Oral Cancer

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

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

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The collective knowledge generated from academic and applied research summarized in various references has been critical in the creation of this book which is best viewed as a comprehensive compilation and collection of information prepared by various official agencies which produce publications on oral cancer. Books in this series draw from various agencies and institutions associated with the United States Department of Health and Human Services, and in particular, the Office of the Secretary of Health and Human Services (OS), the Administration for Children and Families (ACF), the Administration on Aging (AOA), the Agency for Healthcare Research and Quality (AHRQ), the Agency for Toxic Substances and Disease Registry (ATSDR), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Healthcare Financing Administration (HCFA), the Health Resources and Services Administration (HRSA), the Indian Health Service (IHS), the institutions of the National Institutes of Health (NIH), the Program Support Center (PSC), and the Substance Abuse and Mental Health Services Administration (SAMHSA). In addition to these sources, information gathered from the National Library of Medicine, the United States Patent Office, the European Union, and their related organizations has been invaluable in the creation of this book. Some of the work represented was financially supported by the Research and Development Committee at INSEAD. This support is gratefully acknowledged. Finally, special thanks are owed to Tiffany Freeman for her excellent editorial support.

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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 oral cancer is indexed in search engines, such as **www.google.com** or others, a non-systematic approach to Internet research can be not only time consuming, but also incomplete. This book was created for medical professionals, students, and members of the general public who want to know as much as possible about oral cancer, using the most advanced research tools available and spending the least amount of time doing so.

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

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

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

The Editors

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

CHAPTER 1. STUDIES ON ORAL CANCER

Overview

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

The Combined Health Information Database

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

- **Perform a Death-Defying Act: The 90-second Oral Cancer Examination**

  Source: JADA. Journal of the American Dental Association. 132 (Supplement): 36S-40S. November 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

  Summary: A comprehensive **oral cancer** examination takes approximately 90 seconds and includes a review of the patient's medical and dental history, extraoral and intraoral inspections of the head and neck, and manual palpation of related specific sites. This article reviews each step of an **oral cancer** examination. Each step is described and illustrated with a full color photograph. The article is included in a special supplement to the Journal of the American Dental Association (JADA) that presents eight articles on

the topic of the dentist's role in preventing and detecting **oral cancer.** This summary of the **oral cancer** examination is also available in poster form from the National Institute of Dental and Craniofacial Research (www.nohic.nidcr.nih.gov/pubs/detect). The author stresses that all adult patients should receive this part of a comprehensive oral examination on a routine basis. All lesions that have not resolved within two weeks of manifestation warrant a biopsy or referral to an appropriate provider. One sidebar lists points to remember when screening for **oral cancer.** 15 figures. 1 table. 3 references.

- **Oral Cancer: Practical Prevention and Early Detection for the Dental Team**

  Source: New York State Dental Journal (NYSDJ). 68(7): 44-54. August-September 2002.

  Contact: Available from Dental Society of the State of New York. 7 Elk Street, Albany, NY 12207. (518) 465-0044.

  Summary: Approximately 2,000 patients a year are diagnosed with **oral cancer** in New York state. In an effort to control this deadly disease, Governor George Pataki has taken a leadership role in the United States by mandating and funding training for dentists in the prevention and early detection of **oral cancer.** The purpose of this article is to highlight the epidemiology of **oral cancer,** to show how the dental profession can contribute to the health of the citizens of New York state, and to provide practical guidelines for both tobacco cessation intervention and utilization of existing technology for the early detection of **oral cancer** and precancerous conditions in the general dental practice setting. 11 figures. 6 tables. 44 references.

- **Oral Cancer and its Detection: History-taking and the Diagnostics Phase of Management**

  Source: JADA. Journal of the American Dental Association. 132 (Supplement): 12S-18S. November 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

  Summary: Comprehensive patient evaluation begins with an accurate analysis of all factors of the patient's history before the physical examination is performed. Risk factor identification is particularly important in most cases of oral mucosal dysplasia (abnormal cells in the mucosal tissue of the mouth) and carcinoma (cancer), as it alerts the clinician to an increased susceptibility for such alterations. In this article, the author identifies the factors a clinician should consider when evaluating the dental patient, from initial presentation and risk factor identification to the use of traditional assessment parameters. The article is from a special supplement to the Journal of the American Dental Association (JADA) that presents eight articles on the topic of the dentist's role in preventing and detecting **oral cancer.** The author presents methods of assessing and analyzing a patient's oral health status. The author discusses carcinogens and cofactors, as well as dietary considerations, in the development of oral mucosal pre-cancer and cancer. New and evolving diagnostic tools, coupled with cell and tissue characterization by an oral and maxillofacial pathologist, remain critical in terms of patient management and in maintaining optimum standards of care. The authors concludes that a comprehensive oral examination must include integration of each patient's in depth health history and the physical findings. Appreciation of subtle surface changes as a possible harbinger of pathology and the traditional process of observation combined with these new diagnostic tools can result in earlier diagnosis and thus, improved outcomes. The article is illustrated with full color photographs of oral and histological findings. 7 figures. 32 references.

