded by the EBV BamHI rightward transcripts (BARTs) to BL-cell tumorigenic potential, and in particular whether any of these proteins are responsible for the enhanced survival conferred upon BL cells by EBV that is attributed to viral-enforced down-regulation of the c-MYC proto-oncoprotein under growth-limiting conditions. Under Aim 3, we will assess the importance of EBV genes expressed in BL cell lines to actual lymphomagenesis using the murine model of BL, the Emu-myc transgenic mouse, in which expression of the c-myc proto-oncogene, as in BL, is constitutively overexpressed in B lymphocytes. Specifically, we will express the EBV genes within the B cells of these mice to determine whether this accelerates c-Myc-induced lymphomagenesis, and if so, we will identify the genetic and biochemical basis for this contribution to lymphoma.

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- **Project Title: ROLE OF THE BCL 6 PROTO ONCOGENE IN B CELL LYMPHOMAS**

  Principal Investigator & Institution: Ye, B H.; Cell Biology; Yeshiva University 500 W 185Th St New York, Ny 10033

  Timing: Fiscal Year 2002; Project Start 01-MAY-2000; Project End 30-APR-2005

Summary: (Adapted from the investigator's abstract) Aggressive non Hodgkin's B-cell lymphomas often carry chromosomal translocations in the proto-oncogene BCL-6 locus. Translocations deregulate BCL-6 expression via promoter substitution, leading to constitutive high levels of the wild type BCL-6 protein in lymphoma B cells. In normal B cells, the BCL-6 protein is expressed only at the germinal center stage. BCL-6 is a zinc finger-containing transcription repressor. Knock out studies in mice have suggested important regulatory functions for BCL-6 in the immune system. Still, very little is known about how its expression is normally regulated in B as well as in non-B cells. In addition, the mechanism by which abnormal BCL-6 expression contributes to lymphomagenesis is still unclear. The first specific aim will attempt to characterize a negative autoregulatory mechanism governing BCL-6 transcription. Experiments are designed to first firmly establish its existence in B cells with a wild type BCL-6 gene. Its integrity in tumor B cells with genetically altered BCL-6 gene will then studied. In the second aim, we will test our hypothesis that continued expression of the BCL-6 protein is essential for maintaining the tumorigenicity of lymphoma cell lines. We will attempt to downregulate the activity of BCL-6 protein by expression of either the antisense or dominant negative BCL-6 mutants (knock down approach). Corresponding changes in the cellular phenotype of lymphoma cells will be studied. As our preliminary data suggests a role of BCL-6 in preventing apoptosis, identifying a link between BCL-6 and apoptosis regulators will be a priority. In the third aim, effort will be made to search for BCL-6 genes genes based upon this knock down approach. A combination of cDNA RDA and the cDNA microarray techniques will be used. The last specific aim is to establish the causative role of BCL-6 in lymphomagenesis in vivo by generating conditional BCL-6 transgenic mice using the cre-lox system. Phenotypes to be analyzed include germinal center enter function, B cell proliferation and tumorigenesis.

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- **Project Title: TCL1 ONCOGENE IN B LYMPHOCYTE DEVELOPMENT AND NEOPLASIA**

  Principal Investigator & Institution: Teitell, Michael A.; Associate Professor, Departments of Path; Anesthesiology; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2002; Project Start 05-AUG-2002; Project End 30-JUN-2007

  Summary: (provided by the applicant): A new direction in determining the role of the TCL1 (T cell leukemia-1) oncogene in B-cell development and neoplasia is highlighted by this application. We found that TCL1 expression is normally extinguished during B-lymphocyte maturation to memory or plasma cells in reactive germinal centers (GC) of lymphoid tissues. However, using subtractive hybridization, we also identified aberrant, high level TCL1 expression in -~8O% of post-GC-derived AIDS diffuse large **B-cell lymphoma** patient samples. This discovery makes TCL1 the most prevalent oncogene associated with this large subgroup of B-lymphomas and strongly implicates its role in AIDS-lymphomagenesis. The pattern of regulated expression led us to propose a model in which TCL1 primarily functions in cell survival and to a lesser extent in cell proliferation. We further propose that the normal mechanisms that down-regulate TCL1 expression are mainly epigenetic and are disrupted in AIDS, resulting in sustained, high level expression in B-cells. Increased protection and proliferation of B-cells that otherwise would be eliminated or kept quiescent would yield a survival advantage and, over the long-term, allow accumulated mutations to yield aggressive B-cell tumors, as seen in many AIDS patients. Support for this model has now been obtained by our group and by others who have shown an interaction between Tc11 and Akt (protein

kinase B). Akt functions as an essential cellular kinase that mainly promotes cell survival. Our approach for testing the hypothesis that dysregulated TCL1 expression alters normal B-cell homeostasis and promotes lymphomas is straightforward. We will determine key features of the epigenetic regulatory mechanisms we believe are controlling TCL1 expression and investigate the biological significance of dysregulation in an animal model system. Accordingly, specific aim 1 studies the epigenetic mechanisms regulating TCL1 gene activity while specific aim II assesses the impact of abnormal regulation in our now established transgenic mouse model. Then, specific aim III determines how TCL1 initiates B-cell transformation by examining the development of autoantibodies and the role of additional mutations from errors in the mechanisms that normally operate in GCs to drive antibody diversity. Because of its strategic position down-stream of PTEN and other known tumor promoting proteins in the Akt activation cascade, these studies also presage future evaluations of TCL1 as a potential diagnostic or therapeutic target molecule.

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- **Project Title: TRANSCRIPTIONAL SILENCING BY THE BCL-6 ONCOPROTEIN**

  Principal Investigator & Institution: Melnick, Ari M.; Belfer Scholar; Developmtl & Molecular Biology; Yeshiva University 500 W 185Th St New York, Ny 10033

  Timing: Fiscal Year 2004; Project Start 06-APR-2004; Project End 31-JAN-2009

  Summary: (provided by applicant): The Bcl-6 transcriptional repressor is the most commonly mutated oncoprotein in B-cell lymphomas. Mutations of its regulatory regions occur in approximately 50% of patients, leading to deregulated expression of Bcl-6 with consequent differentiation block and aberrant cell survival. The N-terminal BTB/POZ domain of Bcl-6 is required for its transcriptional functions. By X-ray crystallography we found that the Bcl-6 BTB domain binds directly to its co-repressor partner proteins through a non-conserved "lateral groove" motif. The reciprocal surface is provided by a short sequence present in the SMRT, N-CoR and BCoR corepressors. Point mutations in this "COW' motif cause loss of physical and functional interactions between corepressors and Bcl-6 in vitro and in vivo. This could be of major functional relevance for Bcl-6, since corepressor interaction is required for this protein to mediate transcriptional repression. We hypothesize that the lateral groove plays a critical role in Bcl-6 dependent repression. Therefore, we designed peptide inhibitors that prevent co-repressor interaction with Bcl-6. These reagents will be used to "conditionally knock out" the contribution of the SMRT/N-CoRJBCoR co-repressors to silencing by Bcl-6. This will allow us to determine the relative contribution of these corepressors to the genomic and epigenomic transcriptional mechanisms of Bcl-6. Such results can be obtained by combining high-throughput chromatin structure analysis by ChIP on chip and differential methylation hybridization with standard expression arrays. Validation through specific studies on independent loci is also required. Finally, we predict that lateral groove blockade of Bcl-6 will counteract the oncogenic activity of Bcl-6 and constitutes a novel and specific transcription therapy approach for B-cell lymphomas. We will assess the ability of lateral groove blockade to reverse the malignant phenotype of **B-cell lymphoma** cells as well as its capacity to alter the course of disease in pre-clinical animal models of this disease. Collectively, these results will reveal novel and important insights into the mechanism of action of Bcl-6 transcriptional repression, as well as provide the basis for a novel and specific molecular therapeutic modality for patients with B-cell lymphomas.

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

- **Project Title: VH IG PEPTIDE VACCINES FOR HUMAN B CELL MALIGNANCIES**

  Principal Investigator & Institution: Bankert, Richard B.; Associate Professor; Microbiology and Immunology; State University of New York at Buffalo Suite 211 Ub Commons Buffalo, Ny 14228

  Timing: Fiscal Year 2002; Project Start 01-APR-2000; Project End 31-MAR-2004

  Summary: Human B-cell malignancies display on their surface, membrane-associated immunoglobulin (Ig). The variable regions at the amino terminal ends of both heavy and light chains (VH and VL) of Ig contain clonal specific epitopes that represent tumor specific antigens. The cloning and sequencing of VH cDNAs from tumor specimens of patients with B-cell lymphomas allow us to generate different synthetic peptides based upon these sequences. This will be exploited to test vaccination strategies in which patients' dendritic cells are pulsed with these peptides and their ability to induce tumor specific immunity will be examined. In Aim 1, peptides corresponding to hypervariable (CDR1-3) regions of B-cell lymphomas that have either germline or somatically mutated sequences are being tested. In Aim 2 peptides corresponding to the more conserved germline and somatically mutated framework VH regions are being tested for immunogenicity. In these first two vaccination strategies (Aims l and 2) we will use synthetic peptides of 11-30 amino acids to pulse DC's which would be expected to take up (by macropinocytosis), process and present small peptides in the context of MHC Class 1 and ll to autologous lymphocytes. In Aim 3, smaller synthetic peptides (9-mers) which are expected to bind directly to Class I on dendritic cells without processing, are selected from the entire tumor-associated VH region based upon optimal MHC Class I binding strengths that are predicted by peptide binding motifs specific for an HLA allele expressed by the patient. In Aim 4, patients' dendritic cells are transfected with mammalian expression vectors encoding either selected VH region peptides or the entire tumor associated VH region and the transfected dendritic cells tested for immunogenicity. In all 4 Aims, the vaccination strategies are evaluated for their ability to induce protective anti-tumor immunity using a human/SCID mouse chimeric model in which patients' peptide-pulsed or transfected dendritic cells, along with patients' lymphocytes, are engrafted in SCID mice and subsequently challenged with autologous tumor cells. Peptide pulsed or transfected D.C. are also evaluated in vitro for their ability to provoke tumor specific cytotoxic T lymphocytes. These results are expected to define immunogenic VH region peptides and to establish an optimal clinical strategy for the vaccination of patients with B cell malignancies. Valuable insights are also anticipated with respect to designing vaccination protocols for other tumors where a tumor specific antigen has been identified.

  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

[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.

unrestricted.[5] To search, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Pmc**, and type "B-cell lymphoma" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for B-cell lymphoma in the PubMed Central database:

- **A subpopulation of normal B cells latently infected with Epstein-Barr virus resembles Burkitt lymphoma cells in expressing EBNA-1 but not EBNA-2 or LMP1.** by Chen F, Zou JZ, di Renzo L, Winberg G, Hu LF, Klein E, Klein G, Ernberg I.; 1995 Jun; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=189092
- **Antibody coating and agglutination of virus particles separated from the EB3 line of Burkitt lymphoma cells.** by Henle W, Hummeler K, Henle G.; 1966 Jul; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=276225
- **Characterization of two related Epstein-Barr virus-encoded membrane proteins that are differentially expressed in Burkitt lymphoma and in vitro-transformed cell lines.** by Modrow S, Wolf H.; 1986 Aug; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=386357
- **Clustered somatic mutations in and around first exon of non-rearranged c-myc in Burkitt lymphoma with t(8;22) translocation.** by Szajnert MF, Saule S, Bornkamm GW, Wajcman H, Lenoir GM, Kaplan JC.; 1987 Jun 11; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=340879
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[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.

- **Down-regulation of class I HLA antigens and of the Epstein-Barr virus-encoded latent membrane protein in Burkitt lymphoma lines.** by Masucci MG, Torsteindottir S, Colombani J, Brautbar C, Klein E, Klein G.; 1987 Jul; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=305131
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- **Epstein-Barr Virus Small RNAs Potentiate Tumorigenicity of Burkitt Lymphoma Cells Independently of an Effect on Apoptosis.** by Ruf IK, Rhyne PW, Yang C, Cleveland JL, Sample JT.; 2000 Nov 1; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=102063
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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 B-cell lymphoma, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "B-cell lymphoma" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for B-cell lymphoma (hyperlinks lead to article summaries):

- **A case of a diffuse large B-cell lymphoma of plasmablastic type associated with the t(2;5)(p23;q35) chromosome translocation.**
  Author(s): Adam P, Katzenberger T, Seeberger H, Gattenlohner S, Wolf J, Steinlein C, Schmid M, Muller-Hermelink HK, Ott G.
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  Author(s): Yanagihori H, Oyama N, Kawakami Y, Sakuma-Oyama Y, Nakamura K, Iwatsuki K, Kaneko F.
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  Author(s): Shim CS, Lee JS, Kim JO, Cho JY, Lee MS, Jin SY, Youm W.
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[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.

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  Author(s): Parrens M, Vergier B, Fitoussi O, Lahet C, Belleannee G, Marit G, Dubus P, de Mascarel A, Delfau-Larue MH, Merlio JP.
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  Author(s): Fierro MT, Savoia P, Quaglino P, Novelli M, Barberis M, Bernengo MG.
  Source: Journal of the American Academy of Dermatology. 2003 August; 49(2): 281-7.
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  Author(s): Pai RR, Khadilkar UN, Pai MR, Dinesh M.
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- **T-cell-rich large B-cell lymphoma in children and adolescents: a clinicopathologic report of six cases from the Children's Cancer Group Study CCG-5961.**
  Author(s): Lones MA, Cairo MS, Perkins SL.
  Source: Cancer. 2000 May 15; 88(10): 2378-86.
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- **Telomerase activity and proliferation index in aggressive mature B-cell lymphoma: comparison to germinal center phenotypic markers.**
  Author(s): Chiu KC, Fine M, Ikle D, Slovak ML, Arber DA.
  Source: Human Pathology. 2003 December; 34(12): 1259-64.
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- **Uncommon hematologic malignancies. Case 2. Calcification in untreated primary mediastinal large B-cell lymphoma with sclerosis.**
  Author(s): Oo TH, Aish LS, Schneider D, Hesketh PJ.
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  Author(s): Quintini G, Barbera V, Franco V, Florena AM, Spadola V, Mariani G.
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- **Unusual locations for lymphomas. Case 3. Successive occurrence of peripheral T-cell lymphoma with bilateral conjuctival involvement in a patient with low-grade B-cell lymphoma.**
  Author(s): Akpek G, Akpek EK, Li S, Green RW, O'Brien TP, Borowitz MJ.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 2001 June 1; 19(11): 2964-6.
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- **Ureteric obstruction due to B-cell lymphoma.**
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  Source: Leukemia & Lymphoma. 1998 January; 28(3-4): 295-306.
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  Author(s): Arsos G, Garypidou V, Al-Mousa G, Iakovou I, Karakatsanis C.
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- **Very late relapse in diffuse large B-cell lymphoma represents clonally related disease and is marked by germinal center cell features.**
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  Source: American Journal of Clinical Pathology. 2002 March; 117(3): 495-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11888093

- **Waldenstrom macroglobulinemia caused by extranodal marginal zone B-cell lymphoma: a report of six cases.**
  Author(s): Valdez R, Finn WG, Ross CW, Singleton TP, Tworek JA, Schnitzer B.
  Source: American Journal of Clinical Pathology. 2001 November; 116(5): 683-90.
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- **Yttrium-90-labeled anti-CD20 monoclonal antibody therapy of recurrent B-cell lymphoma.**
  Author(s): Knox SJ, Goris ML, Trisler K, Negrin R, Davis T, Liles TM, Grillo-Lopez A, Chinn P, Varns C, Ning SC, Fowler S, Deb N, Becker M, Marquez C, Levy R.
  Source: Clinical Cancer Research : an Official Journal of the American Association for Cancer Research. 1996 March; 2(3): 457-70.
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- **Zosteriform relapse of B-cell lymphoma.**
  Author(s): Au WY, Chan AC, Kwong YL.
  Source: The British Journal of Dermatology. 2000 January; 142(1): 180-2.
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CHAPTER 2. NUTRITION AND B-CELL LYMPHOMA

Overview

In this chapter, we will show you how to find studies dedicated specifically to nutrition and B-cell lymphoma.