- **Comment On: Oral Cancer in Young Adults**

  Source: British Dental Journal. 188(7): 366. April 8, 2000.

  Contact: Available from Stockton Press. Houndmills, Basingstoke, Hampshire, RG21 6XS, United Kingdom. E-mail: subscriptions@nature.com.

  Summary: Malignancy of the mouth in childhood and early adulthood is uncommon. This commentary accompanies an article presenting three cases of **oral cancer** in young adults. The commentary stresses that there is a need to establish the precise cancer causing mechanisms that underly such disease, as they may be different than those of oral squamous cell carcinoma (SCC) in older individuals. The authors of the commentary stress that the low incidence of oral SCC and other malignant or potentially malignant disease in young adults indicates strongly that specific screening programs in this population is neither realistic nor cost effective. However, dental health care staff have an important role in the care of young adults with possible malignant disease. The social history of all patients should be carefully reviewed, and appropriate preventive advice provided regarding tobacco and alcohol habits. In addition, all patients should be advised to maintain a high standard of oral hygiene. Delay in referral of individuals (regardless of patient age) with a potentially malignant lesion can limit potential treatment options, and ultimately adversely affect prognosis. 27 references.

- **Perspectives of Maryland Dentists on Oral Cancer**

  Source: JADA. Journal of the American Dental Association. 132(1): 65-72. January 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

  Summary: Maryland's mortality rate for oral and pharyngeal cancer is seventh highest overall in the United States, sixth highest for men and third highest for African American men. As part of a statewide needs assessment and in follow up to a mail survey of Maryland general dentists, focus groups were conducted to obtain more in depth information about why dentists do not provide a comprehensive **oral cancer** examination for most of their patients and how to solve this problem from a dentist's perspective. This article reports on the findings of these focus groups. A trained focus group moderator conducted two focus groups of general practice dentists in two locations in Maryland. Five major themes emerged from the two focus groups: inaccurate knowledge about **oral cancer;** inconsistency in **oral cancer** examinations; lack of confidence in when and how to palpate for abnormalities; lack of time to routinely provide **oral cancer** examinations; and recommendations to help resolve these issues. The focus groups provided a rich source of ideas on how to best provide dentists with continuing education about **oral cancer** prevention and early detection. Participants also provided opinions about the need to improve the public's awareness of **oral cancer** and its prevention. The authors conclude that dentists need to include comprehensive **oral cancer** examinations as part of their routine oral examinations for all appropriate patients. 21 references.

- **Professional and Community Efforts to Prevent Morbidity and Mortality from Oral Cancer**

  Source: JADA. Journal of the American Dental Association. 132 (Supplement): 24S-29S. November 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

Summary: Oral and pharyngeal (throat) cancers cause significant morbidity (related illness) and mortality (death); indeed, there has been little improvement in survival rates in the past 30 years. Because early diagnosis can significantly increase survival rates, the authors of this article summarize several approaches to educating and mobilizing the dental profession and the public about this problem. The article is included in a special supplement to the Journal of the American Dental Association (JADA) that presents eight articles on the topic of the dentist's role in preventing and detecting **oral cancer.** In this article, the authors report on their findings of many different approaches that have been used to define the problem and initiate change. These approaches include surveys, focus groups, development of consortia, media programs, flyers, leaflets, prescription pads, legislation, and professional endorsements. The authors report results of some survey research. For example, in Maryland in 1996, only 20 percent of adults reported receiving an **oral cancer** examination, and most oral cancers were diagnosed at late stages by physicians, not dentists. Results of the public educational campaigns in the regions of New York, New Jersey, and Maryland have not been formally evaluated, but there is a developing consensus that **oral cancer** diagnostic practices in the regions with active educational programs are increasing. The authors conclude that coalitions or partnerships among individuals and organizations from government, academia, private practice, industry, the general community, and the media can affect awareness about **oral cancer** prevention and early detection on a regional basis. The authors also note that providing **oral cancer** diagnostic services as a routine part of an oral examination also may motivate patients to visit the dentist at least once a year. 1 figure. 19 references.

- **Chronic Alcoholism: A Common Risk Factor in Oral Cancer and Alcoholic Cirrhosis**

  Source: Compendium of Continuing Education in Dentistry. 22(3): 49-51. July 2001.

  Contact: Available from Dental Learning Systems. 241 Forsgate Drive, Jamesburg, NJ 08831. (800) 926-7636.

  Summary: Oral cancer and alcoholic cirrhosis are relatively common diseases encountered in medical and dental practices. This continuing education article reviews the clinical, pathophysiological, and epidemiological characteristics of these two conditions. A major risk factor common to both **oral cancer** and alcoholic cirrhosis (liver scarring) is the excessive use of alcohol. A challenge for practitioners and researchers is to become mindful of the connection between **oral cancer** and alcoholic cirrhosis. The authors discuss earlier studies exploring these relationships and the potential mechanisms for development of these diseases. The authors conclude by encouraging dentists to educate and counsel their patients regarding the effects of alcohol, tobacco, diet, and lifestyle on **oral cancer** and other systemic diseases, including alcoholic cirrhosis. Patients with risk factors who have not yet developed any clinical disease should be advised to change their lifestyle and behavior (cease excessive drinking and smoking immediately). A healthy diet, risk in fruits and vegetables, should be instituted into a daily routine. These measures, in combination with regular visits to the dentist and physician for routine examinations, can prevent **oral cancer,** alcoholic cirrhosis, and many other systemic diseases, especially within the African American community.