Finding Nutrition Studies on B-Cell Lymphoma

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 "B-cell lymphoma" (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 "B-cell lymphoma" (or a synonym):

- **A case of cutaneous B-cell lymphoma treated successfully with MACOP-B.**
  Author(s): Department of Dermatology, Yokohama City University School of Medicine, Japan.
  Source: Nagatani, T Miyazawa, M Matsuzaki, T Hayakawa, H Iemoto, G Kim, S T Baba, N Sugiyama, A Aihara, M Miyamoto, H et al. J-Dermatol. 1993 January; 20(1): 40-4 0385-2407

- **Bilateral, primary, low-grade, diffuse B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) of the breast.**
  Author(s): Department of Surgery, 251 Hellenic Air Force Hospital, Athens, Greece.
  Source: Zobolas, B Sakorafas, G H Kourakli, I Tsiotou, A G Breast-J. 2002 Nov-December; 8(6): 382 1075-122X

- **Cerebral B-cell lymphoma following treatment for Tolosa-Hunt syndrome.**
  Author(s): Department of Neuropathology, Neurological Institute, Faculty of Medicine, Kyushu University, Fukuoka, Japan.
  Source: Takao, T Kaku, S Tashima, T Iwaki, T Clin-Neuropathol. 1999 Mar-April; 18(2): 87-92 0722-5091

- **Diffuse large B-cell lymphoma with fibrillary matrix.**
  Author(s): Laboratoire d'Anatomie Pathologique, CHU Saint-Pierre/Institut Jules Bordet, Universite Libre de Bruxelles, Brussels, Belgium. jldargent@hotmail.com
  Source: Dargent, J L Meiers, I Lespagnard, L Ma, Y Dehou, M F Verhest, A Diagn-Cytopathol. 2002 October; 27(4): 223-6 8755-1039

- **Epstein-Barr virus associated diffuse large B-cell lymphoma complicated by autoimmune hemolytic anemia and pure red cell aplasia.**
  Author(s): Department of Internal Medicine, National Sanatrium Minami Okayama Hospital, 4066 Hayashima Cho, Tsukubo Gun, Okayama 701-0304, Japan.
  Source: Katayama, H Takeuchi, M Yoshino, T Munemasa, M Tada, A Soda, R Takahashi, K Leuk-Lymphoma. 2001 July; 42(3): 539-42 1042-8194

- **Hodgkin's disease following extranodal marginal zone B-cell lymphoma in remission.**
  Author(s): Department of Medicine, Nagoya City Higashi General Hospital, Nagoya, Japan.
  Source: Shimizu, K Hara, K Yatabe, Y Int-J-Hematol. 1999 February; 69(2): 96-100 0925-5710

- **In vitro and in vivo effect of HPMA copolymer-bound doxorubicin targeted to transferrin receptor of B-cell lymphoma 38C13.**
  Author(s): Department of Immunology, Institute of Microbiology, Academy of Sciences of the Czech Republic, Prague. makovar@biomed.cas.cz
  Source: Kovar, M Strohalm, J Ulbrich, K Rihova, B J-Drug-Target. 2002 February; 10(1): 23-30 1061-186X

- **Major prognostic factors of adult patients with advanced B-cell lymphoma treated with vincristine, cyclophosphamide, prednisone and doxorubicin (VEPA) or VEPA plus methotrexate (VEPA-M).**
  Author(s): Department of Internal Medicine, National Cancer Center Hospital, Tokyo.
  Source: Shimoyama, M Ota, K Kikuchi, M Yunoki, K Konda, S Takatsuki, K Ogawa, M Tominaga, S Tsugane, S Minato, K et al. Jpn-J-Clin-Oncol. 1988 June; 18(2): 113-24 0368-2811

- **Measurements of IL-6, soluble IL-6 receptor and soluble gp130 in sera of B-cell lymphoma patients. Does viscum album treatment affect these parameters?**
  Author(s): Society of Cancer Research, Kirschweg, Arlesheim, Switzerland. evakovacsbenke@hotmail.com
  Source: Kovacs, E Kuehn, J J Biomed-Pharmacother. 2002 May; 56(3): 152-8 0753-3322

- **Modulation of apoptosis and enhancement of chemosensitivity by decreasing cellular thiols in a mouse B-cell lymphoma cell line that overexpresses bcl-2.**
  Author(s): Department of Experimental Radiation Oncology, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA. mstory@mdanderson.org
  Source: Story, M D Meyn, R E Cancer-Chemother-Pharmacol. 1999; 44(5): 362-6 0344-5704

- **Occurrence of Hodgkin's disease and cutaneous B-cell lymphoma in the same patient: a report of two cases.**
  Author(s): Department of Dermatology and Pathology, Hospital Princeps d'Espanya, CSUB. Feixa Llarga s/n L'Hospitalet de Llobregat, 08907 Barcelona, Spain. oservitje@csub.scs.es.
  Source: Servitje, O Marti, R M Estrach, T Palou, J Gallardo, F Limon, A Romagosa, V Eur-J-Dermatol. 2000 Jan-February; 10(1): 43-6 1167-1122

- **Presentation of T-cell-rich B-cell lymphoma mimicking acute hepatitis.**
  Author(s): Division of Gastroenterology, Complejo Hospitalario Universitario, Santiago de Compostela, Spain.
  Source: Castroagudin, J F Gonzalez Quintela, A Fraga, M Forteza, J Barrio, E Hepatogastroenterology. 1999 May-June; 46(27): 1710-3 0172-6390

- **Primary Mediastinal B-cell lymphoma with sclerosis: clinical and therapeutic evaluation of 22 patients.**
  Author(s): Institute of Hematology Seragnoli, University of Bologna, Italy.
  Source: Zinzani, P L Bendandi, M Frezza, G Gherlinzoni, F Merla, E Salvucci, M Magagnoli, M Babini, L Tura, S Leuk-Lymphoma. 1996 April; 21(3-4): 311-6 1042-8194

- **Response of B-cell lymphoma to a combination of bispecific antibodies and saporin.**
  Author(s): Lymphoma Research Unit, Tenovus Research Laboratory, Southampton General Hospital, U.K.
  Source: French, R R Bell, A J Hamblin, T J Tutt, A L Glennie, M J Leuk-Res. 1996 July; 20(7): 607-17 0145-2126

- **Secondary pancreatic involvement by diffuse large B-cell lymphoma presenting as acute pancreatitis: treatment and outcome.**
  Author(s): Department of Gastroenterology and Hepatology, Henry Mondor University Hospital, Creteil, France.
  Source: Bernardeau, M Auroux, J Cavicchi, M Haioun, C Tsakiris, L Delchier, J C Pancreatology. 2002; 2(4): 427-30 1424-3903

- **Treatment and clinical management of primary mediastinal large B-cell lymphoma with sclerosis: MACOP-B regimen and mediastinal radiotherapy monitored by (67)Gallium scan in 50 patients.**
  Author(s): Institute of Hematology and Medical Oncology “Seragnoli,” University of Bologna, Bologna, Italy.
  Source: Zinzani, P L Martelli, M Magagnoli, M Pescarmona, E Scaramucci, L Palombi, F Bendandi, M Martelli, M P Ascani, S Orcioni, G F Pileri, S A Mandelli, F Tura, S Blood. 1999 November 15; 94(10): 3289-93 0006-4971

- **Treatment of patients with low-grade B-cell lymphoma with the combination of chimeric anti-CD20 monoclonal antibody and CHOP chemotherapy.**
  Author(s): Department of Hematologic Oncology and Bone Marrow Transplantation, Roswell Park Cancer Institute, Buffalo, NY 14263, USA.
  Source: Czuczman, M S Grillo Lopez, A J White, C A Saleh, M Gordon, L LoBuglio, A F Jonas, C Klippenstein, D Dallaire, B Varns, C J-Clin-Oncol. 1999 January; 17(1): 268-76 0732-183X
- **Two different IFN-gamma nonresponsive variants derived from the B-cell lymphoma 70Z/3.**
  Author(s): Department of Biological Structure, University of Washington, Seattle 98195.
  Source: Rhodes, L D Paull, A T Sibley, C H Immunogenetics. 1994; 40(3): 199-209 0093-7711
- **Urate-oxidase in the prevention and treatment of metabolic complications in patients with B-cell lymphoma and leukemia, treated in the Societe Francaise d'Oncologie Pediatrique LMB89 protocol.**
  Author(s): Institut Gustave Roussy, Villejuif, France. patte@igr.fr
  Source: Patte, C Sakiroglu, C Ansoborlo, S Baruchel, A Plouvier, E Pacquement, H Babin Boilletot, A Ann-Oncol. 2002 May; 13(5): 789-95 0923-7534

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**

CHAPTER 3. ALTERNATIVE MEDICINE AND B-CELL LYMPHOMA

Overview

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

National Center for Complementary and Alternative Medicine

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

- **A phase I/II trial of iodine-131-tositumomab (anti-CD20), etoposide, cyclophosphamide, and autologous stem cell transplantation for relapsed B-cell lymphomas.**
  Author(s): Press OW, Eary JF, Gooley T, Gopal AK, Liu S, Rajendran JG, Maloney DG, Petersdorf S, Bush SA, Durack LD, Martin PJ, Fisher DR, Wood B, Borrow JW, Porter B, Smith JP, Matthews DC, Appelbaum FR, Bernstein ID.
  Source: Blood. 2000 November 1; 96(9): 2934-42.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11049969

- **Additional chemotherapy agents improve treatment outcome for children and adults with advanced B-cell lymphomas.**
  Author(s): Adde M, Shad A, Venzon D, Arndt C, Gootenberg J, Neely J, Nieder M, Owen W, Seibel N, Wilson W, Horak ID, Magrath I.

Source: Seminars in Oncology. 1998 April; 25(2 Suppl 4): 33-9; Discussion 45-8.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9578060

- **Age-adjusted International Prognostic Index predicts autologous stem cell transplantation outcome for patients with relapsed or primary refractory diffuse large B-cell lymphoma.**
Author(s): Hamlin PA, Zelenetz AD, Kewalramani T, Qin J, Satagopan JM, Verbel D, Noy A, Portlock CS, Straus DJ, Yahalom J, Nimer SD, Moskowitz CH.
Source: Blood. 2003 September 15; 102(6): 1989-96. Epub 2003 April 03.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12676776

- **Autologous bone marrow transplant in a patient with sickle cell disease and diffuse large B-cell lymphoma.**
Author(s): Onitilo AA, Lazarchick J, Brunson CY, Frei-Lahr D, Stuart RK.
Source: Transplantation Proceedings. 2003 December; 35(8): 3089-92.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14697986

- **B-cell lymphoma with extensive cutaneous involvement presenting to the ENT surgeon.**
Author(s): Hughes RG, Morgan DW.
Source: The Journal of Laryngology and Otology. 1998 February; 112(2): 186-8.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9578884

- **BCL6 overexpression prevents increase in reactive oxygen species and inhibits apoptosis induced by chemotherapeutic reagents in B-cell lymphoma cells.**
Author(s): Kurosu T, Fukuda T, Miki T, Miura O.
Source: Oncogene. 2003 July 17; 22(29): 4459-68.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12881702

- **Beta-HCG aberrant expression in primary mediastinal large B-cell lymphoma.**
Author(s): Fraternali-Orcioni G, Falini B, Quaini F, Campo E, Piccioli M, Gamberi B, Pasquinelli G, Poggi S, Ascani S, Sabattini E, Pileri SA.
Source: The American Journal of Surgical Pathology. 1999 June; 23(6): 717-21.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10366155

- **Bilateral, primary, low-grade, diffuse B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) of the breast.**
Author(s): Zobolas B, Sakorafas GH, Kourakli I, Tsiotou AG.
Source: The Breast Journal. 2002 November-December; 8(6): 382.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12390362

- **CD5+ T-cell/histiocyte-rich large B-cell lymphoma.**
Author(s): Chang CC, Bunyi-Teopengco E, Eshoa C, Chitambar CR, Kampalath B.

Source: Modern Pathology : an Official Journal of the United States and Canadian Academy of Pathology, Inc. 2002 October; 15(10): 1051-7.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12379751

- **Chemotherapy for management of localised high-grade gastric B-cell lymphoma: how much is necessary?**
  Author(s): Raderer M, Chott A, Drach J, Montalban C, Dragosics B, Jager U, Puspok A, Osterreicher C, Zielinski CC.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2002 July; 13(7): 1094-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12176789

- **Chemotherapy for the treatment of patients with primary high grade gastric B-cell lymphoma of modified Ann Arbor Stages IE and IIE.**
  Author(s): Raderer M, Valencak J, Osterreicher C, Drach J, Hejna M, Kornek G, Scheithauer W, Brodowicz T, Chott A, Dragosics B.
  Source: Cancer. 2000 May 1; 88(9): 1979-85.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10813708

- **CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma.**
  Author(s): Coiffier B, Lepage E, Briere J, Herbrecht R, Tilly H, Bouabdallah R, Morel P, Van Den Neste E, Salles G, Gaulard P, Reyes F, Lederlin P, Gisselbrecht C.
  Source: The New England Journal of Medicine. 2002 January 24; 346(4): 235-42.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11807147

- **CHOP plus rituximab chemoimmunotherapy of indolent B-cell lymphoma.**
  Author(s): Czuczman MS.
  Source: Seminars in Oncology. 1999 October; 26(5 Suppl 14): 88-96.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10561023

- **Clinical relevance of the lung resistance protein in diffuse large B-cell lymphomas.**
  Author(s): Filipits M, Jaeger U, Simonitsch I, Chizzali-Bonfadin C, Heinzl H, Pirker R.
  Source: Clinical Cancer Research : an Official Journal of the American Association for Cancer Research. 2000 September; 6(9): 3417-23.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10999723

- **Clinicopathologic, immunophenotypic, and molecular characterization of primary cutaneous follicular B-cell lymphoma.**
  Author(s): Bergman R, Kurtin PJ, Gibson LE, Hull PR, Kimlinger TK, Schroeter AL.
  Source: Archives of Dermatology. 2001 April; 137(4): 432-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11295923

- **Coexistent rearrangements of c-MYC, BCL2, and BCL6 genes in a diffuse large B-cell lymphoma.**
  Author(s): Ueda C, Nishikori M, Kitawaki T, Uchiyama T, Ohno H.
  Source: International Journal of Hematology. 2004 January; 79(1): 52-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14979479

- **Coincidental detection of T-cell rich B-cell lymphoma in the paraaortic lymph nodes of a woman undergoing lymph node dissection for cervical cancer.**
  Author(s): Abali H, Eren OO, Erman M, Uner AH, Kose F, Guler N.
  Source: International Journal of Gynecological Cancer : Official Journal of the International Gynecological Cancer Society. 2003 July-August; 13(4): 548-50.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12911737

- **Combined therapy in the treatment of primary mediastinal B-cell lymphoma: conventional versus escalated chemotherapy.**
  Author(s): Aviles A, Garcia EL, Fernandez R, Gonzalez JL, Neri N, Diaz-Maqueo JC.
  Source: Annals of Hematology. 2002 July; 81(7): 368-73. Epub 2002 June 21.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12185505

- **Complete remission of generalized relapsed extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue type of the gastrointestinal tract after high-dose chemotherapy and autologous peripheral stem cell transplantation.**
  Author(s): Neumeister P, Hoefler G, Beham-Schmid C, Sill H, Linkesch W.
  Source: Annals of Hematology. 2000 December; 79(12): 703-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11195010

- **Consolidation radiotherapy following brief chemotherapy for localized diffuse large B-cell lymphoma: a prospective study.**
  Author(s): Isobe K, Kawakami H, Tamaru J, Yasuda S, Uno T, Aruga T, Kawata T, Shigematsu N, Hatano K, Takagi T, Mikata A, Ito H.
  Source: Leukemia & Lymphoma. 2003 September; 44(9): 1535-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14565656

- **Diabetes insipidus in a patient with a highly malignant B-cell lymphoma and stomatitis.**
  Author(s): Breidert M, Schimmelpfennig C, Kittner T, Helwig A, Ehninger G.
  Source: Experimental and Clinical Endocrinology & Diabetes : Official Journal, German Society of Endocrinology [and] German Diabetes Association. 2000; 108(1): 54-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10768833

- **Diffuse large B-cell lymphoma outcome prediction by gene-expression profiling and supervised machine learning.**
  Author(s): Shipp MA, Ross KN, Tamayo P, Weng AP, Kutok JL, Aguiar RC, Gaasenbeek

M, Angelo M, Reich M, Pinkus GS, Ray TS, Koval MA, Last KW, Norton A, Lister TA, Mesirov J, Neuberg DS, Lander ES, Aster JC, Golub TR.
Source: Nature Medicine. 2002 January; 8(1): 68-74.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11786909

- **Diffuse large B-cell lymphoma with fibrillary matrix.**
  Author(s): Dargent JL, Meiers I, Lespagnard L, Ma Y, Dehou MF, Verhest A.
  Source: Diagnostic Cytopathology. 2002 October; 27(4): 223-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12357500

- **Dose-adjusted EPOCH chemotherapy for untreated large B-cell lymphomas: a pharmacodynamic approach with high efficacy.**
  Author(s): Wilson WH, Grossbard ML, Pittaluga S, Cole D, Pearson D, Drbohlav N, Steinberg SM, Little RF, Janik J, Gutierrez M, Raffeld M, Staudt L, Cheson BD, Longo DL, Harris N, Jaffe ES, Chabner BA, Wittes R, Balis F.
  Source: Blood. 2002 April 15; 99(8): 2685-93.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11929754

- **Doxorubicin-based chemotherapy for diffuse large B-cell lymphoma in elderly patients: comparison of treatment outcomes between young and elderly patients and the significance of doxorubicin dosage.**
  Author(s): Lee KW, Kim DY, Yun T, Kim DW, Kim TY, Yoon SS, Heo DS, Bang YJ, Park S, Kim BK, Kim NK.
  Source: Cancer. 2003 December 15; 98(12): 2651-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14669285

- **Efficacy of carboplatin with an MEP (mitoxantrone, etoposide and prednisone) regimen for relapsed and CHOP-resistant diffuse large B-cell lymphomas.**
  Author(s): Murohashi I, Kashimura T, Tominaga K, Wakao D, Takahashi T, Akiba M, Kishimoto K, Yoshida K, Yagasaki F, Itoh Y, Sakata T, Kawai N, Itoh K, Suzuki T, Matsuda A, Hirashima K, Bessho M.
  Source: Leukemia Research. 2002 March; 26(3): 229-34.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11792410

- **Elevated serum CA-125 concentrations due to expression by a diffuse large B-cell lymphoma.**
  Author(s): Vlasveld LT, Ermens AA, Sonnenberg AA, Pauwels P.
  Source: Annals of Clinical Biochemistry. 2000 July; 37 (Pt 4): 545-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10902875

- **Epstein-Barr virus associated diffuse large B-cell lymphoma complicated by autoimmune hemolytic anemia and pure red cell aplasia.**
  Author(s): Katayama H, Takeuchi M, Yoshino T, Munemasa M, Tada A, Soda R, Takahashi K.