- **Oral Cancer in Young Adults: Reports of Three Cases and Review of the Literature**

  Source: British Dental Journal. 188(7): 362-365. April 8, 2000.

  Contact: Available from Stockton Press. Houndmills, Basingstoke, Hampshire, RG21 6XS, United Kingdom. E-mail: subscriptions@nature.com.

Summary: Oral cancer in young adults in not common in the United Kingdom. However, since it is so rare, when cases present they are often misdiagnosed and inappropriately treated, leading to delay in definitive treatment. This may, in turn, lead to a poorer prognosis for these patients. This article presents three cases of **oral cancer** in young adults (aged under 30 years) and reviews the literature with respect to **oral cancer** in this group of patients. The authors note that it is debatable if **oral cancer** in younger adults carries an inherently poor prognosis and presents with more aggressive tumors. Young adult patients who develop **oral cancer** often are not exposed to the traditional risk factors of tobacco and alcohol. The authors conclude that **oral cancer** should always be considered as part of the differential diagnosis in patients who present with persistent ulceration, leukoplakia, erythroplakia, or swellings with no obvious local cause, particularly in high risk sites of the tongue and floor of the mouth. Accompanying this article is a brief commentary article. 2 figures. 1 table. 21 references.

- **Molecular Markers of the Risk of Oral Cancer (editorial)**

  Source: New England Journal of Medicine. 344(17): 1323-1325. April 26, 2001.

  Contact: Available from New England Journal of Medicine. 10 Shattuck Street, Boston, MA 02115-6094.

  Summary: Oral leukoplakia (white patches on the oral mucosa) may develop into squamous cell carcinoma, which has a poor prognosis. Risk factors for oral carcinoma (cancer) have been identified, but there are no reliable predictors of the outcome in individual patients with oral leukoplakia. This editorial comments on an article in the same issue in which the authors conclude that the DNA content in cells of oral leukoplakia can be used to predict the risk of oral carcinoma. The editorial notes that these findings represent an important advance in the molecular assessment of the risk of **oral cancer** in patients with leukoplakia. Surprisingly, the degree of dysplasia (abnormal tissue development) did not correlate with DNA content or the risk of cancer. The editorial authors note that only half of oral cancers develop at the site of leukoplakia. The rest occur at different sites because in these cases the carcinogenic process is multi-focal. The new molecular data have important implications for the standard of care of patients with oral leukoplakia. Local management ranges from watchful waiting to resection with widely varying margin widths, depending on histologic and clinical features. Molecular information can redefine the assessment of the risk of **oral cancer** and even guide treatment. The authors call for the establishment of standard molecular assays to help plan the management of oral leukoplakia. Although not perfect or generally available, assays that identify loss of heterozygosity and determine ploidy (nuclear DNA content) are an improvement on current ways of assessing the risk of **oral cancer** in patients with leukoplakia. 1 figure.

- **Classification and Identification of Genes Associated With Oral Cancer Based on Gene Expression Profiles: A Preliminary Study**

  Source: New York State Dental Journal. NYSDJ. 69(2): 23-26. February 2003.

  Contact: Available from Dental Society of the State of New York. 7 Elk Street, Albany, NY 12207. (518) 465-0044.

  Summary: Oral squamous cell carcinoma (OSCC) is an aggressive cancer (malignancy). The five year survival rate remains largely unchanged for the past 40 years. Early diagnosis has been shown to correlate with increased survival. In order to improve current treatment strategies for OSCC, it is necessary to understand the genetic and molecular networks underlying this disease. In this article, the authors report on a

preliminary study of the application of DNA microarrays to study OSCC. Using computational and statistical algorithms, the authors were able to differentiate (or classify) 'cancer' and 'normal' samples based on the behavior of the gene expression profiles. The authors found 651 genes to be associated with cancer. The article describes a preliminary study of current developments from the Human Genome Project (HGP) and its application to OSCC. 2 figures. 21 references.

- **Oral Cancer Prevention and Early Detection: The Role of the Dental Hygienist**

  Source: Journal of Practical Hygiene. 12(2): 28-30. March-April 2003.

  Contact: Available from Montage Media Corporation. 1000 Wyckoff Avenue, Mahwah, NJ 07430-3164. (201) 891-3200.

  Summary: The high morbidity rates for **oral cancer** are cause for a major paradigm shift in how dental teams view oral lesions. Working beyond early detection to actual prevention, dental hygienists are among the first to view potential cancerous sites. The three primary detection and control programs include: the participation of dental professionals in promoting smoking cessation; the recognition and treatment of premalignant oral lesions (primarily leukoplakia); and the early detection of **oral cancer.** This article reviews the problem of **oral cancer** control, the risk factors, and the recommended approaches to reduce the risk of morbidity and mortality associated with **oral cancer.** An adequate oral soft tissue examination is essential and can result in an encompassing differential diagnosis which, in turn, will facilitate approaches in the diagnosis of premalignant and early malignant lesions, and accelerate a confirmable biopsy (brush biopsy) for definitive diagnosis and appropriate treatment. The authors stress the importance of the dental hygienist as a significant member of the patient education and care team. 6 figures. 11 references.