Source: Leukemia & Lymphoma. 2001 July; 42(3): 539-42.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11699422

- **Epstein-Barr virus-induced transformation of cutaneous plasmacytoma into CD30+ diffuse large B-cell lymphoma.**
  Author(s): Donner LR.
  Source: The American Journal of Dermatopathology. 2004 February; 26(1): 63-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14726824

- **Favorable response to treatment of a child with T-cell-rich large B-cell lymphoma presenting with liver failure.**
  Author(s): Sathiapalan RK, Hainau B, Al-Mane K, Belgaumi AF.
  Source: Journal of Pediatric Hematology/Oncology : Official Journal of the American Society of Pediatric Hematology/Oncology. 2003 October; 25(10): 809-12.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14528106

- **Ga-67 scintigraphy in a patient with B-cell lymphoma.**
  Author(s): Waldherr C, Otte A, Mueller-Brand J.
  Source: Clinical Nuclear Medicine. 2000 May; 25(5): 389.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10795710

- **Hemophagocytic syndrome in ileum-origin B-cell lymphoma.**
  Author(s): Motegi S, Nishizaki Y, Muramatsu C, Nakamura H, Kobayashi F, Shiozawa H, Kamochi J, Itakura M, Shibuya M, Ogawa T, Matsuzaki S.
  Source: Journal of Gastroenterology. 2003; 38(10): 995-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14614609

- **High dose radioimmunotherapy in relapsed B-cell lymphoma with I-131 rituximab.**
  Author(s): Becker W, Behr T.
  Source: Annals of Hematology. 2001; 80 Suppl 3: B130-1. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11757696

- **High-dose chemotherapy for relapsed and refractory diffuse large B-cell lymphoma: mediastinal localization predicts for a favorable outcome.**
  Author(s): Popat U, Przepiork D, Champlin R, Pugh W, Amin K, Mehra R, Rodriguez J, Giralt S, Romaguera J, Rodriguez A, Preti A, Andersson B, Khouri I, Claxton D, de Lima M, Donato M, Anderlini P, Gajewski J, Cabanillas F, van Besien K.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1998 January; 16(1): 63-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9440724

- **Hodgkin's disease following extranodal marginal zone B-cell lymphoma in remission.**
  Author(s): Shimizu K, Hara K, Yatabe Y.
  Source: International Journal of Hematology. 1999 February; 69(2): 96-100. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10071458

- **Idiotype vaccination following ABMT can stimulate specific anti-idiotype immune responses in patients with B-cell lymphoma.**
  Author(s): Davis TA, Hsu FJ, Caspar CB, van Beckhoven A, Czerwinsk DK, Liles TM, Taidi B, Benike CJ, Engleman EG, Levy R.
  Source: Biology of Blood and Marrow Transplantation : Journal of the American Society for Blood and Marrow Transplantation. 2001; 7(9): 517-22.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11669219

- **Immunogenicity of a plasmid DNA vaccine encoding chimeric idiotype in patients with B-cell lymphoma.**
  Author(s): Timmerman JM, Singh G, Hermanson G, Hobart P, Czerwinski DK, Taidi B, Rajapaksa R, Caspar CB, Van Beckhoven A, Levy R.
  Source: Cancer Research. 2002 October 15; 62(20): 5845-52.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12384547

- **Inability of short-term, low-dose hydroxychloroquine to resolve vitamin D-mediated hypercalcemia in patients with B-cell lymphoma.**
  Author(s): Adams JS, Kantorovich V.
  Source: The Journal of Clinical Endocrinology and Metabolism. 1999 February; 84(2): 799-801.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10022456

- **Incidence and risk factors for central nervous system occurrence in elderly patients with diffuse large-B-cell lymphoma: influence of rituximab.**
  Author(s): Feugier P, Virion JM, Tilly H, Haioun C, Marit G, Macro M, Bordessoule D, Recher C, Blanc M, Molina T, Lederlin P, Coiffier B.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2004 January; 15(1): 129-33.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14679132

- **Interferon alfa 2b as maintenance therapy in poor risk diffuse large B-cell lymphoma in complete remission after intensive CHOP-BLEO regimens.**
  Author(s): Aviles A, Cleto S, Huerta-Guzman J, Neri N.
  Source: European Journal of Haematology. 2001 February; 66(2): 94-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11168516

- **International prognostic index-based outcomes for diffuse large B-cell lymphomas.**
  Author(s): Wilder RB, Rodriguez MA, Medeiros LJ, Tucker SL, Ha CS, Romaguera JE, Pro B, Hess MA, Cabanillas F, Cox JD.
  Source: Cancer. 2002 June 15; 94(12): 3083-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12115338

- **Large B-cell lymphoma of thyroid. Two cases with a marginal zone distribution of the neoplastic cells.**
  Author(s): Higgins JP, Warnke RA.
  Source: American Journal of Clinical Pathology. 2000 August; 114(2): 264-70.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10941342

- **MACOP-B and involved field radiation therapy is an effective therapy for primary mediastinal large B-cell lymphoma with sclerosis.**
  Author(s): Martelli MP, Martelli M, Pescarmona E, De Sanctis V, Donato V, Palombi F, Todisco E, Rendina EA, Pau FM, Mandelli F.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 1998 September; 9(9): 1027-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9818079

- **Measurements of IL-6, soluble IL-6 receptor and soluble gp130 in sera of B-cell lymphoma patients. Does viscum album treatment affect these parameters?**
  Author(s): Kovacs E, Kuehn JJ.
  Source: Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie. 2002 May; 56(3): 152-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12046687

- **Mechanistic aspects of the induction of apoptosis by lauryl gallate in the murine B-cell lymphoma line Wehi 231.**
  Author(s): Roy G, Lombardia M, Palacios C, Serrano A, Cespon C, Ortega E, Eiras P, Lujan S, Revilla Y, Gonzalez-Porque P.
  Source: Archives of Biochemistry and Biophysics. 2000 November 15; 383(2): 206-14.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11185555

- **Modified chop-chemotherapy plus rituximab for diffuse large B-cell lymphoma complicating ataxia-telangiectasia.**
  Author(s): Rossi G, Zecca M, Marchi A, de Stefano P, Sammarchi L, Locatelli F.
  Source: British Journal of Haematology. 2003 January; 120(2): 369-71.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12542504

- **Modulation of apoptosis and enhancement of chemosensitivity by decreasing cellular thiols in a mouse B-cell lymphoma cell line that overexpresses bcl-2.**
  Author(s): Story MD, Meyn RE.

Source: Cancer Chemotherapy and Pharmacology. 1999; 44(5): 362-6.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10501908

- **Occurrence of Hodgkin's disease and cutaneous B-cell lymphoma in the same patient: a report of two cases.**
  Author(s): Servitje O, Marti RM, Estrach T, Palou J, Gallardo F, Limon A, Romagosa V.
  Source: European Journal of Dermatology : Ejd. 2000 January-February; 10(1): 43-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10694298

- **Pegylated liposomal doxorubicin in combination chemotherapy in the treatment of previously untreated aggressive diffuse large-B-cell lymphoma.**
  Author(s): Aviles A, Neri N, Castaneda C, Talavera A, Huerta-Guzman J, Gonzalez M.
  Source: Medical Oncology (Northwood, London, England). 2002; 19(1): 55-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12025891

- **Presentation of T-cell-rich B-cell lymphoma mimicking acute hepatitis.**
  Author(s): Castroagudin JF, Gonzalez-Quintela A, Fraga M, Forteza J, Barrio E.
  Source: Hepatogastroenterology. 1999 May-June; 46(27): 1710-3.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10430328

- **Primary cutaneous CD30 (Ki-1)-positive non-anaplastic B-cell lymphoma.**
  Author(s): Herrera E, Gallardo M, Bosch R, Cabra B, Aneri V, Sanchez P.
  Source: Journal of Cutaneous Pathology. 2002 March; 29(3): 181-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11972717

- **Primary mediastinal large B-cell lymphoma (PMLBCL): long-term results from a retrospective multicentre Italian experience in 138 patients treated with CHOP or MACOP-B/VACOP-B.**
  Author(s): Todeschini G, Secchi S, Morra E, Vitolo U, Orlandi E, Pasini F, Gallo E, Ambrosetti A, Tecchio C, Tarella C, Gabbas A, Gallamini A, Gargantini L, Pizzuti M, Fioritoni G, Gottin L, Rossi G, Lazzarino M, Menestrina F, Paulli M, Palestro M, Cabras MG, Di Vito F, Pizzolo G.
  Source: British Journal of Cancer. 2004 January 26; 90(2): 372-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14735179

- **Primary mediastinal large B-cell lymphoma with sclerosis in pediatric and adolescent patients: treatment and results from three therapeutic studies of the Berlin-Frankfurt-Munster Group.**
  Author(s): Seidemann K, Tiemann M, Lauterbach I, Mann G, Simonitsch I, Stankewitz K, Schrappe M, Zimmermann M, Niemeyer C, Parwaresch R, Riehm H, Reiter A; NHL Berlin-Frankfurt-Munster Group.

Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 2003 May 1; 21(9): 1782-9.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12721255

- **Primary mediastinal large B-cell lymphoma with sclerosis: a clinical study of 89 patients treated with MACOP-B chemotherapy and radiation therapy.**
  Author(s): Zinzani PL, Martelli M, Bendandi M, De Renzo A, Zaccaria A, Pavone E, Bocchia M, Falini B, Gobbi M, Gherlinzoni F, Stefoni V, Tani M, Tura S.
  Source: Haematologica. 2001 February; 86(2): 187-91.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11224489

- **Primary mediastinal large B-cell lymphoma.**
  Author(s): Ergul SM, Lal A, Afri L, Frei-Lahr D.
  Source: Southern Medical Journal. 2002 September; 95(9): 1005-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12356098

- **Primary mediastinal large B-cell lymphoma: the need for prospective controlled clinical trials.**
  Author(s): Bieri S, Roggero E, Zucca E, Bertoni F, Pianca S, Sanna P, Pedrinis E, Bernier J, Cavalli F.
  Source: Leukemia & Lymphoma. 1999 November; 35(5-6): 537-44. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10609791

- **Prognostic implications of BCL6 rearrangement in uniformly treated patients with diffuse large B-cell lymphoma--a Nordic Lymphoma Group study.**
  Author(s): Jerkeman M, Aman P, Cavallin-Stahl E, Torlakovic E, Akerman M, Mitelman F, Fioretos T.
  Source: International Journal of Oncology. 2002 January; 20(1): 161-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11743658

- **Prognostic models for diffuse large B-cell lymphoma.**
  Author(s): Conconi A, Zucca E, Roggero E, Bertoni F, Bernasconi A, Mingrone W, Pedrinis E, Cavalli F.
  Source: Hematological Oncology. 2000 June; 18(2): 61-73.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10960876

- **Pure red cell aplasia due to parvovirus following treatment with CHOP and rituximab for B-cell lymphoma.**
  Author(s): Song KW, Mollee P, Patterson B, Brien W, Crump M.
  Source: British Journal of Haematology. 2002 October; 119(1): 125-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12358915

- **Reversible posterior leukoencephalopathy syndrome following CHOP chemotherapy for diffuse large B-cell lymphoma.**
  Author(s): Edwards MJ, Walker R, Vinnicombe S, Barlow C, MacCallum P, Foran JM.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2001 September; 12(9): 1327-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11697848

- **Rituximab in heavily pretreated cutaneous B-cell lymphoma.**
  Author(s): Zinzani PL, Stefoni V, Alinari L, Vianelli N, Baccarani M.
  Source: Leukemia & Lymphoma. 2003 September; 44(9): 1637-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14565673

- **Rituximab plus CHOP (R-CHOP) overcomes bcl-2--associated resistance to chemotherapy in elderly patients with diffuse large B-cell lymphoma (DLBCL).**
  Author(s): Mounier N, Briere J, Gisselbrecht C, Emile JF, Lederlin P, Sebban C, Berger F, Bosly A, Morel P, Tilly H, Bouabdallah R, Reyes F, Gaulard P, Coiffier B.
  Source: Blood. 2003 June 1; 101(11): 4279-84. Epub 2003 February 06.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12576316

- **Rituximab plus CHOP for diffuse large-B-cell lymphoma.**
  Author(s): Akhtar S, Maghfoor I.
  Source: The New England Journal of Medicine. 2002 June 6; 346(23): 1830-1; Author Reply 1830-1.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12050349

- **Sarcomatoid variant of B-cell lymphoma of the uterine cervix.**
  Author(s): Kahlifa M, Buckstein R, Perez-Ordonez B.
  Source: International Journal of Gynecological Pathology : Official Journal of the International Society of Gynecological Pathologists. 2003 July; 22(3): 289-93.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12819398

- **Secondary pancreatic involvement by diffuse large B-cell lymphoma presenting as acute pancreatitis: treatment and outcome.**
  Author(s): Bernardeau M, Auroux J, Cavicchi M, Haioun C, Tsakiris L, Delchier JC.
  Source: Pancreatology : Official Journal of the International Association of Pancreatology (Iap). [et Al.]. 2002; 2(4): 427-30.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12138234

- **Severe hypercalcaemia in B-cell lymphoma: combined effects of PTH-rP, IL-6 and TNF.**
  Author(s): Daroszewska A, Bucknall RC, Chu P, Fraser WD.

Source: Postgraduate Medical Journal. 1999 November; 75(889): 672-4.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10621879

- **Specificity of PCR-based clonality analysis of immunoglobulin heavy chain gene rearrangements for the detection of bone marrow involvement by low-grade B-cell lymphomas.**
  Author(s): Brinckmann R, Kaufmann O, Reinartz B, Dietel M.
  Source: The Journal of Pathology. 2000 January; 190(1): 55-60.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10640992

- **Successful treatment of diffuse large B-cell lymphoma following Waldenstrom's macroglobulinemia with CHOP chemotherapy followed by combination therapy of CHOP with rituximab.**
  Author(s): Uchino K, Sameshima H, Miyamoto T, Iino T, Kato K, Henzan H, Aoki K, Nagafuji K, Gondo H, Harada M.
  Source: Intern Med. 2004 February; 43(2): 131-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15005256

- **Systemic therapy with 3BIT, a triple combination cocktail of anti-CD19, -CD22, and -CD38-saporin immunotoxins, is curative of human B-cell lymphoma in severe combined immunodeficient mice.**
  Author(s): Flavell DJ, Noss A, Pulford KA, Ling N, Flavell SU.
  Source: Cancer Research. 1997 November 1; 57(21): 4824-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9354445

- **T-cell-rich B-cell lymphoma. Analysis of clinical features, response to treatment, survival and comparison with diffuse large B-cell lymphoma.**
  Author(s): Tsirigotis P, Economopoulos T, Rontogianni D, Dervenoulas J, Papageorgiou E, Bollas G, Mantzios G, Kalantzis D, Koumarianou A, Raptis S.
  Source: Oncology. 2001; 61(4): 257-64.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11721171

- **T-cell-rich B-cell lymphoma: a clinicopathologic study of 21 cases and comparison with 43 cases of diffuse large B-cell lymphoma.**
  Author(s): Aki H, Tuzuner N, Ongoren S, Baslar Z, Soysal T, Ferhanoglu B, Sahinler I, Aydin Y, Ulku B, Aktuglu G.
  Source: Leukemia Research. 2004 March; 28(3): 229-36. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14687617

- **Testicular ischemia due to intravascular large B-cell lymphoma: a novel presentation in an immunosuppressed individual.**
  Author(s): Tranchida P, Bayerl M, Voelpel MJ, Palutke M.

Source: International Journal of Surgical Pathology. 2003 October; 11(4): 319-24.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14615832

- **The rapidly expanding role of rituximab in the treatment of aggressive B-cell lymphoma.**
  Author(s): Cooper D.
  Source: Cancer Journal (Sudbury, Mass.). 2002 September-October; 8(5): 364-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12416891

- **The role of rituximab and chemotherapy in aggressive B-cell lymphoma: a preliminary report of dose-adjusted EPOCH-R.**
  Author(s): Wilson WH, Gutierrez M, O'Connor P, Frankel S, Jaffe E, Chabner BA, Grossbard ML.
  Source: Seminars in Oncology. 2002 February; 29(1 Suppl 2): 41-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11842388

- **The Societe Francaise d'Oncologie Pediatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burden and initial response in 561 unselected children with B-cell lymphomas and L3 leukemia.**
  Author(s): Patte C, Auperin A, Michon J, Behrendt H, Leverger G, Frappaz D, Lutz P, Coze C, Perel Y, Raphael M, Terrier-Lacombe MJ; Societe Francaise d'Oncologie Pediatrique.
  Source: Blood. 2001 June 1; 97(11): 3370-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11369626

- **Transformation of Hodgkin's disease to high-grade B-cell lymphoma: remission after Rituximab monotherapy.**
  Author(s): Kirchner EM, Ebsen M, Kirchner J, Theegarten D, Voigtmann R.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2001 August; 12(8): 1169-71.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11583202

- **Transfusion-associated graft vs. host disease in a patient with high-grade B-cell lymphoma. Should cellular products for patients with non-Hodgkin's lymphoma be irradiated?**
  Author(s): Gelly KJ, Kerr R, Rawlinson S, Norris A, Bowen DT.
  Source: British Journal of Haematology. 2000 July; 110(1): 228-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10931004

- **Treatment and clinical management of primary mediastinal large B-cell lymphoma with sclerosis: MACOP-B regimen and mediastinal radiotherapy monitored by (67)Gallium scan in 50 patients.**
  Author(s): Zinzani PL, Martelli M, Magagnoli M, Pescarmona E, Scaramucci L, Palombi F, Bendandi M, Martelli MP, Ascani S, Orcioni GF, Pileri SA, Mandelli F, Tura S.

Source: Blood. 1999 November 15; 94(10): 3289-93.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10552937

- **Treatment of multifocal primary cutaneous B-cell lymphoma: a clinical follow-up study of 29 patients.**
  Author(s): Bekkenk MW, Vermeer MH, Geerts ML, Noordijk EM, Heule F, van Voorst Vader PC, van Vloten WA, Meijer CJ, Willemze R.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1999 August; 17(8): 2471-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10561311

- **Treatment of patients with low-grade B-cell lymphoma with the combination of chimeric anti-CD20 monoclonal antibody and CHOP chemotherapy.**
  Author(s): Czuczman MS, Grillo-Lopez AJ, White CA, Saleh M, Gordon L, LoBuglio AF, Jonas C, Klippenstein D, Dallaire B, Varns C.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1999 January; 17(1): 268-76.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10458242

- **Treatment of splenic marginal zone B-cell lymphoma: an analysis of 81 patients.**
  Author(s): Thieblemont C, Felman P, Berger F, Dumontet C, Arnaud P, Hequet O, Arcache J, Callet-Bauchu E, Salles G, Coiffier B.
  Source: Clinical Lymphoma. 2002 June; 3(1): 41-7. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12141954

- **Urate-oxidase in the prevention and treatment of metabolic complications in patients with B-cell lymphoma and leukemia, treated in the Societe Francaise d'Oncologie Pediatrique LMB89 protocol.**
  Author(s): Patte C, Sakiroglu C, Ansoborlo S, Baruchel A, Plouvier E, Pacquement H, Babin-Boilletot A; Societe Francaise d'Oncologie Pediatrique.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 2002 May; 13(5): 789-95.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12075750

Additional Web Resources

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

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

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

General References

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

CHAPTER 4. DISSERTATIONS ON B-CELL LYMPHOMA

Overview

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

Dissertations on B-Cell Lymphoma

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

- **Pathways leading to apoptosis resistance in a murine B-cell lymphoma cell system** by Kurland, John Ford; PhD from The Univ. of Texas H.S.C. at Houston Grad. Sch. of Biomed. Sci., 2003, 124 pages
  http://wwwlib.umi.com/dissertations/fullcit/3083497

Keeping Current

Ask the medical librarian at your library if it has full and unlimited access to the *ProQuest Digital Dissertations* database. From the library, you should be able to do more complete searches via **http://wwwlib.umi.com/dissertations**.

CHAPTER 5. PATENTS ON B-CELL LYMPHOMA

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

Patents on B-Cell Lymphoma

By performing a patent search focusing on B-cell lymphoma, 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.

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

The following is an example of the type of information that you can expect to obtain from a patent search on B-cell lymphoma:

- **Anti-idiotype antibodies reactive with shared idiotopes expressed by B cell lymphomas and autoantibodies**

  Inventor(s): Miller; Richard A. (8 Ohlone, Portola Valley, CA 94025)

  Assignee(s): none reported

  Patent Number: 5,227,159

  Date filed: June 12, 1992

  Abstract: B-cell lymphomas express surface immunoglobulin (immunoglobulin) containing unique idiotypic (idiotype) determinants which may be exploited as tumor specific markers. The inventor has produced murine monoclonal antibodies (MAbs) reactive with the idiotype marker derived from 67 patients with low grade, follicular, small cleaved cell lymphoma. Out of 199 monoclonal antibodies, 47 (24%) were found to react with pooled normal human serum immunoglobulin in concentrations ranging from 0.6.mu.g/ml to 160.mu.g/ml. Of these 40 monoclonal antibodies, 90% cross-reacted with idiotype present in normal serum in levels <50.mu.g/ml. Thirty-two of these anti-idiotypes were directed against a shared idiotope expressed on another patient's lymphoma cells. The frequency of shared idiotope expression defined by each antibody ranged from 0.26% to 3.9% of the B-cell lymphomas tested. A panel of five anti-idiotype antibodies reacted with 80% of AIDS associated lymphomas. Based on the reactivity with these monoclonal antibodies, tumors could be grouped into distinct families. In aggregate, these 32 monoclonal antibodies reacted with a total of 108 of 332 B cell lymphoma cases (32.5%), including 35 of 116 follicular, small cleaved cell lymphomas (30%). Many of these anti-shared idiotopes reacted with more than one histopathologic subtype of lymphoma. Anti-idiotypes have been used in **B-cell lymphoma** diagnosis and therapy. Moreover, applicant has discovered at least seven anti-shared idiotype antibodies that cross react with autoantibodies, e.g., 16.6 and RF. The development of a library of anti-idiotypes reactive with shared idiotopes should facilitate these clinical studies by obviating the need to develop a customized hybridoma for each patient.

  Excerpt(s): The present invention is in the field of immunodiagnosis and immuno-therapy. Specifically, the invention relates to the discovery of antibodies that may be used in the prevention, diagnosis, monitoring, treatment, and amelioration of autoimmune diseases, HIV associated B-cell lymphomas, and B-cell lymphomas generally. Antibodies (immunoglobulins) are produced by the B-cells (B-lymphocytes) of the immune system of animals for the purpose of recognizing and contributing to the elimination of foreign substances found within the host mammal. Any foreign substance, typically but not exclusively a protein, that induces such an antibody response by the host, is termed an antigen. Upon antigen stimulation, mature B-cells differentiate into plasma cells that proliferate and secrete antigen specific antibodies into the serum. Immunoglobulins are Y-shaped, tetrameric molecules consisting of two relatively long polypeptide chains called heavy (H) chains and two shorter polypeptide chains called light (L) chains. Each pair of arms of the Y-shaped structure has specific antigen binding properties and each arm is referred to as an antigen-binding fragment (Fab region). The tail (or base) of the Y structure is a crystallizable fragment (Fc) that includes the binding site for activating cytolytic activity (the Fc region).

  Web site: http://www.delphion.com/details?pn=US05227159__

- **Bispecific antibody effective to treat B-cell lymphoma and cell line**

  Inventor(s): Gingrich; Roger (Iowa City, IA), Link; Brian K. (Carlville, IA), Tso; J. Yun (Menlo Park, CA), Weiner; George (Iowa City, IA)

  Assignee(s): Protein Design Labs, Inc. (Fremont, CA)

  Patent Number: 6,129,914

  Date filed: March 1, 1995

  Abstract: The invention provides bispecific antibodies with selective cytotoxicity against malignant B-cells. The bispecific antibodies bind to an effector cell antigen and to a 28/32 kDa heterodimeric protein on the surface of malignant B-cells. The invention also includes the monospecific components of the bispecific antibodies, humanized versions thereof, and humanized bispecific antibodies. The invention further provides therapeutic and diagnostic methods employing these antibodies.

  Excerpt(s): Administration of monoclonal antibodies (MoAb) has shown promise as a new treatment modality for human malignancy. However, destruction of malignant cells by MoAb does not always occur, even after successful binding of the antibody to the target cell. A second approach to immunotherapy of malignancy involves the manipulation of the cellular immune system. Lymphokines, such as IL-2, can be used to activate both NK cells and T cells isolated from the blood, spleen, or malignant tumors themselves. The anti-tumor effects of such cells have been well documented both in vitro and in vivo. Toxicity of therapy based on IL-2 alone can be severe and may well limit the clinical utility of this therapy. Various forms of bispecific antibodies have been produced. These include BSIgG, which are IgG molecules comprising two distinct heavy chains and two distinct light chains that are secreted by so-called "hybrid hybridomas", and heteroantibody conjugates produced by the chemical conjugation of antibodies or antibody fragments of different specificities. Several investigators have evaluated anti-CD3/anti-tumor bispecific antibody structures as immunotherapeutic agents. Such studies have reported in vitro cytolysis of renal cell carcinoma, melanoma, glioma, lymphoma, leukemia and cells expressing the multidrug-resistance-related glycoprotein. IL-2-activated human peripheral lymphocytes directed by certain anti-CD3/anti-tumor-specific heteroantibody conjugates have also been reported to prevent the growth of human cancer xenografts in nude mice. Studies in vitro, and in vivo in immunodeficient mice bearing human xenografts have reported that certain bispecific antibodies are capable of blocking the growth of both tumor cells bearing certain target antigens and, to some extend, bystander tumor cells that are not recognized by the therapeutic antibody.

  Web site: http://www.delphion.com/details?pn=US06129914__

- **Monoclonal antibody recognizing a surface molecule on a subset of antigen-stimulated T cells and on certain malignancies of T and B cell origin**

  Inventor(s): Bock; Glenn H. (Bethesda, MD), Fleisher; Thomas A. (Bethesda, MD), Kurman; Carole C. (Potomac, MD), Nelson; David L. (Bethesda, MD)

  Assignee(s): The United States of America as represented by the Department of Health (Washington, DC)

  Patent Number: 5,556,947

  Date filed: August 9, 1994

Abstract: This invention provides an IL-6 dependent **B-cell lymphoma** cell line designated DS-1 deposited with the American Type Culture Collection, wherein the cell line is reactive with a monoclonal antibody produced by a hybridoma cell line designated 10D2F6 deposited with the American Type Culture Collection. The invention also provides a purified antigen reactive with a monoclonal antibody produced by 10D2F6. The antigen also exists on DS-1. Also provided is a method of detecting the presence of an antigen-stimulated T-cell comprising detecting the presence of the antigen on a lymphocyte. In addition, the invention provides a method of detecting the presence of a neoplastic cell comprising detecting the presence of the antigen on a cell which is not normal a T-cell.

Excerpt(s): Lymphocytes of B-cell lineage, with the proper cellular signals, ultimately mature into cells which secrete immunoglobulin molecules. Cell lines of B-cell lineage have been commonly produced by infecting cells with Epstein-Barr virus, but this technique produces cell lines at the B-cell stage of development which are not of tumor cell origin. While pre-B-cell lines such as REH and NALM-6 have been described, more mature B-cell lines which have not been Epstein-Barr virus-infected have been more difficult to obtain. Generally, most of the work on plasma cells has depended upon short-term culture of plasma cells from the bone marrow of patients with multiple myeloma. These cells live weeks to months in vitro. While a number of tumor cell antigens have been described for epithelial cell tumors, few have been described for B-cell lineage malignancies. Many of these cells will express protein antigens on their surface during the active growth characteristic of malignant cells. In general, however, these antigens have proven to be upregulated receptors for cytokines (interleukin-2 and transferrin as examples) and not antigens unique to the tumor per se. A cascade of events occurs which leads to the induction and maintenance of T- and B-lymphocyte activation. In general, these events are the result of the encounter, by T-cells, of a variety of stimuli. In vitro, stimuli which induce proliferation include mitogens, antibodies to specific T-cell receptors (such as to the T3 receptor) or reactivation of a subset of normal circulating lymphocytes by previously-encountered antigen (immunologic memory). With stimulation of these memory cells, a variety of surface proteins is expressed which participate in cellular activation and adhesion events. In general, these proteins are not unique to memory cells and can also be induced on the surface of nonmemory lymphocytes upon activation. The identification of a cell surface antigen which is uniquely associated with cells participating in the immunological memory response would be valuable for lymphocyte subpopulation manipulation in vitro and in vivo.

Web site: http://www.delphion.com/details?pn=US05556947__

- **Processes and intermediates for synthetic antibody derivatives**

Inventor(s): Stevenson; George T. (Southampton, GB)

Assignee(s): Imperial College Innovations Limited (London, GB)

Patent Number: 6,136,313

Date filed: March 13, 1995

Abstract: This invention is directed to intermediates for use in the preparation of chimeric antibodies and synthetic antibody derivatives. The intermediates are open- or closed-hinge Fc fragments that have at least one alkylated external sulphydryl group. The invention is also directed to processes for making such intermediates, chimeric antibodies or synthetic antibody derivatives produced from the intermediates, and to

methods of treating **B-Cell Lymphoma** by administering chimeric antibodies or synthetic antibody derivatives produced using the intermediates of the invention.

Excerpt(s): This invention is in the field of antibodies, specifically directed to antibody intermediates which are Fc fragments having a controlled number of chemically functional groups. The Fc antibody intermediates of this invention can be used to build chimeric antibodies and synthetic antibody derivatives that exhibit Fc regions. Antibody derivatives with multiple Fc fragments have a variety of therapeutic applications, especially when the Fc fragments are linked to Fab fragments or functionally similar moieties to form combinations having "chimeric" properties. When chimeric antibodies are used as immunotherapeutic agents, the Fc fragments used to make the intermediates should be derived from the same species as the intended recipient to minimize antigenicity and maximize recruitment of natural effectors. Thus, human Fc fragments are preferred for making chimeric antibodies that are intended for use as immunotherapeutic agents in humans. Chimeric antibodies in which the Fc fragments are derived from normal human IgG and the Fab fragments are derived from xenogeneic antibody (usually mouse monoclonal IgG) maximize cytotoxicity mediated via recruitment of natural effectors. The preparation of chimeric antibodies in which the antigen binding (Fab) arms of rodent IgG antibody are chemically linked by thioether bonds to human IgG, or to the Fc-gamma portion of human IgG, has been reported in Stevenson et al., "Surface Immunoglobulin of B-lymphocytic Tumours as a Therapeutic Target," Cancer Surveys, 4:213 (1985). A chemically synthesized FabFc chimera was prepared in quantity from monoclonal anti-Id and used in the treatment of human lymphoma as described in Hamblin et al., Blood, 42:495 (1987).

Web site: http://www.delphion.com/details?pn=US06136313__

Patent Applications on B-Cell Lymphoma

As of December 2000, U.S. patent applications are open to public viewing.[9] 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 B-cell lymphoma:

- **B-cell lymphoma specific antigen for use in diagnosis and treatment of B-cell malignancies**

  Inventor(s): Hu, Guanghui; (Houston, TX), Li, Yucheng; (Houston, TX), Wang, Shen-Wu; (Sugar Land, TX), Yao, Zhengbin; (Sugar Land, TX)

  Correspondence: Tanox, INC.; 10301 Stella Link; Houston; TX; 77025; US

  Patent Application Number: 20030147887

  Date filed: November 2, 2002

  Abstract: The present invention provides vaccines, antibodies, and diagnostic tools for the diagnosis and/or treatment of B-cell mediated diseases, particularly B-cell lymphomas.

  Excerpt(s): This application claims priority to U.S. Provisional Application No. 60/337,542, filed Nov. 2, 2001. This invention relates generally to molecules, e.g., peptides and antibodies, that interact with **B-Cell Lymphoma** Specific Antigen

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

("BLSA"). Malignant tumors often express characteristic antigens or "markers" which offer a mechanism for tumor prevention, resistance or treatment. The antigens which are characteristic of the tumor may be purified and formulated into vaccines. This may stimulate an antibody response and a cellular immune response which are helpful in controlling tumor growth. At a minimum, the antibodies raised by these antigens can be used as detection tools to monitor the level of lymphoma-associated marker in the host to track the course of the disease, identify patients that have an early stage of the disease that are currently asymptomatic, or to monitor the effectiveness of treatment.