- **Ask the Expert: What Are the Diagnostic Protocols for Oral Cancer Screenings?**

  Source: JADA. Journal of the American Dental Association. 132(1): 83-84. January 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

  Summary: There has been a great deal of attention to the need for dentists to provide **oral cancer** screenings as part of their routine clinical examinations. This article answers the question of the dentist's responsibilities regarding the diagnosis of oral lesions and outlines a diagnostic protocol that should be followed. The author stresses that the clinical oral examination is by far the dentist's most potent tool for discovering oral lesions. The dentist should begin by observing the face, head and neck, with particular emphasis placed on the vermillion of the lips. The systematic intraoral examination should include all mucous membrane and gingival surfaces, with emphasis placed on the lateral border of the tongue, floor of the mouth, and pharynx, which are prime sites for **oral cancer.** For any observed lesion, the dentist must decide who is best suited to diagnose and, if necessary, treat the observed lesion. The author also describes the role of recordkeeping. 1 reference.

- **Oral Cancer: A Self-Assessment Quiz**

  Source: CDA Journal. Journal of the California Dental Association. 29(8): 608-617, 625. August 2001.

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

Summary: This article consists of a quiz for dental professionals to test their **oral cancer** knowledge. The goals of the quiz are to reinforce known cancer information and to present new information. Full color photographs are used to bring a sense of the practical problems that clinical pathology presents. Also, a number of real life case situations are presented with their corresponding illustrations so that the readers may use their clinical judgement and experience in choosing an answer. The quiz is divided into five sections: epidemiology and biology, etiology and prevention, precancer, early detection and diagnosis, and treatment and complications. An answer key is appended to the article. 29 figures.

- **Current Management of Oral Cancer: A Multidisciplinary Approach**

  Source: JADA. Journal of the American Dental Association. 132 (Supplement): 19S-23S. November 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

  Summary: This article evaluates and summarizes current approaches to the management of **oral cancer,** emphasizing the multidisciplinary team approach to coordinate surgery, radiation therapy, and chemotherapy. The article is from a special supplement to the Journal of the American Dental Association (JADA) that presents eight articles on the topic of the dentist's role in preventing and detecting **oral cancer.** The authors describe current concepts in management, including complications of therapy. State of the art surgical techniques can spare patients with **oral cancer** much of the morbidity (related illness and complications) common in the past. The refinement of treatment strategies reduces complications and improves efficacy. The mainstay of current therapy for **oral cancer** is surgery and radiation treatment. New research in the areas of gene therapy and immunomodulation is also showing promise. Discoveries in molecular biology, diagnosis, surgery, radiation therapy, and medical oncology have altered many traditional concepts and practices. The authors conclude that general dental practitioners need to understand current treatment modalities for oral and pharyngeal (throat) cancers to determine to whom they should refer patients for the most appropriate treatment, and to make recommendations regarding complications associated with these cancers. 34 references.

- **Maryland Dental Hygienists' Views of Oral Cancer Prevention and Early Detection**

  Source: Journal of Dental Hygiene. 76(3): 186-191. Summer 2002.

  Contact: Available from American Dental Hygienists' Association. 444 North Michigan Avenue, Chicago, IL 60611. (312) 440-8900. Website: www.adha.org.

  Summary: This article reports on a qualitative study undertaken to obtain in-depth information on dental hygienists' awareness and opinions of **oral cancer, oral cancer** examinations, and related factors. These findings are intended to supplement a previous statewide survey of Maryland dental hygienists on this subject. The study included two types of focus groups: in person (n = 10) and telephone (n = 7). Six major themes emerged from the focus groups: dental hygienists' lack of awareness of Maryland's **oral cancer** statistics, level of training to provide **oral cancer** examinations, provision of **oral cancer** examinations and barriers for not providing them, reactions to Maryland surveys of dental hygienists and dentists, assessment of **oral cancer** risk factors, and interest in additional training. In addition, some participants recommended that updates on how to conduct an **oral cancer** examination be a requirement, as updates on infection control are now. The findings strongly suggest that **oral cancer** prevention and early detection

need to be addressed by continuing education courses, as well as by professional entry-level schools of dental hygiene and schools of dentistry. Emphasis should be placed on providing hands-on training. 24 references.