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

- **CLONING AND USES OF THE GENETIC LOCUS BCL-6**

  Inventor(s): DALLA-FAVERA, RICCARDO; (NEW YORK, NY), NIU, HUIFENG; (NEW YORK, NY)

  Correspondence: John P White; Cooper & Dunham; 1185 Avenue OF The Americas; New York; NY; 10036

  Patent Application Number: 20010010922

  Date filed: June 30, 1998

  Abstract: This invention provides an isolated vertebrate nucleic acid molecule the bcl-6 locus. This invention also provides an isolated human nucleic acid molecule of bcl-6 locus. This invention further provides a nucleic acid molecule comprising a nucleic acid molecule of at least 15 nucleotides capable of specifically hybridizing with a sequence included within the sequence of the nucleic acid molecule of bcl-6 locus. This invention provides an isolated vertebrate nucleic acid molecule of bcl-6 operatively linked to a promoter of RNA transcription. This invention provides a vector which comprises the nucleic acid molecule of bcl-6 locus. This invention provides a host vector system for the production of a polypeptide encoded by bcl-6 locus, which comprises the vector of bcl-6 locus in a suitable host. This invention provides a polypeptide encoded by the isolated vertebrate nucleic acid molecule of bcl-6 locus. This invention provides an antibody capable of binding to polypeptide encoded by bcl-6 locus. This invention provides an antagonist capable of blocking the expression of the polypeptide encoded by bcl-6. This invention provides an antisense molecule capable of hybridizing to the nucleic acid molecule of bcl-6. This invention provides an assay for non-Hodgkin's lymphoma, a method for screening putative therapeutic agents for treatment of non-Hodgkin's lymphoma and a method for diagnosing **B-cell lymphoma** in a subject. Finally, this invention provides a method of treating a subject with non-Hodgkin's lymphoma.

  Excerpt(s): This application is a continuation-in-part of U.S. application Ser. No. 08/074,967, filed on Jun. 9, 1993, the contents of which are hereby incorporated by reference. Throughout this application various references are referred to within parenthesis. Disclosures of these publications in their entireties are hereby incorporated by reference into this application to more fully describe the state of the art to which this invention pertains. Full bibliographic citation for these references may be found at the end of each Experimental Detail Section. Non-random chromosomal abnormalities are found in up to 90% of patients with non-Hodgkin's lymphoma (NHL) and have been shown to play an important role in lymphomagenesis by activating proto-oncogenes (1). Some of these translocations, which are associated with specific histologic subsets of NHL, have been characterized at the molecular level. In the t(8;14), t(8;22), and t(2;8) translocations associated with **Burkitt Lymphoma,** L.sub.3-type acute lymphoblastic leukemia and AIDS-associated non-Hodgkin lymphoma (NHL), a known proto-

oncogene, c-myc, was found juxtaposed to the immunoglobulin (Ig) loci (2,3). In the t(14;18) translocation, which is implicated in follicular-type NHL, molecular analysis of the sequences linked to the Ig locus led to the identification of a novel proto-oncogene, bcl-2 (4-6). The t(11;14)(q13;q32), mainly associated with "mantle zone" lymphoma, appears to involve the juxtaposition of the Ig heavy-chain locus with the bcl-1 locus, the site of the candidate proto-oncogene PRAD-1/cyclin D1 (7,8). These well characterized chromosome translocations are associated, however, with only a fraction of NHL cases, while a number of other recurrent translocations remain to be characterized for their genetic components.

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

- **Immunoconjugates and humanized antibodies specific for B-cell lymphoma and leukemia cells**

  Inventor(s): Hansen, Hans; (Mystic Island, NJ), Leung, Shui-on; (Madison, NJ)

  Correspondence: Bernhard D. Saxe; Foley & Lardner; Washington Harbour; 3000 K Street, N.W, Suite 500; Washington; DC; 20007-5109; US

  Patent Application Number: 20020102254

  Date filed: December 22, 2000

  Abstract: A chimeric LL2 monoclonal antibody is described in which the complementarity determining regions (CDRs) of the light and heavy chains of the murine LL2 anti-B-lymphoma, anti-leukemia cell monoclonal antibody has been recombinantly joined to the human kappa and IgG.sub.1 constant region domains, respectively, which retains the immunospecificity and **B-cell lymphoma** and leukemia cell internalization capacity of the parental murine LL2 monoclonal antibody, and which has the potential of exhibiting reduced human anti-mouse antibody production activity. A humanized LL2 monoclonal antibody is described in which the CDRs of the light and heavy chains have been recombinantly joined to a framework sequence of human light and heavy chains variable regions, respectively, and subsequently linked to human kappa and IgG.sub.1 constant region domains, respectively, which retains the immunospecificity and B-lymphoma and leukemia cell internalization capacities of the parental murine and chimeric LL2 monoclonal antibodies, and which has the potential for exhibiting reduced human anti-mouse antibody production activity. Vectors for producing recombinant chimeric and humanized chimeric monoclonal antibodies are provided. Isolated DNAs encoding the amino acid sequences of the LL2 variable light and heavy chain and CDR framework regions are described. Conjugates of chimeric and humanized chimeric LL2 antibodies with cytotoxic agents or labels find use in therapy and diagnosis of B-cell lymphomas and leukemias.

  Excerpt(s): The invention relates generally to immunoconjugates for diagnostic and therapeutic uses in cancer. In particular, the invention relates to recombinantly produced chimeric and humanized monoclonal antibodies directed against **B-cell lymphoma** and leukemia cells, which antibodies can be covalently conjugated to a diagnostic or therapeutic reagent without loss of antibody binding and internalization function and with reduced production of human anti-mouse antibodies. Non-Hodgkins lymphoma (NHL) and chronic lymphocytic leukemia are B-cell malignancies that remain important contributors to cancer mortality. The response of these malignancies to various forms of treatment is mixed. They respond reasonably well to chemotherapy, and, in cases where adequate clinical staging of NHL is possible, as for patients with localized disease, satisfactory treatment may be provided using field radiation therapy

(Hall et al., Radiology for the Radiologist, Lippincott, Philadelphia, 1989, pp 365-376). However, the toxic side effects associated with chemotherapy and the toxicity to the hematopoietic system from local, as well as whole body, radiotherapy, limits the use of these therapeutic methods. About one-half of the patients die from the disease (Posner et al., Blood, 61: 705 (1983)). The use of targeting monoclonal antibodies conjugated to radionuclides or other cytotoxic agents offers the possibility of delivering such agents directly to the tumor site, thereby limiting the exposure of normal tissues to toxic agents (Goldenberg, Semin. Nucl. Med., 19: 332 (1989)). In recent years, the potential of antibody-based therapy and its accuracy in the localization of tumor-associated antigens have been demonstrated both in the laboratory and clinical studies (see., e.g., Thorpe, TIBTECH, 11: 42 (1993); Goldenberg, Scientific American, Science & Medicine, 1: 64 (1994); Baldwin et al., U.S. Pat. Nos. 4,925,922 and 4,916,213; Young, U.S. Pat. No. 4,918,163; U.S. Pat. No. 5,204,095; Irie et al., U.S. Pat. No. 5,196,337; Hellstrom et al., U.S. Pat. No. 5,134,075 and 5,171,665). In general, the use of radio-labeled antibodies or antibody fragments against tumor-associated markers for localization of tumors has been more successful than for therapy, in part because antibody uptake by the tumor is generally low, ranging from only 0.01% to 0.001% of the total dose injected (Vaughan et al., Brit. J. Radiol., 60: 567 (1987)). Increasing the concentration of the radiolabel to increase the dosage to the tumor is counterproductive generally as this also increases exposure of healthy tissue to radioactivity.

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 B-cell lymphoma, 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 "B-cell lymphoma" (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 B-cell lymphoma.

You can also use this procedure to view pending patent applications concerning B-cell lymphoma. 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 6. BOOKS ON B-CELL LYMPHOMA

Overview

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

- **The Clinical Spectrum of AIDS**

  Source: AIDS: A Health Care Management Response.

  Contact: Aspen Publishers, 200 Orchard Ridge Dr, Gaithersburg, MD, 20878, (301) 417-7500, http://www.aspenpub.com.

  Summary: This paper describes the nature of HIV (human immunodeficiency virus) infection and its immunological and clinical manifestations. It also explains the distinct clinical syndromes associated with HIV infection and the signs, course, and treatment of the 12 secondary infectious diseases and 2 malignancies that, alone or in combination, establish that a patient has AIDS (acquired immunodeficiency syndrome). These are pneumocystis carinii pneumonia, other protozoan infections, fungal infections, viral infections, Kaposi's sarcoma, and **B-cell lymphoma.** A variety of other infections, immune-mediated problems, and neurological diseases that are not AIDS-defining but

that are common to patients with HIV infection are also explained. The lack of a cure and the importance of providing the entire population with explicit information about AIDS transmission and behavioral changes needed to avoid contracting it are emphasized.

CHAPTER 7. PERIODICALS AND NEWS ON B-CELL LYMPHOMA

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover B-cell lymphoma.

News Services and Press Releases

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

- **Diffuse large B-cell lymphoma appears to be two distinct diseases**
  Source: Reuters Medical News
  Date: February 03, 2000

- **Radioimmunotherapy of relapsed B-cell lymphoma yields good long-term results**
  Source: Reuters Medical News
  Date: October 02, 1998
- **Case Report: T-Cell-Rich B-Cell Lymphoma In Postmenopausal Woman With IUD**
  Source: Reuters Medical News
  Date: April 27, 1998
- **Link Between Helicobacter Pylori And B-Cell Lymphoma Demonstrated**
  Source: Reuters Medical News
  Date: March 27, 1996

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 "B-cell lymphoma" (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 "B-cell lymphoma" (or synonyms). If you know the name of a company that is relevant to B-cell lymphoma, 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 "B-cell lymphoma" (or synonyms).

Academic Periodicals covering B-Cell Lymphoma

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to B-cell lymphoma. In addition to these sources, you can search for articles covering B-cell lymphoma 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 B-cell lymphoma. 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).

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. Or, you may be able to access these sources from your local medical library.

Mosby's Drug Consult™

Mosby's Drug Consult™ database (also available on CD-ROM and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Subscription information is available at the following hyperlink: **http://www.mosbysdrugconsult.com/**.

PDR*health*

The PDR*health* database is a free-to-use, drug information search engine that has been written for the public in layman's terms. It contains FDA-approved drug information adapted from the Physicians' Desk Reference (PDR) database. PDR*health* can be searched by brand name, generic name, or indication. It features multiple drug interactions reports. Search PDR*health* at **http://www.pdrhealth.com/drug_info/index.html**.

Other Web Sites

Drugs.com (**www.drugs.com**) reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. (**http://www.medletter.com/**) which allows users to download articles on various drugs and therapeutics for a nominal fee.

Researching Orphan Drugs

Although the list of orphan drugs is revised on a daily basis, you can quickly research orphan drugs that might be applicable to B-cell lymphoma by using the database managed by the National Organization for Rare Disorders, Inc. (NORD), at **http://www.rarediseases.org/**. Scroll down the page, and on the left toolbar, click on "Orphan Drug Designation Database." On this page (**http://www.rarediseases.org/search/noddsearch.html**), type "B-cell lymphoma" (or synonyms) into the search box, and click "Submit Query." When you receive your results, note that not all of the drugs may be relevant, as some may have been withdrawn from orphan status. Write down or print out the name of each drug and the relevant contact information. From there, visit the Pharmacopeia Web site and type the name of each orphan drug into the search box at **http://www.nlm.nih.gov/medlineplus/druginformation.html**. You may need to contact the sponsor or NORD for further information.

NORD conducts "early access programs for investigational new drugs (IND) under the Food and Drug Administration's (FDA's) approval 'Treatment INDs' programs which allow for a limited number of individuals to receive investigational drugs before FDA marketing approval." If the orphan product about which you are seeking information is approved for

marketing, information on side effects can be found on the product's label. If the product is not approved, you may need to contact the sponsor.

The following is a list of orphan drugs currently listed in the NORD Orphan Drug Designation Database for B-cell lymphoma:

- **Iodine I 131 murine monoclonal antibody IgG2a to B (trade name: Immurait, L1-2-I-131)**
  http://www.rarediseases.org/nord/search/nodd_full?code=146
- **Technetium Tc-99m murine monoclonal antibody (IgG2 (trade name: LymphoScan)**
  http://www.rarediseases.org/nord/search/nodd_full?code=311
- **Chimeric (murine variable human constant) MAb (C2B**
  http://www.rarediseases.org/nord/search/nodd_full?code=628
- **I-131 radiolabeled B1 monoclonal antibody**
  http://www.rarediseases.org/nord/search/nodd_full?code=772
- **Iodine I 131 murine monoclonal antibody IgG2a to B (trade name: Immurait, L1-2-I-131)**
  http://www.rarediseases.org/nord/search/nodd_full?code=782

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[10]:

- 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/**

[10] 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.[11] 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:[12]

- **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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[11] 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**).

[12] 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[13]

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.[14] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "B-cell lymphoma" (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	18479
Books / Periodicals / Audio Visual	7
Consumer Health	942
Meeting Abstracts	57
Other Collections	125
Total	19610

HSTAT[15]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[16] 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.[17] Simply search by "B-cell lymphoma" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

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

[14] 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).

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

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

[17] 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[18]

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.[19] 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.[20] 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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[18] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[19] 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.

[20] 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 B-cell lymphoma 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 B-cell lymphoma. 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 B-cell lymphoma. 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 "B-cell lymphoma":

- Guides on B-cell lymphoma

  Hodgkin's Disease
  http://www.nlm.nih.gov/medlineplus/hodgkinsdisease.html

  Lymphoma
  http://www.nlm.nih.gov/medlineplus/lymphoma.html

- Other guides

  Stem Cells and Stem Cell Transplantation
  http://www.nlm.nih.gov/medlineplus/stemcellsandstemcelltransplantation.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 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 B-cell lymphoma. 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 B-cell lymphoma. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with B-cell lymphoma.

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 B-cell lymphoma. 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 "B-cell lymphoma" (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 "B-cell lymphoma". 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 "B-cell lymphoma" (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 "B-cell lymphoma" (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.[21]

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

[21] 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)[22]:

- **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/**

[22] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), **http://hml.org/CHIS/**
- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Chicago), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center, Peoria), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), **http://www.centralbap.com/education/community/library.cfm**
- **Kentucky:** University of Kentucky - Health Information Library (Chandler Medical Center, Lexington), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center, Portland), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital (Brunswick), **http://www.parkviewhospital.org/**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), **http://www.wmhcc.org/Library/**

- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), **http://www.deerlodge.mb.ca/crane_library/about.asp**
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School, Worchester), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information (Detroit), **http://www.henryford.com/body.cfm?id=39330**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**

- **Nevada:** Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital, Rahway), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York, Syracuse), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), **http://www.sfh-tulsa.com/services/healthinfo.asp**
- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), **http://www.hsls.pitt.edu/guides/chi/hopwood/index_html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System, Williamsport), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://www.mghlib.mcgill.ca/**

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), **http://www.rcrh.org/Services/Library/Default.asp**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), **http://www.swmedicalcenter.com/body.cfm?id=72**

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://cancerweb.ncl.ac.uk/omd/**
- Rare Diseases Terms (Office of Rare Diseases): **http://ord.aspensys.com/asp/diseases/diseases.asp**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a**). The NIH suggests the following Web sites in the ADAM Medical Encyclopedia when searching for information on B-cell lymphoma:

- **Basic Guidelines for B-Cell Lymphoma**

  Burkitt lymphoma
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001308.htm

- **Signs & Symptoms for B-Cell Lymphoma**

  Swelling
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003103.htm

  Swollen lymph nodes
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003097.htm

- **Diagnostics and Tests for B-Cell Lymphoma**

  Bone marrow biopsy
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003934.htm

  Bone scan
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003833.htm

Chest X-ray
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003804.htm

Lymph node biopsy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003933.htm

Peritoneal fluid analysis
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003626.htm

Pleural fluid analysis
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003624.htm

- **Background Topics for B-Cell Lymphoma**

Chemotherapy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002324.htm

Radiation therapy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001918.htm

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

B-CELL LYMPHOMA 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]

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]

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]

Acute lymphoblastic leukemia: ALL. A quickly progressing disease in which too many immature white blood cells called lymphoblasts are found in the blood and bone marrow. Also called acute lymphocytic leukemia. [NIH]

Acute lymphocytic leukemia: ALL. A quickly progressing disease in which too many immature white blood cells called lymphoblasts are found in the blood and bone marrow. Also called acute lymphoblastic leukemia. [NIH]

Acute myelogenous leukemia: AML. A quickly progressing disease in which too many immature blood-forming cells are found in the blood and bone marrow. Also called acute myeloid leukemia or acute nonlymphocytic leukemia. [NIH]

Acute myeloid leukemia: AML. A quickly progressing disease in which too many immature blood-forming cells are found in the blood and bone marrow. Also called acute myelogenous leukemia or acute nonlymphocytic leukemia. [NIH]