- **Computer-Assisted Analysis of Oral Brush Biopsies at an Oral Cancer Screening Program**

  Source: JADA. Journal of the American Dental Association. 133(3): 357-362. March 2002.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

  Summary: This article reports on a study in which dentists and dental hygienists attending a health screening program were screened for **oral cancer.** Select oral epithelial lesions were evaluated by oral brush biopsy with a computer-assisted method of analysis (OralCDx, OralScan Laboratories). After those who had oral epithelial lesions were identified, the clinical characteristics of each lesion were recorded. Participants with abnormal oral brush biopsy results ('positive' or 'atypical') subsequently underwent incisional biopsy of their lesions by an oral surgeon. A total of 930 dentists and dental hygienists were screened over a four day period at each of the American Dental Association's 1999 and 2000 annual sessions. Of those, 89 people (9.7 percent) with 93 oral epithelial lesions were identified and evaluated by brush biopsy. Seven of the 93 oral lesions, all benign appearing in their clinical appearance, were determined to be positive or atypical. Of these, three were diagnosed as precancerous by scalpel biopsy and histologic evaluation. The author concludes that computer assisted brush biopsy analysis is a valuable adjunct to the oral screening examination. The identification of three innocuous looking precancerous lesions in this low risk group of dentists and dental hygienists underscores the necessity of evaluating all oral lesions of unknown etiology. 2 figures. 3 tables. 27 references.

- **Maryland Dental Hygienists' Assessment of Patients' Risk Behaviors for Oral Cancer**

  Source: Journal of Dental Hygiene. 75(1): 25-38. Winter 2001.

  Contact: Available from American Dental Hygienists' Association. 444 North Michigan Avenue, Chicago, IL 60611. (312) 440-8900. Website: www.adha.org.

  Summary: This article reports on a study that examined Maryland dental hygienists' knowledge of tobacco and alcohol use as **oral cancer** risk behaviors; the practice of obtaining comprehensive medical histories regarding patients' current, past, and type or amount of alcohol and tobacco used; and their opinions about the adequacy of their tobacco and alcohol cessation education preparation in a state that ranks unusually high for **oral cancer** mortality (death) rates. Data were collected with a 40 item self administered mailed questionnaire; 331 surveys were returned (a 60 percent response rate). Nearly all of the responding dental hygienists knew that tobacco is an **oral cancer** risk factor. Most probed their patients' present use of tobacco in medical histories. However, fewer hygienists assessed patients' past use and type or amount of tobacco used. Very few hygienists believed that they were adequately prepared to provide tobacco cessation education, although the majority agreed that dental hygienists should be prepared to provide this type of information. The majority of respondents also knew that alcohol use is an **oral cancer** risk factor; however, less probed their patients' present use of alcohol in medical histories compared to assessing present tobacco use. Even fewer assessed patients' past use and type or amount of alcohol used. A very small minority believed that they were adequately prepared to provide alcohol cessation education. Yet, in contrast to tobacco cessation counseling preparations, few

respondents believed that dental hygienists should be prepared to provide alcohol cessation education. 7 figures. 2 tables. 46 references.

- **Follow-Up in Patients with Oral Cancer**

  Source: Journal of Oral and Maxillofacial Surgery. 60(4): 380-386. April 2002.

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

  Summary: This article reports on a study undertaken to establish and provide standardized follow up of patients who underwent **oral cancer** treatment. The German-Austrian-Swiss Cooperative Group on Tumors of the Maxillofacial Region (DOSAK) established a schedule of check-up examinations for a 5 year period. On the basis of a questionnaire, the authors investigated oncologic follow up in respect to the early detection of recurrences, cost and outcome efficiencies, and physician and patient judgment in the development of impairments. Only 11 percent of all operated patients participated regularly in the follow up program within the first 3 years. Ultrasound was the most effective imaging for the detection of recurrences. Swallowing, speaking, tongue mobility, and facial appearance were the most common problems. Troubles with swallowing were mainly induced by poorly fitted dentures, discontinuity of the mandible, osteomyelitis, and xerostomia (dry mouth). Other appearance was mostly impaired by scars, missing facial muscle function, and edema. The problem of chronic pain remained unsolved. Due to the sequelae of treatment, this study shows the need for close medical and psychological follow up. 7 tables. 20 references.

- **Oral and Maxillofacial Surgeon's Role in the Diagnosis and Treatment of Oral Cancer**

  Source: Journal of the Tennessee Dental Association. 82(3): 34-38. Fall 2002.

  Contact: Available from Journal of the Tennessee Dental Association. 2104 Sunset Place, Nashville, TN 37212. E-mail: tda@tenndental.org.

  Summary: This article reviews the oral and maxillofacial surgeon's role in the diagnosis and treatment of **oral cancer. Oral cancer** sites include the tongue, palate, oropharynx, buccal mucosa, gingiva, and alveolar mucosa; cancers of the dorsal tongue, as well as the hard palate, are quite uncommon however. The author first reviews the epidemiology of **oral cancer,** then considers the prognosis, noting that the five year survival rate for **oral cancer** has not markedly improved in 30 years. The author describes the clinical appearance of both malignant and premalignant lesions of the oral cavity. The five year survival rate of **oral cancer** patients is directly related to the cancer stage at the time of diagnosis. For this reason, early detection, recognition, and treatment have the potential to not only increase the survival of patients with **oral cancer,** but also to decrease the incidence of malignant change of premalignant lesions. The author also outlines treatment options (generally surgical), the typical training of oral and maxillofacial surgeons, management of disease in the neck, basic surgical procedures, reconstruction of the oral cavity, and wound healing considerations. 12 figures. 11 references.