Acute nonlymphocytic leukemia: A quickly progressing disease in which too many immature blood-forming cells are found in the blood and bone marrow. Also called acute myeloid leukemia or acute myelogenous leukemia. [NIH]

Acute renal: A condition in which the kidneys suddenly stop working. In most cases, kidneys can recover from almost complete loss of function. [NIH]

Adaptability: Ability to develop some form of tolerance to conditions extremely different from those under which a living organism evolved. [NIH]

Adenocarcinoma: A malignant epithelial tumor with a glandular organization. [NIH]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

Adipose Tissue: Connective tissue composed of fat cells lodged in the meshes of areolar tissue. [NIH]

Adnexa: The appendages of the eye, as the lacrimal apparatus, the eyelids, and the extraocular muscles. [NIH]

Adverse Effect: An unwanted side effect of treatment. [NIH]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [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]

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]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH2) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amplification: The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

Amyloid: A general term for a variety of different proteins that accumulate as extracellular fibrils of 7-10 nm and have common structural features, including a beta-pleated sheet conformation and the ability to bind such dyes as Congo red and thioflavine (Kandel, Schwartz, and Jessel, Principles of Neural Science, 3rd ed). [NIH]

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]

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]

Anaplasia: Loss of structural differentiation and useful function of neoplastic cells. [NIH]

Anaplastic: A term used to describe cancer cells that divide rapidly and bear little or no resemblance to normal cells. [NIH]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

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]

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]

Antibody Diversity: The phenomenon of immense variability characteristic of antibodies, which enables the immune system to react specifically against the essentially unlimited kinds of antigens it encounters. Antibody diversity is accounted for by three main theories: 1) the germ line theory, which holds that each antibody-producing cell has genes coding for all possible antibody specificities, but expresses only the one stimulated by antigen; 2) the somatic mutation theory, which holds that antibody-producing cells contain only a few genes, which produce antibody diversity by mutation; and 3) the gene rearrangement theory, which holds that antibody diversity is generated by the rearrangement of variable region gene segments during the differentiation of the antibody-producing cells. [NIH]

Antibody therapy: Treatment with an antibody, a substance that can directly kill specific tumor cells or stimulate the immune system to kill tumor cells. [NIH]

Antibody-Producing Cells: Cells of the lymphoid series that can react with antigen to produce specific cell products called antibodies. Various cell subpopulations, often B-lymphocytes, can be defined, based on the different classes of immunoglobulins that they synthesize. [NIH]

Anticoagulant: A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble

substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antigen-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]

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]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anus: The opening of the rectum to the outside of the body. [NIH]

Aplasia: Lack of development of an organ or tissue, or of the cellular products from an organ or tissue. [EU]

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]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Artery: Vessel-carrying blood from the heart to various parts of the body. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Ataxia: Impairment of the ability to perform smoothly coordinated voluntary movements. This condition may affect the limbs, trunk, eyes, pharnyx, larnyx, and other structures. Ataxia may result from impaired sensory or motor function. Sensory ataxia may result from posterior column injury or peripheral nerve diseases. Motor ataxia may be associated with cerebellar diseases; cerebral cortex diseases; thalamic diseases; basal ganglia diseases; injury to the red nucleus; and other conditions. [NIH]

Auditory: Pertaining to the sense of hearing. [EU]

Auditory nerve: The eight cranial nerve; also called vestibulocochlear nerve or acoustic nerve. [NIH]

Autoantibodies: Antibodies that react with self-antigens (autoantigens) of the organism that produced them. [NIH]

Autoantigens: Endogenous tissue constituents that have the ability to interact with autoantibodies and cause an immune response. [NIH]

Autodigestion: Autolysis; a condition found in disease of the stomach: the stomach wall is

digested by the gastric juice. [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 bone marrow transplantation: A procedure in which bone marrow is removed from a person, stored, and then given back to the person after intensive treatment. [NIH]

Autologous lymphocytes: A person's white blood cells. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and disease. [NIH]

Autologous tumor cells: Cancer cells from an individual's own tumor. [NIH]

Avian: A plasmodial infection in birds. [NIH]

Avian Leukosis: A group of transmissible viral diseases of chickens and turkeys. Liver tumors are found in most forms, but tumors can be found elsewhere. [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]

Bacterium: Microscopic organism which may have a spherical, rod-like, or spiral unicellular or non-cellular body. Bacteria usually reproduce through asexual processes. [NIH]

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

Basal Ganglia Diseases: Diseases of the basal ganglia including the putamen; globus pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [NIH]

Base: In chemistry, the nonacid part of a salt; a substance that combines with acids to form salts; a substance that dissociates to give hydroxide ions in aqueous solutions; a substance whose molecule or ion can combine with a proton (hydrogen ion); a substance capable of donating a pair of electrons (to an acid) for the formation of a coordinate covalent bond. [EU]

Basilar Artery: The artery formed by the union of the right and left vertebral arteries; it runs from the lower to the upper border of the pons, where it bifurcates into the two posterior cerebral arteries. [NIH]

BCL-1: Codes for cyclin D1, a stimulatory component of the cell cycle clock. Involved in breast, head and neck cancers. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Beta Rays: A stream of positive or negative electrons ejected with high energy from a disintegrating atomic nucleus; most biomedically used isotopes emit negative particles (electrons or negatrons, rather than positrons). Cathode rays are low-energy negative electrons produced in cathode ray tubes, also called television tubes or oscilloscopes. [NIH]

Beta-pleated: Particular three-dimensional pattern of amyloidoses. [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]

Biliary: Having to do with the liver, bile ducts, and/or gallbladder. [NIH]

Biliary Tract: The gallbladder and its ducts. [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]

Biomarkers: Substances sometimes found in an increased amount in the blood, other body fluids, or tissues and that may suggest the presence of some types of cancer. Biomarkers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and GI tract cancers), and PSA (prostate cancer). Also called tumor markers. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

Biopsy specimen: Tissue removed from the body and examined under a microscope to determine whether disease is present. [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]

Bispecific antibodies: Antibodies developed in the laboratory to recognize more than one protein on the surface of different cells. Examples include bispecific antibodies 2B1, 520C9xH22, mDX-H210, and MDX447. [NIH]

Bladder: The organ that stores urine. [NIH]

Blast Crisis: Rapid increase in the proportion of blast cells in the blood and bone marrow. [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]

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 biopsy: The removal of a sample of tissue from the bone marrow with a needle for examination under a microscope. [NIH]

Bone Marrow Transplantation: The transference of bone marrow from one human or animal to another. [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]

Bronchi: The larger air passages of the lungs arising from the terminal bifurcation of the trachea. [NIH]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Calcium: A basic element found in nearly all organized tissues. It is a member of the alkaline earth family of metals with the atomic symbol Ca, atomic number 20, and atomic weight 40. Calcium is the most abundant mineral in the body and combines with phosphorus to form calcium phosphate in the bones and teeth. It is essential for the normal functioning of nerves and muscles and plays a role in blood coagulation (as factor IV) and in many enzymatic processes. [NIH]

Carboplatin: An organoplatinum compound that possesses antineoplastic activity. [NIH]

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]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Case series: A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. [NIH]

Caspase: Enzyme released by the cell at a crucial stage in apoptosis in order to shred all cellular proteins. [NIH]

Catabolism: Any destructive metabolic process by which organisms convert substances into excreted compounds. [EU]

Cathode: An electrode, usually an incandescent filament of tungsten, which emits electrons in an X-ray tube. [NIH]

Caudal: Denoting a position more toward the cauda, or tail, than some specified point of reference; same as inferior, in human anatomy. [EU]

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Celiac Disease: A disease characterized by intestinal malabsorption and precipitated by gluten-containing foods. The intestinal mucosa shows loss of villous structure. [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 Division: The fission of a cell. [NIH]

Cell Lineage: The developmental history of cells as traced from the first division of the original cell or cells in the embryo. [NIH]

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]

Central Nervous System: The main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebral Cortex: The thin layer of gray matter on the surface of the cerebral hemisphere that develops from the telencephalon and folds into gyri. It reaches its highest development in man and is responsible for intellectual faculties and higher mental functions. [NIH]

Cervical: Relating to the neck, or to the neck of any organ or structure. Cervical lymph nodes are located in the neck; cervical cancer refers to cancer of the uterine cervix, which is the lower, narrow end (the "neck") of the uterus. [NIH]

Cervix: The lower, narrow end of the uterus that forms a canal between the uterus and vagina. [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]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Chimera: An individual that contains cell populations derived from different zygotes. [NIH]

Chlorambucil: An anticancer drug that belongs to the family of drugs called alkylating agents. [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 leukemia: A slowly progressing cancer of the blood-forming tissues. [NIH]

Clathrin: The main structural coat protein of coated vesicles which play a key role in the intracellular transport between membranous organelles. Clathrin also interacts with cytoskeletal proteins. [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 study: A research study in which patients receive treatment in a clinic or other

medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

Clinical trial: A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

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]

Coated Vesicles: Vesicles formed when cell-membrane coated pits invaginate and pinch off. The outer surface of these vesicles are covered with a lattice-like network of coat proteins, such as clathrin, coat protein complex proteins, or caveolins. [NIH]

Colon: The long, coiled, tubelike organ that removes water from digested food. The remaining material, solid waste called stool, moves through the colon to the rectum and leaves the body through the anus. [NIH]

Combination chemotherapy: Treatment using more than one anticancer drug. [NIH]

Combination Therapy: Association of 3 drugs to treat AIDS (AZT + DDC or DDI + protease inhibitor). [NIH]

Combinatorial: A cut-and-paste process that churns out thousands of potentially valuable compounds at once. [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]

Complementarity Determining Regions: Three regions (CDR1, CDR2 and CDR3) of amino acid sequence in theimmunoglobulin variable region that are highly divergent. Together the CDRs from the light and heavy immunoglobulin chains form a surface that is complementary to the antigen. These regions are also present in other members of the immunoglobulin superfamily, for example, T-cell receptors (receptors, antigen, T-cell). [NIH]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices

are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complementary medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complete remission: The disappearance of all signs of cancer. Also called a complete response. [NIH]

Complete response: The disappearance of all signs of cancer in response to treatment. This does not always mean the cancer has been cured. [NIH]

Computational Biology: A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

Conception: The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

Concomitant: Accompanying; accessory; joined with another. [EU]

Conjugated: Acting or operating as if joined; simultaneous. [EU]

Conjugation: 1. The act of joining together or the state of being conjugated. 2. A sexual process seen in bacteria, ciliate protozoa, and certain fungi in which nuclear material is exchanged during the temporary fusion of two cells (conjugants). In bacterial genetics a form of sexual reproduction in which a donor bacterium (male) contributes some, or all, of its DNA (in the form of a replicated set) to a recipient (female) which then incorporates differing genetic information into its own chromosome by recombination and passes the recombined set on to its progeny by replication. In ciliate protozoa, two conjugants of separate mating types exchange micronuclear material and then separate, each now being a fertilized cell. In certain fungi, the process involves fusion of two gametes, resulting in union of their nuclei and formation of a zygote. 3. In chemistry, the joining together of two compounds to produce another compound, such as the combination of a toxic product with some substance in the body to form a detoxified product, which is then eliminated. [EU]

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]

Constriction: The act of constricting. [NIH]

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]

Controlled clinical trial: A clinical study that includes a comparison (control) group. The comparison group receives a placebo, another treatment, or no treatment at all. [NIH]

Cortisone: A natural steroid hormone produced in the adrenal gland. It can also be made in the laboratory. Cortisone reduces swelling and can suppress immune responses. [NIH]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Crossing-over: The exchange of corresponding segments between chromatids of homologous chromosomes during meiosia, forming a chiasma. [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]

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

Cytogenetic Analysis: Examination of chromosomes to diagnose, classify, screen for, or manage genetic diseases and abnormalities. Following preparation of the sample, karyotyping is performed and/or the specific chromosomes are analyzed. [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]

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]

Cytoskeletal Proteins: Major constituent of the cytoskeleton found in the cytoplasm of eukaryotic cells. They form a flexible framework for the cell, provide attachment points for organelles and formed bodies, and make communication between parts of the cell possible. [NIH]

Cytotoxic: Cell-killing. [NIH]

Cytotoxicity: Quality of being capable of producing a specific toxic action upon cells of special organs. [NIH]

Daunorubicin: Very toxic anthracycline aminoglycoside antibiotic isolated from Streptomyces peucetius and others, used in treatment of leukemias and other neoplasms. [NIH]

De novo: In cancer, the first occurrence of cancer in the body. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Deletion: A genetic rearrangement through loss of segments of DNA (chromosomes), bringing sequences, which are normally separated, into close proximity. [NIH]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [NIH]

Denaturation: Rupture of the hydrogen bonds by heating a DNA solution and then cooling it rapidly causes the two complementary strands to separate. [NIH]

Dendrites: Extensions of the nerve cell body. They are short and branched and receive stimuli from other neurons. [NIH]

Dendritic: 1. Branched like a tree. 2. Pertaining to or possessing dendrites. [EU]

Dendritic cell: A special type of antigen-presenting cell (APC) that activates T lymphocytes. [NIH]

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]

Desensitization: The prevention or reduction of immediate hypersensitivity reactions by administration of graded doses of allergen; called also hyposensitization and immunotherapy. [EU]

Diagnostic procedure: A method used to identify a disease. [NIH]

Diffusion: The tendency of a gas or solute to pass from a point of higher pressure or concentration to a point of lower pressure or concentration and to distribute itself throughout the available space; a major mechanism of biological transport. [NIH]

Digestion: The process of breakdown of food for metabolism and use by the body. [NIH]

Digestive tract: The organs through which food passes when food is eaten. These organs are the mouth, esophagus, stomach, small and large intestines, and rectum. [NIH]

Dimerization: The process by which two molecules of the same chemical composition form a condensation product or polymer. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Discrete: Made up of separate parts or characterized by lesions which do not become blended; not running together; separate. [NIH]

Disease Progression: The worsening of a disease over time. This concept is most often used for chronic and incurable diseases where the stage of the disease is an important determinant of therapy and prognosis. [NIH]

Dissection: Cutting up of an organism for study. [NIH]

Dissociation: 1. The act of separating or state of being separated. 2. The separation of a molecule into two or more fragments (atoms, molecules, ions, or free radicals) produced by the absorption of light or thermal energy or by solvation. 3. In psychology, a defense mechanism in which a group of mental processes are segregated from the rest of a person's mental activity in order to avoid emotional distress, as in the dissociative disorders (q.v.), or in which an idea or object is segregated from its emotional significance; in the first sense it is roughly equivalent to splitting, in the second, to isolation. 4. A defect of mental integration in which one or more groups of mental processes become separated off from normal consciousness and, thus separated, function as a unitary whole. [EU]

Distal: Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

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]

Doxorubicin: Antineoplastic antibiotic obtained from Streptomyces peucetics. It is a

hydroxy derivative of daunorubicin and is used in treatment of both leukemia and solid tumors. [NIH]

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 Interactions: The action of a drug that may affect the activity, metabolism, or toxicity of another drug. [NIH]

Duct: A tube through which body fluids pass. [NIH]

Duodenum: The first part of the small intestine. [NIH]

Dyes: Chemical substances that are used to stain and color other materials. The coloring may or may not be permanent. Dyes can also be used as therapeutic agents and test reagents in medicine and scientific research. [NIH]

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

Effector cell: A cell that performs a specific function in response to a stimulus; usually used to describe cells in the immune system. [NIH]

Efficacy: The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

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]

Electrophoresis: An electrochemical process in which macromolecules or colloidal particles with a net electric charge migrate in a solution under the influence of an electric current. [NIH]

Elementary Particles: Individual components of atoms, usually subatomic; subnuclear particles are usually detected only when the atomic nucleus decays and then only transiently, as most of them are unstable, often yielding pure energy without substance, i.e., radiation. [NIH]

Emaciation: Clinical manifestation of excessive leanness usually caused by disease or a lack of nutrition. [NIH]

Embolus: Bit of foreign matter which enters the blood stream at one point and is carried until it is lodged or impacted in an artery and obstructs it. It may be a blood clot, an air bubble, fat or other tissue, or clumps of bacteria. [NIH]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

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]

Endometrium: The layer of tissue that lines the uterus. [NIH]

Enhancer: Transcriptional element in the virus genome. [NIH]

Environmental Exposure: The exposure to potentially harmful chemical, physical, or

biological agents in the environment or to environmental factors that may include ionizing radiation, pathogenic organisms, or toxic chemicals. [NIH]

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

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]

Epithelial: Refers to the cells that line the internal and external 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]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [NIH]

Esophageal: Having to do with the esophagus, the muscular tube through which food passes from the throat to the stomach. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Etoposide: A semisynthetic derivative of podophyllotoxin that exhibits antitumor activity. Etoposide inhibits DNA synthesis by forming a complex with topoisomerase II and DNA. This complex induces breaks in double stranded DNA and prevents repair by topoisomerase II binding. Accumulated breaks in DNA prevent entry into the mitotic phase of cell division, and lead to cell death. Etoposide acts primarily in the G2 and S phases of the cell cycle. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Evoke: The electric response recorded from the cerebral cortex after stimulation of a peripheral sense organ. [NIH]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Exon: The part of the DNA that encodes the information for the actual amino acid sequence of the protein. In many eucaryotic genes, the coding sequences consist of a series of exons alternating with intron sequences. [NIH]

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]

Extraocular: External to or outside of the eye. [NIH]

Extremity: A limb; an arm or leg (membrum); sometimes applied specifically to a hand or foot. [EU]

Eye socket: One of the two cavities in the skull which contains an eyeball. Each eye is located in a bony socket or orbit. [NIH]

Facial: Of or pertaining to the face. [EU]

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]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Flow Cytometry: Technique using an instrument system for making, processing, and displaying one or more measurements on individual cells obtained from a cell suspension. Cells are usually stained with one or more fluorescent dyes specific to cell components of interest, e.g., DNA, and fluorescence of each cell is measured as it rapidly transverses the excitation beam (laser or mercury arc lamp). Fluorescence provides a quantitative measure of various biochemical and biophysical properties of the cell, as well as a basis for cell sorting. Other measurable optical parameters include light absorption and light scattering, the latter being applicable to the measurement of cell size, shape, density, granularity, and stain uptake. [NIH]

Foramen: A natural hole of perforation, especially one in a bone. [NIH]

Gallate: Antioxidant present in tea. [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]

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]

Gastric: Having to do with the stomach. [NIH]

Gastric Mucosa: Surface epithelium in the stomach that invaginates into the lamina propria, forming gastric pits. Tubular glands, characteristic of each region of the stomach (cardiac, gastric, and pyloric), empty into the gastric pits. The gastric mucosa is made up of several different kinds of cells. [NIH]

Gastritis: Inflammation of the stomach. [EU]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [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 Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Gene Expression Profiling: The determination of the pattern of genes expressed i.e., transcribed, under specific circumstances or in a specific cell. [NIH]

Gene Fusion: Fusion of structural genes to analyze protein behavior or fusion of regulatory sequences with structural genes to determine mechanisms of regulation. [NIH]

Gene Rearrangement: The ordered rearrangement of gene regions by DNA recombination such as that which occurs normally during development. [NIH]

Gene Silencing: Interruption or suppression of the expression of a gene at transcriptional or translational levels. [NIH]

Gene Targeting: The integration of exogenous DNA into the genome of an organism at sites where its expression can be suitably controlled. This integration occurs as a result of

homologous recombination. [NIH]

Gene Therapy: The introduction of new genes into cells for the purpose of treating disease by restoring or adding gene expression. Techniques include insertion of retroviral vectors, transfection, homologous recombination, and injection of new genes into the nuclei of single cell embryos. The entire gene therapy process may consist of multiple steps. The new genes may be introduced into proliferating cells in vivo (e.g., bone marrow) or in vitro (e.g., fibroblast cultures) and the modified cells transferred to the site where the gene expression is required. Gene therapy may be particularly useful for treating enzyme deficiency diseases, hemoglobinopathies, and leukemias and may also prove useful in restoring drug sensitivity, particularly for leukemia. [NIH]

Gene-modified: Cells that have been altered to contain different genetic material than they originally contained. [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]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genomics: The systematic study of the complete DNA sequences (genome) of organisms. [NIH]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Germinal Center: The activated center of a lymphoid follicle in secondary lymphoid tissue where B-lymphocytes are stimulated by antigens and helper T cells (T-lymphocytes, helper-inducer) are stimulated to generate memory cells. [NIH]

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]

Glomerular: Pertaining to or of the nature of a glomerulus, especially a renal glomerulus. [EU]

Glomeruli: Plural of glomerulus. [NIH]

Glomerulonephritis: Glomerular disease characterized by an inflammatory reaction, with leukocyte infiltration and cellular proliferation of the glomeruli, or that appears to be the result of immune glomerular injury. [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]

Gluten: The protein of wheat and other grains which gives to the dough its tough elastic character. [EU]

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]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

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]

Hairy cell leukemia: A type of chronic leukemia in which the abnormal white blood cells appear to be covered with tiny hairs when viewed under a microscope. [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]

Hemato: A selective mechanism opposing the passage of most large-molecular compounds from the blood to the cerebro-spinal fluid and brain tissue; offers some protection against intoxication. [NIH]

Hematologic malignancies: Cancers of the blood or bone marrow, including leukemia and lymphoma. Also called hematologic cancers. [NIH]

Hematopoietic Stem Cell Transplantation: The transference of stem cells from one animal or human to another (allogeneic), or within the same individual (autologous). The source for the stem cells may be the bone marrow or peripheral blood. Stem cell transplantation has been used as an alternative to autologous bone marrow transplantation in the treatment of a variety of neoplasms. [NIH]

Hematopoietic Stem Cells: Progenitor cells from which all blood cells derive. [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]

Hemoglobinopathies: A group of inherited disorders characterized by structural alterations within the hemoglobin molecule. [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]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatocytes: The main structural component of the liver. They are specialized epithelial

cells that are organized into interconnected plates called lobules. [NIH]

Hepatologist: A doctor who specializes in liver diseases. [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]

Heterochromatin: The portion of chromosome material that remains condensed and is transcriptionally inactive during interphase. [NIH]

Heteroduplex Analysis: A method of detecting gene mutation by mixing PCR-amplified mutant and wild-type DNA followed by denaturation and reannealing. The resultant products are resolved by gel electrophoresis, with single base substitutions detectable under optimal electrophoretic conditions and gel formulations. Large base pair mismatches may also be analyzed by using electron microscopy to visualize heteroduplex regions. [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]

Histones: Small chromosomal proteins (approx 12-20 kD) possessing an open, unfolded structure and attached to the DNA in cell nuclei by ionic linkages. Classification into the various types (designated histone I, histone II, etc.) is based on the relative amounts of arginine and lysine in each. [NIH]

Homeobox: Distinctive sequence of DNA bases. [NIH]

Homeostasis: The processes whereby the internal environment of an organism tends to remain balanced and stable. [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]

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-cell: A cell whose metabolism is used for the growth and reproduction of a virus. [NIH]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used of endocrine factors as opposed to neural or somatic. [EU]

Humour: 1. A normal functioning fluid or semifluid of the body (as the blood, lymph or bile) especially of vertebrates. 2. A secretion that is itself an excitant of activity (as certain hormones). [EU]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

Hybridization: The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

Hybridoma: A hybrid cell resulting from the fusion of a specific antibody-producing spleen cell with a myeloma cell. [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]

Hypercalcemia: Abnormally high level of calcium in the blood. [NIH]

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]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hypoxia: Reduction of oxygen supply to tissue below physiological levels despite adequate perfusion of the tissue by blood. [EU]

Idiotype: The unique antigenic determinant in the variable region. [NIH]

Ileum: The lower end of the small intestine. [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]

Immunoconjugates: Combinations of diagnostic or therapeutic substances linked with specific immune substances such as immunoglobulins, monoclonal antibodies or antigens. Often the diagnostic or therapeutic substance is a radionuclide. These conjugates are useful tools for specific targeting of drugs and radioisotopes in the chemotherapy and radioimmunotherapy of certain cancers. [NIH]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [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]

Immunogenic: Producing immunity; evoking an immune response. [EU]

Immunoglobulins: Glycoproteins present in the blood (antibodies) and in other tissue. They are classified by structure and activity into five classes (IgA, IgD, IgE, IgG, IgM). [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]

Immunologic Memory: The altered state of immunologic responsiveness resulting from initial contact with antigen, which enables the individual to produce antibodies more rapidly and in greater quantity in response to secondary antigenic stimulus. [NIH]

Immunology: The study of the body's immune system. [NIH]

Immunophenotyping: Process of classifying cells of the immune system based on structural and functional differences. The process is commonly used to analyze and sort T-lymphocytes into subsets based on CD antigens by the technique of flow cytometry. [NIH]

Immunosuppressant: An agent capable of suppressing immune responses. [EU]

Immunosuppression: Deliberate prevention or diminution of the host's immune response. It may be nonspecific as in the administration of immunosuppressive agents (drugs or radiation) or by lymphocyte depletion or may be specific as in desensitization or the simultaneous administration of antigen and immunosuppressive drugs. [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]

Immunotoxins: Semisynthetic conjugates of various toxic molecules, including radioactive isotopes and bacterial or plant toxins, with specific immune substances such as immunoglobulins, monoclonal antibodies, and antigens. The antitumor or antiviral immune substance carries the toxin to the tumor or infected cell where the toxin exerts its poisonous effect. [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]

Incidental: 1. Small and relatively unimportant, minor; 2. Accompanying, but not a major part of something; 3. (To something) Liable to occur because of something or in connection with something (said of risks, responsibilities, .) [EU]

Incision: A cut made in the body during surgery. [NIH]

Indolent: A type of cancer that grows slowly. [NIH]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators

or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Infarction: A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

Infection: 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

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]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

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]

Intercellular Adhesion Molecule-1: A cell-surface ligand with a role in leukocyte adhesion and inflammation. Its production is induced by gamma-interferon and it is required for neutrophil migration into inflamed tissue. [NIH]

Interferon: A biological response modifier (a substance that can improve the body's natural response to disease). Interferons interfere with the division of cancer cells and can slow tumor growth. There are several types of interferons, including interferon-alpha, -beta, and -gamma. These substances are normally produced by the body. They are also made in the laboratory for use in treating cancer and other diseases. [NIH]

Interferon-alpha: One of the type I interferons produced by peripheral blood leukocytes or lymphoblastoid cells when exposed to live or inactivated virus, double-stranded RNA, or bacterial products. It is the major interferon produced by virus-induced leukocyte cultures and, in addition to its pronounced antiviral activity, it causes activation of NK cells. [NIH]

Interleukin-2: Chemical mediator produced by activated T lymphocytes and which regulates the proliferation of T cells, as well as playing a role in the regulation of NK cell activity. [NIH]

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]

Interphase: The interval between two successive cell divisions during which the chromosomes are not individually distinguishable and DNA replication occurs. [NIH]

Intestinal: Having to do with the intestines. [NIH]

Intestinal Mucosa: The surface lining of the intestines where the cells absorb nutrients. [NIH]

Intestine: A long, tube-shaped organ in the abdomen that completes the process of digestion. There is both a large intestine and a small intestine. Also called the bowel. [NIH]

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intravascular: Within a vessel or vessels. [EU]

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]

Iodine: A nonmetallic element of the halogen group that is represented by the atomic symbol I, atomic number 53, and atomic weight of 126.90. It is a nutritionally essential element, especially important in thyroid hormone synthesis. In solution, it has anti-infective properties and is used topically. [NIH]

Iodine-131: Radioactive isotope of iodine. [NIH]

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]

Ischemia: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

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]

Kidney Transplantation: The transference of a kidney from one human or animal to another. [NIH]

Kinesin: A microtubule-associated mechanical adenosine triphosphatase, that uses the energy of ATP hydrolysis to move organelles along microtubules toward the plus end of the microtubule. The protein is found in squid axoplasm, optic lobes, and in bovine brain. Bovine kinesin is a heterotetramer composed of two heavy (120 kDa) and two light (62 kDa) chains. EC 3.6.1.-. [NIH]

Lacrimal: Pertaining to the tears. [EU]

Lacrimal Apparatus: The tear-forming and tear-conducting system which includes the lacrimal glands, eyelid margins, conjunctival sac, and the tear drainage system. [NIH]

Lacrimal gland: The small almond-shaped structure that produces tears; located just above the outer corner of the eye. [NIH]

Large Intestine: The part of the intestine that goes from the cecum to the rectum. The large intestine absorbs water from stool and changes it from a liquid to a solid form. The large intestine is 5 feet long and includes the appendix, cecum, colon, and rectum. Also called colon. [NIH]

Larynx: An irregularly shaped, musculocartilaginous tubular structure, lined with mucous membrane, located at the top of the trachea and below the root of the tongue and the hyoid bone. It is the essential sphincter guarding the entrance into the trachea and functioning

secondarily as the organ of voice. [NIH]

Latent: Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

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]

Leiomyosarcoma: A tumor of the muscles in the uterus, abdomen, or pelvis. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukoencephalopathy: A condition with spongy holes in the brain's white matter. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Lipid: Fat. [NIH]

Lipopolysaccharide: Substance consisting of polysaccaride and lipid. [NIH]

Liposomal: A drug preparation that contains the active drug in very tiny fat particles. This fat-encapsulated drug is absorbed better, and its distribution to the tumor site is improved. [NIH]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Liver Transplantation: The transference of a part of or an entire liver from one human or animal to another. [NIH]

Local therapy: Treatment that affects cells in the tumor and the area close to it. [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]

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]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphoblastic: One of the most aggressive types of non-Hodgkin lymphoma. [NIH]

Lymphoblasts: Interferon produced predominantly by leucocyte cells. [NIH]

Lymphocyte Count: A count of the number of lymphocytes in the blood. [NIH]

Lymphocyte Depletion: Immunosuppression by reduction of circulating lymphocytes or by T-cell depletion of bone marrow. The former may be accomplished in vivo by thoracic duct drainage or administration of antilymphocyte serum. The latter is performed ex vivo on bone marrow before its transplantation. [NIH]

Lymphocytes: White blood cells formed in the body's lymphoid tissue. The nucleus is round or ovoid with coarse, irregularly clumped chromatin while the cytoplasm is typically pale blue with azurophilic (if any) granules. Most lymphocytes can be classified as either T or B (with subpopulations of each); those with characteristics of neither major class are called null cells. [NIH]

Lymphocytic: Referring to lymphocytes, a type of white blood cell. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphoma: A general term for various neoplastic diseases of the lymphoid tissue. [NIH]

Lysogeny: The phenomenon by which a temperate phage incorporates itself into the DNA of a bacterial host, establishing a kind of symbiotic relation between prophage and bacterium which results in the perpetuation of the prophage in all the descendants of the bacterium until induction by various agents, such as ultraviolet radiation, releases the phage, which then becomes virulent and lyses the bacterium. [NIH]

Maintenance therapy: Treatment that is given to help a primary (original) treatment keep working. Maintenance therapy is often given to help keep cancer in remission. [NIH]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malignancy: A cancerous tumor that can invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant tumor: A tumor capable of metastasizing. [NIH]

Meatus: A canal running from the internal auditory foramen through the petrous portion of the temporal bone. It gives passage to the facial and auditory nerves together with the auditory branch of the basilar artery and the internal auditory veins. [NIH]

Mediastinum: The area between the lungs. The organs in this area include the heart and its large blood vessels, the trachea, the esophagus, the bronchi, and lymph nodes. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [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 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]

Meningitis: Inflammation of the meninges. When it affects the dura mater, the disease is termed pachymeningitis; when the arachnoid and pia mater are involved, it is called leptomeningitis, or meningitis proper. [EU]

Meningoencephalitis: An inflammatory process involving the brain (encephalitis) and meninges (meningitis), most often produced by pathogenic organisms which invade the central nervous system, and occasionally by toxins, autoimmune disorders, and other conditions. [NIH]

Mental: Pertaining to the mind; psychic. 2. (L. mentum chin) pertaining to the chin. [EU]

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]

Methotrexate: An antineoplastic antimetabolite with immunosuppressant properties. It is an inhibitor of dihydrofolate reductase and prevents the formation of tetrahydrofolate, necessary for synthesis of thymidylate, an essential component of DNA. [NIH]

Methyltransferase: A drug-metabolizing enzyme. [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]

Microorganism: An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

Microscopy: The application of microscope magnification to the study of materials that cannot be properly seen by the unaided eye. [NIH]

Microtubules: Slender, cylindrical filaments found in the cytoskeleton of plant and animal cells. They are composed of the protein tubulin. [NIH]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Mitosis: A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

Mitotic: Cell resulting from mitosis. [NIH]

Mitoxantrone: An anthracenedione-derived antineoplastic agent. [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]

Monotherapy: A therapy which uses only one drug. [EU]

Morphology: The science of the form and structure of organisms (plants, animals, and other forms of life). [NIH]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Mucositis: A complication of some cancer therapies in which the lining of the digestive system becomes inflamed. Often seen as sores in the mouth. [NIH]

Multiple Myeloma: A malignant tumor of plasma cells usually arising in the bone marrow; characterized by diffuse involvement of the skeletal system, hyperglobulinemia, Bence-Jones proteinuria, and anemia. [NIH]

Myelin: The fatty substance that covers and protects nerves. [NIH]

Myeloma: Cancer that arises in plasma cells, a type of white blood cell. [NIH]

Myopathy: Any disease of a muscle. [EU]

Nasolacrimal: Pertaining to the nose and lacrimal apparatus. [EU]

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]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

Neoplasm: A new growth of benign or malignant tissue. [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]

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]

Neurosyphilis: A late form of syphilis that affects the brain and may lead to dementia and death. [NIH]

Neutrons: Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier nuclei during their decay. [NIH]

Neutrophil: A type of white blood cell. [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]