- **Educational Resources on Oral Cancer**

  Source: JADA. Journal of the American Dental Association. 129(Supplement): 45S-46S. November 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

Summary: This brief article offers a list of educational resources on **oral cancer.** The article includes publications and web sites on **oral cancer,** the oral complications of cancer treatment, tobacco control, continuing education courses (for dental professionals), and resource organizations. The contact information is provided for each of the organizations; the publications are available through these organizations. Each item in the list is also marked to note whether it is aimed at an audience of consumers or health care providers.

- **Primary Care Study of Dentists' and Doctors' Knowledge of Oral Cancer**

  Source: British Dental Journal. 191(9): 507. November 10, 2001.

  Contact: Available from Stockton Press. Houndmills, Basingstoke, Hampshire, RG21 6XS, United Kingdom. E-mail: subscriptions@nature.com.

  Summary: This brief article summarizes on a study undertaken to compare the knowledge of **oral cancer** and related issues of general dental and general medical practitioners (GDPs and GMPs) working in primary care. Knowledge levels are important since either group of practitioners may see such patients at first presentation. A questionnaire was sent to 420 primary care clinicians, half to dentists and half to doctors. The response rate was 68.1 percent for GDPs and 71.9 percent for GMPs. Dental practitioners were significantly more likely to have diagnosed cases of **oral cancer** than medical practitioners. Dental practitioners were significantly more likely to name alcohol as a risk factor than medical practitioners. Dental practitioners showed a preference for examining areas related to the tooth bearing or potentially denture bearing tissues rather than some of the more high risk sites (e.g., floor of the mouth). The authors conclude that knowledge levels were generally good, but there were some important differences mainly relating to risk factor knowledge and clinical examination techniques. A commentary on the study results is included. 3 references.

- **Want Some Life Saving Advice?: Ask Your Dental Hygienist About Oral Cancer**

  Source: Access. 16(8): 36-38. September-October 2002.

  Contact: Available from American Dental Hygienists' Association. 444 North Michigan Avenue, Chicago, IL 60611.

  Summary: This continuing education article reminds dental hygienists of the vital role that dental care providers play in screening and providing information about **oral cancer.** The author emphasizes that in the early stages, **oral cancer** can be treated in up to 90 percent of cases. Therefore, the **oral cancer** screening is one of the most critical components of a routine dental hygiene and dental exam. Dental hygienists and dentists can alert patients to suspicious growths and changes, noted during head and neck exams, and urge them to seek medical care. The author reviews the signs and symptoms of **oral cancer,** and outlines an **oral cancer** self-examination that can be taught to patients. The author also briefly reviews the treatment options available for **oral cancer.**

- **Treatment of Early Stage Oral Cancer**

  Source: Pennsylvania Dental Journal. p. 25-37. September-October 2002.

  Contact: Available from Pennsylvania Dental Association. P.O. Box 3341, 3501 North Front Street, Harrisburg, PA 17105. (717) 234-5941. Fax 717) 232-7169. Website: www.padental.org.

Summary: This lengthy journal article reviews the treatment of early stage **oral cancer.** Therapy depends on the site, stage, and patient's general condition and wishes. The treatment usually consists of surgery and, in some cases, adjunctive postoperative radiotherapy (radiation). The authors review treatments for cancers of the lips, floor of the mouth, oral tongue, alveolar ridge, buccal (cheek) mucosa, and hard palate. The authors conclude that through patient education, thorough examination of the oral cavity by the dentist and oral hygienist, and early referral to an otolaryngologist, it is possible to detect and treat these tumors at earlier stages and reduce their morbidity and mortality. Appended to the article are three additional items: a detailed review of **oral cancer** screening recommendations; a summary of oral precancerous lesions (leukoplakia and erythroplakia); and a description of the indications and use of the oral brush biopsy for early **oral cancer** detection. 17 figures. 68 references.

- **Combating Oral Cancer: The Dentist's Role in Preventing, Detecting a Deadly Disease**

  Source: JADA. Journal of the American Dental Association. 132 (Supplement): 1S-48S. November 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

  Summary: This special supplement to the Journal of the American Dental Association (JADA) presents eight articles on the topic of the dentist's role in preventing and detecting **oral cancer.** After a letter from the ADA President stressing the important role of the dental profession in the early detection and treatment of **oral cancer,** the supplement offers an editorial on some of the recent strides made in combating **oral cancer;** the editorial reiterates the need for dentists to perform comprehensive **oral cancer** examinations for all adult patients. Six articles follow: the demographics and occurrence of oral and pharyngeal cancers; **oral cancer** and its detection (history taking and the diagnostic phase of management); a multidisciplinary approach to managing **oral cancer;** professional and community efforts to prevent morbidity (related illness or complications) and mortality (death) from **oral cancer;** dentistry's role in tobacco control; and the use of a 90 second **oral cancer** examination. The supplement also includes a review of the JADA's continuing education program on **oral cancer,** a listing of educational resources for health care professionals and patients, and a patient education handout reviewing the basics of screening for **oral cancer.** The articles include full color photographs and lists of references.

Federally Funded Research on Oral Cancer

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

[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).