Nonmalignant: Not cancerous. [NIH]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleic Acid Hybridization: The process whereby two single-stranded polynucleotides form a double-stranded molecule, with hydrogen bonding between the complementary bases in the two strains. [NIH]

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]

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]

Oncogene: A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens. [NIH]

Oncogenic: Chemical, viral, radioactive or other agent that causes cancer; carcinogenic. [NIH]

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]

Operon: The genetic unit consisting of a feedback system under the control of an operator gene, in which a structural gene transcribes its message in the form of mRNA upon blockade of a repressor produced by a regulator gene. Included here is the attenuator site of bacterial operons where transcription termination is regulated. [NIH]

Opportunistic Infections: An infection caused by an organism which becomes pathogenic under certain conditions, e.g., during immunosuppression. [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]

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]

Overall survival: The percentage of subjects in a study who have survived for a defined period of time. Usually reported as time since diagnosis or treatment. Often called the survival rate. [NIH]

Palate: The structure that forms the roof of the mouth. It consists of the anterior hard palate and the posterior soft palate. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatitis: Acute or chronic inflammation of the pancreas, which may be asymptomatic or symptomatic, and which is due to autodigestion of a pancreatic tissue by its own enzymes. It is caused most often by alcoholism or biliary tract disease; less commonly it may be associated with hyperlipaemia, hyperparathyroidism, abdominal trauma (accidental or operative injury), vasculitis, or uraemia. [EU]

Panniculitis: General term for inflammation of adipose tissue, usually of the skin, characterized by reddened subcutaneous nodules. [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]

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]

Partial remission: The shrinking, but not complete disappearance, of a tumor in response to therapy. Also called partial response. [NIH]

Particle: A tiny mass of material. [EU]

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]

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]

Pathophysiology: Altered functions in an individual or an organ due to disease. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Pelvis: The lower part of the abdomen, located between the hip bones. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Perfusion: Bathing an organ or tissue with a fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread. [NIH]

Periorbital: Situated around the orbit, or eye socket. [EU]

Peripheral blood: Blood circulating throughout the body. [NIH]

Peripheral Neuropathy: Nerve damage, usually affecting the feet and legs; causing pain, numbness, or a tingling feeling. Also called "somatic neuropathy" or "distal sensory polyneuropathy." [NIH]

Peripheral stem cell transplantation: A method of replacing blood-forming cells destroyed by cancer treatment. Immature blood cells (stem cells) in the circulating blood that are similar to those in the bone marrow are given after treatment to help the bone marrow recover and continue producing healthy blood cells. Transplantation may be autologous (an individual's own blood cells saved earlier), allogeneic (blood cells donated by someone else), or syngeneic (blood cells donated by an identical twin). Also called peripheral stem cell support. [NIH]

Petroleum: Naturally occurring complex liquid hydrocarbons which, after distillation, yield combustible fuels, petrochemicals, and lubricants. [NIH]

Pharmacodynamic: Is concerned with the response of living tissues to chemical stimuli, that is, the action of drugs on the living organism in the absence of disease. [NIH]

Pharmacokinetic: The mathematical analysis of the time courses of absorption, distribution, and elimination of drugs. [NIH]

Pharmacologic: Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

Pharynx: The hollow tube about 5 inches long that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach). [NIH]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

Phorbol: Class of chemicals that promotes the development of tumors. [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]

Pigment: A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair. [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]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

Plasmacytoma: Any discrete, presumably solitary, mass of neoplastic plasma cells either in bone marrow or various extramedullary sites. [NIH]

Plasmid: An autonomously replicating, extra-chromosomal DNA molecule found in many bacteria. Plasmids are widely used as carriers of cloned genes. [NIH]

Pneumonia: Inflammation of the lungs. [NIH]

Podophyllotoxin: The main active constituent of the resin from the roots of may apple or mandrake (Podophyllum peltatum and P. emodi). It is a potent spindle poison, toxic if taken internally, and has been used as a cathartic. It is very irritating to skin and mucous membranes, has keratolytic actions, has been used to treat warts and keratoses, and may have antineoplastic properties, as do some of its congeners and derivatives. [NIH]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymerase Chain Reaction: In vitro method for producing large amounts of specific DNA or RNA fragments of defined length and sequence from small amounts of short oligonucleotide flanking sequences (primers). The essential steps include thermal denaturation of the double-stranded target molecules, annealing of the primers to their complementary sequences, and extension of the annealed primers by enzymatic synthesis with DNA polymerase. The reaction is efficient, specific, and extremely sensitive. Uses for the reaction include disease diagnosis, detection of difficult-to-isolate pathogens, mutation analysis, genetic testing, DNA sequencing, and analyzing evolutionary relationships. [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

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]

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]

Practicability: A non-standard characteristic of an analytical procedure. It is dependent on the scope of the method and is determined by requirements such as sample throughout and costs. [NIH]

Practice Guidelines: Directions or principles presenting current or future rules of policy for the health care practitioner to assist him in patient care decisions regarding diagnosis, therapy, or related clinical circumstances. The guidelines may be developed by government agencies at any level, institutions, professional societies, governing boards, or by the convening of expert panels. The guidelines form a basis for the evaluation of all aspects of health care and delivery. [NIH]

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]

Prednisolone: A glucocorticoid with the general properties of the corticosteroids. It is the drug of choice for all conditions in which routine systemic corticosteroid therapy is indicated, except adrenal deficiency states. [NIH]

Prednisone: A synthetic anti-inflammatory glucocorticoid derived from cortisone. It is biologically inert and converted to prednisolone in the liver. [NIH]

Probe: An instrument used in exploring cavities, or in the detection and dilatation of strictures, or in demonstrating the potency of channels; an elongated instrument for exploring or sounding body cavities. [NIH]

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]

Prognostic factor: A situation or condition, or a characteristic of a patient, that can be used to estimate the chance of recovery from a disease, or the chance of the disease recurring (coming back). [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protein C: A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

Protein Conformation: The characteristic 3-dimensional shape of a protein, including the secondary, supersecondary (motifs), tertiary (domains) and quaternary structure of the peptide chain. Quaternary protein structure describes the conformation assumed by multimeric proteins (aggregates of more than one polypeptide chain). [NIH]

Protein S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Proteinuria: The presence of protein in the urine, indicating that the kidneys are not working properly. [NIH]

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]

Protozoa: A subkingdom consisting of unicellular organisms that are the simplest in the animal kingdom. Most are free living. They range in size from submicroscopic to macroscopic. Protozoa are divided into seven phyla: Sarcomastigophora, Labyrinthomorpha, Apicomplexa, Microspora, Ascetospora, Myxozoa, and Ciliophora. [NIH]

Protozoal: Having to do with the simplest organisms in the animal kingdom. Protozoa are single-cell organisms, such as ameba, and are different from bacteria, which are not members of the animal kingdom. Some protozoa can be seen without a microscope. [NIH]

Protozoan: 1. Any individual of the protozoa; protozoon. 2. Of or pertaining to the protozoa; protozoal. [EU]

Protozoan Infections: Infections with unicellular organisms of the subkingdom Protozoa. [NIH]

Provirus: Virus that is integrated into the chromosome of a host cell and is transmitted in that form from one host cell generation to another without leading to the lysis of the host cells. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

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]

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]

Purines: A series of heterocyclic compounds that are variously substituted in nature and are known also as purine bases. They include adenine and guanine, constituents of nucleic acids, as well as many alkaloids such as caffeine and theophylline. Uric acid is the metabolic end product of purine metabolism. [NIH]

Purpura: Purplish or brownish red discoloration, easily visible through the epidermis, caused by hemorrhage into the tissues. [NIH]

Pyrimidines: A family of 6-membered heterocyclic compounds occurring in nature in a wide variety of forms. They include several nucleic acid constituents (cytosine, thymine, and uracil) and form the basic structure of the barbiturates. [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]

Radioactive: Giving off radiation. [NIH]

Radioactivity: The quality of emitting or the emission of corpuscular or electromagnetic radiations consequent to nuclear disintegration, a natural property of all chemical elements of atomic number above 83, and possible of induction in all other known elements. [EU]

Radioimmunotherapy: Radiotherapy where cytotoxic radionuclides are linked to antibodies in order to deliver toxins directly to tumor targets. Therapy with targeted radiation rather than antibody-targeted toxins (immunotoxins) has the advantage that adjacent tumor cells, which lack the appropriate antigenic determinants, can be destroyed by radiation cross-fire. Radioimmunotherapy is sometimes called targeted radiotherapy, but this latter term can also refer to radionuclides linked to non-immune molecules (radiotherapy). [NIH]

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]

Reactive Oxygen Species: Reactive intermediate oxygen species including both radicals and non-radicals. These substances are constantly formed in the human body and have been shown to kill bacteria and inactivate proteins, and have been implicated in a number of diseases. Scientific data exist that link the reactive oxygen species produced by inflammatory phagocytes to cancer development. [NIH]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

Receptors, Antigen: Molecules on the surface of B- and T-lymphocytes that recognize and combine with specific antigens. [NIH]

Recombinant: A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Recombination: The formation of new combinations of genes as a result of segregation in crosses between genetically different parents; also the rearrangement of linked genes due to crossing-over. [NIH]

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]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [NIH]

Red Nucleus: A pinkish-yellow portion of the midbrain situated in the rostral mesencephalic tegmentum. It receives a large projection from the contralateral half of the cerebellum via the superior cerebellar peduncle and a projection from the ipsilateral motor cortex. [NIH]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

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]

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]

Renal cell carcinoma: A type of kidney cancer. [NIH]

Repressor: Any of the specific allosteric protein molecules, products of regulator genes, which bind to the operator of operons and prevent RNA polymerase from proceeding into the operon to transcribe messenger RNA. [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]

Response rate: The percentage of patients whose cancer shrinks or disappears after treatment. [NIH]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

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]

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]

Risk patient: Patient who is at risk, because of his/her behaviour or because of the type of person he/she is. [EU]

Rituximab: A type of monoclonal antibody used in cancer detection or therapy. Monoclonal antibodies are laboratory-produced substances that can locate and bind to cancer cells. [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]

Sarcoma: A connective tissue neoplasm formed by proliferation of mesodermal cells; it is usually highly malignant. [NIH]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Segregation: The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

Semen: The thick, yellowish-white, viscid fluid secretion of male reproductive organs discharged upon ejaculation. In addition to reproductive organ secretions, it contains spermatozoa and their nutrient plasma. [NIH]

Semisynthetic: Produced by chemical manipulation of naturally occurring substances. [EU]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Serine: A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [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]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

Skeletal: Having to do with the skeleton (boney part of the body). [NIH]

Small cell lung cancer: A type of lung cancer in which the cells appear small and round when viewed under the microscope. Also called oat cell lung cancer. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Soft tissue: Refers to muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. [NIH]

Solid tumor: Cancer of body tissues other than blood, bone marrow, or the lymphatic system. [NIH]

Soma: The body as distinct from the mind; all the body tissue except the germ cells; all the axial body. [NIH]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Somatic mutations: Alterations in DNA that occur after conception. Somatic mutations can occur in any of the cells of the body except the germ cells (sperm and egg) and therefore are not passed on to children. These alterations can (but do not always) cause cancer or other diseases. [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]

Sphincter: A ringlike band of muscle fibres that constricts a passage or closes a natural orifice; called also musculus sphincter. [EU]

Spinal cord: The main trunk or bundle of nerves running down the spine through holes in the spinal bone (the vertebrae) from the brain to the level of the lower back. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Statistically significant: Describes a mathematical measure of difference between groups. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone. [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]

Stenosis: Narrowing or stricture of a duct or canal. [EU]

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]

Stimulants: Any drug or agent which causes stimulation. [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]

Stomatitis: Inflammation of the oral mucosa, due to local or systemic factors which may involve the buccal and labial mucosa, palate, tongue, floor of the mouth, and the gingivae. [EU]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Stricture: The abnormal narrowing of a body opening. Also called stenosis. [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]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Survival Analysis: A class of statistical procedures for estimating the survival function (function of time, starting with a population 100% well at a given time and providing the percentage of the population still well at later times). The survival analysis is then used for making inferences about the effects of treatments, prognostic factors, exposures, and other covariates on the function. [NIH]

Survival Rate: The proportion of survivors in a group, e.g., of patients, studied and followed over a period, or the proportion of persons in a specified group alive at the beginning of a time interval who survive to the end of the interval. It is often studied using life table methods. [NIH]

Symphysis: A secondary cartilaginous joint. [NIH]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

Syphilis: A contagious venereal disease caused by the spirochete Treponema pallidum. [NIH]

Systemic: Affecting the entire body. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [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]

Thalamic: Cell that reaches the lateral nucleus of amygdala. [NIH]

Thalamic Diseases: Disorders of the centrally located thalamus, which integrates a wide range of cortical and subcortical information. Manifestations include sensory loss, movement disorders; ataxia, pain syndromes, visual disorders, a variety of neuropsychological conditions, and coma. Relatively common etiologies include cerebrovascular disorders; craniocerebral trauma; brain neoplasms; brain hypoxia; intracranial hemorrhages; and infectious processes. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermal: Pertaining to or characterized by heat. [EU]

Threonine: An essential amino acid occurring naturally in the L-form, which is the active form. It is found in eggs, milk, gelatin, and other proteins. [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]

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]

Thyroid Gland: A highly vascular endocrine gland consisting of two lobes, one on either side of the trachea, joined by a narrow isthmus; it produces the thyroid hormones which are concerned in regulating the metabolic rate of the body. [NIH]

Thyroid Hormones: Hormones secreted by the thyroid gland. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tonsil: A round-to-oval mass of lymphoid tissue embedded in the lateral wall of the pharynx situated on each side of the fauces, between the anterior and posterior pillars of the soft palate. [NIH]

Topical: On the surface of the body. [NIH]

Torsion: A twisting or rotation of a bodily part or member on its axis. [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]

Toxin: A poison; frequently used to refer specifically to a protein produced by some higher plants, certain animals, and pathogenic bacteria, which is highly toxic for other living organisms. Such substances are differentiated from the simple chemical poisons and the vegetable alkaloids by their high molecular weight and antigenicity. [EU]

Trachea: The cartilaginous and membranous tube descending from the larynx and branching into the right and left main bronchi. [NIH]

Transcriptase: An enzyme which catalyses the synthesis of a complementary mRNA molecule from a DNA template in the presence of a mixture of the four ribonucleotides (ATP, UTP, GTP and CTP). [NIH]

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]

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]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Trauma: Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

Treatment Outcome: Evaluation undertaken to assess the results or consequences of management and procedures used in combating disease in order to determine the efficacy, effectiveness, safety, practicability, etc., of these interventions in individual cases or series. [NIH]

Tumor marker: A substance sometimes found in an increased amount in the blood, other body fluids, or tissues and which may mean that a certain type of cancer is in the body. Examples of tumor markers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). Also called biomarker. [NIH]

Tumor 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]

Tunica: A rather vague term to denote the lining coat of hollow organs, tubes, or cavities. [NIH]

Tyramine: An indirect sympathomimetic. Tyramine does not directly activate adrenergic receptors, but it can serve as a substrate for adrenergic uptake systems and monoamine oxidase so it prolongs the actions of adrenergic transmitters. It also provokes transmitter release from adrenergic terminals. Tyramine may be a neurotransmitter in some invertebrate nervous systems. [NIH]

Uraemia: 1. An excess in the blood of urea, creatinine, and other nitrogenous end products

of protein and amino acids metabolism; more correctly referred to as azotemia. 2. In current usage the entire constellation of signs and symptoms of chronic renal failure, including nausea, vomiting anorexia, a metallic taste in the mouth, a uraemic odour of the breath, pruritus, uraemic frost on the skin, neuromuscular disorders, pain and twitching in the muscles, hypertension, edema, mental confusion, and acid-base and electrolyte imbalances. [EU]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [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]

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]

Vagina: The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vasculitis: Inflammation of a blood vessel. [NIH]

Vasodilators: Any nerve or agent which induces dilatation of the blood vessels. [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]

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]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Villous: Of a surface, covered with villi. [NIH]

Vinca Alkaloids: A class of alkaloids from the genus of apocyanaceous woody herbs including periwinkles. They are some of the most useful antineoplastic agents. [NIH]

Vincristine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

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]

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 Integration: Insertion of viral DNA into host-cell DNA. This includes integration of phage DNA into bacterial DNA (lysogeny) to form a prophage or integration of retroviral DNA into cellular DNA to form a provirus. [NIH]

Viscera: Any of the large interior organs in any one of the three great cavities of the body, especially in the abdomen. [NIH]

Viscum: A genus of Old World parasitic plants of the Loranthaceae. Viscum album and Phorandendron flavescens were formerly used as emmenagogues, cardiac stimulants, and vasodilators. The plants contain toxins, lectins, tyramine, phenethylamines, and other useful or dangerous compounds. [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]

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]

Windpipe: A rigid tube, 10 cm long, extending from the cricoid cartilage to the upper border of the fifth thoracic vertebra. [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]

Zygote: The fertilized ovum. [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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