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 oral cancer.

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

- **Project Title: ADENOVIRUS LIMITATIONS AND TUMOR TARGETED GENE THERAPY**

  Principal Investigator & Institution: O'malley, Bert W.; Professor & Chairman; Surgery; University of Maryland Balt Prof School Baltimore, Md 21201

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

  Summary: (provided by applicant): Squamous cell carcinoma of the oral cavity and head and neck (HNSCC) is a devastating disease in which surgery, radiation and/or chemotherapy have not improved the 50 percent overall 5 year survival over the past 20 years. In an attempt to improve survival and reduce morbidity, gone therapy strategies are being developed for **oral cancer.** Despite encouraging preclinical data in many tumor types, initial clinical studies with adenovirus gene therapy have been disappointing. We posit that cellular differences exist even among head and neck cancers of the same histology that limit gone therapy responses. We further posit that variations in shared Coxsackie and adenovirus receptor (CAR) and integrin receptors play a major role in the transduction efficiency and translates to a significant variation in multi-tumor responses to adenovirus gene therapy strategies. We will test five hypotheses by addressing the following Specific Aims: 1) Determine the concentration of CAR, integrins, and FGF2 receptor on fresh human HNSCC samples and derived cell lines; 2) Establish the correlation between expression of CAR or integrin and Ad-tk anti-tumor effects and develop a FGF2 retargeting strategy in vitro that circumvents these limitations; 3) Quantify gene expression and therapeutic response to Ad-tk using both standard adenovirus and FGF2-R retargeted vectors in tumors established from 11NSCC lines. 4) Optimize direct linter-tumor injection therapy using circumventing treatment strategies and introduce systemic FGF2 retargeting therapy. We focus on a newly created fibroblast growth factor (FGF) conjugated adenovirus vector to develop a! Circumventing strategy that will improve gone transfer efficiency and corresponding therapeutic response. This novel FGF-2 receptor-based retargeting strategy may also allow safe and effective systemic delivery of tumor targeted adenovirus vectors. Five investigations regarding the role of adenovirus receptor and integrin expression on tumor cells will provide a platform of important gone therapy information that will lead to more effective and applicable preclinical animal studies and human clinical investigation. Adenovirus receptor or integrin testing prior to enrollment into a clinical trial may provide a means of selecting, stratifying, or assessing outcomes in head and neck cancer patients. This platform of information will also prove valuable to investigators who wish to circumvent limitations by developing and using alternative strategies such as FGF adenovirus retargeting.

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

- **Project Title: ADHESION AND PROLIFERATION IN ORAL CANCER PROGRESSION**

  Principal Investigator & Institution: Kramer, Randall H.; Professor; Stomatology; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 01-JUN-2001; Project End 31-MAY-2006

  Summary: Oral cancer is characterized by relentless growth and invasion, frequently resulting in distant metastasis. While significant progress has been made in defining the clinical and histopathological characteristics of cancer, the molecular mechanisms of tumor progression remain poorly understood. The major focus of the proposed Program Project is to further define the alterations that occur during the stepwise conversion of normal mucosa to oral dysplasia, and finally to invasive squamous cell carcinoma. The project comprises four interactive research laboratories at the University of California San Francisco. That have considerable experience in defining molecules related to tumor progression, including tumor marked analysis, growth factor and adhesion receptor function, signal transduction, and molecular genetics. Moreover, this group has already initiated approaches to the analysis of the complex issues related to the sequential processes characterizing tumor progression. Project I addresses the mechanism of TGF-alpha processing and its regulation by intracellular signaling pathways during carcinoma development. Project II will examine the importance of he alphav class of integrin receptors, which bind extracellular matrix ligands as well as the latent form of TGF- beta, in regulating cell growth and invasion. Project III will define the importance of specific cell adhesion systems in regulating survival, apoptosis and growth in normal and malignant oral keratinocytes. Project IV will analyze the role of human papillomavirus and MRP-8/14 in **oral cancer** pathogenesis. In addition, the Program will support intratumoral seed finding of young investigators proposing basic and clinical research projects in **oral cancer.** The two initial pilot projects will examine (1) p14/ARF status as a molecular predictor of **oral cancer** development, and (2) the role of fibronectin and its receptors in regulating invasion and growth of oral squamous cell carcinoma. These interactive research and feasibility projects will be supported by an administrative core, a cell culture/animal model core, and a histopathology core. Additional infrastructure support will be provided by the specialized cores of the newly established UCSF Comprehensive Cancer Center.

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

- **Project Title: ALCOHOL & TOBACCO CARCINOGENES IN ORAL CANCER ETIOLOGY**

  Principal Investigator & Institution: Timmons, Sherry R.; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002

  Summary: Dr. Sherry Timmons is currently in the Dentist Scientist program at The University of Iowa College of Dentistry. She is continuing her clinical training in Oral Pathology, Radiology and Medicine and is progressing in her research. The broad objective of her research is to examine the interactions between alcohol and tobacco carcinogenes in the etiology of **oral cancer.** Specifically, her research will examine the fundamental mechanisms of alcohol involvement in **oral cancer.** Dr. Timmons attended the Annual IADR meeting in Vancouver, BC March 9-14, 1999 where she participated in an Experimental Pathology Oral Session. Her presentation was, "Effects of Acetaldehyde on c-jun Expression in Squamous Cell Lines." Dr. Timmons co-authored an article accepted for publication in Dental Maxillofacial Radiology: Timmons S, Ruprecht A,

Diehl ST II. "Frequency of Portrayal of Foramen Transversarium of the Second Cervical Vertebra on Rotational Panoramic Radiographs." Projected publication date is May, 1999.

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

- **Project Title: ANGIOGENESIS, ENDOTHELIAL SURVIVAL, AND ORAL CANCER**

  Principal Investigator & Institution: Polverini, Peter J.; Professor and Dean; Oral Sciences; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, Mn 554552070

  Timing: Fiscal Year 2002; Project Start 01-SEP-1999; Project End 31-MAY-2003

  Summary: The development of solid tumors is strictly dependent on the sustained ingrowth of new capillary blood vessels; a process termed angiogenesis. We have recently found that vascular endothelial growth factor (VEGF), a potent proangiogenic mediator that is produced by a variety of normal and tumor cells including oral squamous carcinomas, is able to enhance the survival of endothelial cells (EC) and sustain angiogenesis by upregulating expression of the anti-apoptotic protein Bcl-2. Furthermore, human dermal microvascular EC (HDMEC) genetically engineered to overexpress Bcl-2 exhibit an enhanced ability to organize into functioning capillaries and display prolonged survival in vivo in SCID mice. These results suggest that the unrestrained growth of capillary blood vessels, a hallmark of tumor angiogenesis, may be due to the ability of some proangiogenic factors to confer a survival advantage on EC and thus sustain tumor angiogenesis and growth. The hypothesis underlying the proposed work is that the sustained growth of capillary blood vessels that characterizes solid tumor development is due in part to the ability of some tumor proangiogenic factors to enhance the survival of EC by upregulating Bcl-2. This suggests a mechanism whereby tumor proangiogenic mediators are able to subvert the apoptotic program that normally functions to prevent a protracted angiogenic response and enhance tumor progression by increasing the survival of EC and sustaining angiogenesis. The specific aims of the proposal are to: 1. Determine if Bcl-2 expression is upregulated in endothelial cells that populate tumor vessels. 2. Determine if prolonged expression of Bcl-2 in endothelial cells populating tumor vessels contributes to tumor growth and progression. 3. Define the mechanism(s) by which Bcl-2 enhances endothelial cell survival. 4. Initiate studies designed to attenuate tumor angiogenesis by inducing endothelial cell apoptosis. The studies outlined in this proposal should reveal important new insights into the mechanisms responsible for sustained capillary growth during tumor development, increase our understanding of the mechanism underlying aberrant angiogenesis, and suggest novel strategies for the treatment of solid tumors such as oral squamous carcinoma and other angiogenesis-dependent diseases.

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

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

  Principal Investigator & Institution: Murrah, Valerie A.; Diagnostic Scis/Gen Dentistry; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-JUL-2004

  Summary: (provided by applicant) Oral squamous cell carcinoma is a significant global health problem, comprising one of the ten most common cancers, worldwide. Over the past decade, there has been increased interest in viruses as etiologic agents for cancers of

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

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

- **Project Title: APOPTOTIC PATHWAYS FOLLOWING CHEMOTHERAPY OR GENE THERAPY OF ORAL CANCER**

  Principal Investigator & Institution: Lotze, Michael T.; Professor/ Chief; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

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

  Summary: This abstract is not available.

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

- **Project Title: ARF AS A THERAPEUTIC AGENT IN ORAL MALIGNANCIES**

  Principal Investigator & Institution: Yarbrough, Wendell G.; Associate Professor; Otolaryngology/Head & Neck Surgery; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

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

  Summary: (adapted from the Investigator's abstract): Oral squamous cell carcinoma (SCC) is a debilitating and deadly illness. Despite advances in conventional therapy, **oral cancer** continues to have unacceptable morbidity and mortality. Given the poor prognosis associated with existing therapies, the Principal Investigator's studies will focus on developing more effective treatments premised on reversing the apoptotic and proliferative defects in SCC. The INK4a/ARF gene locus represents the second most frequently altered gene in human cancer and is altered in 80% of SCC, suggesting its

importance in the pathogenesis of this tumor type. Utilizing alternative reading frames, the mammalian ARF-INF4a locus encodes two unrelated proteins that both function in tumor suppression. p16INK4a maintains the retinoblastoma protein in its growth suppressive state through inhibition of cyclin D-dependent kinase activity, while ARF binds with MDM2 and blocks MDM2 and p53 nuclear export, and thus cytoplasmic degradation of p53. These findings implicate both INK4A and ARF in suppressing the development of SCC. Previously, the Principal Investigator and his colleagues (Zhang et al., 1999a) and others (Pomerantz et al., 1998) found that ARF binds the MDM2 oncoprotein leading to stabilization and transcriptional activation of p53 with a resultant proliferative arrest. Recently, the Principal Investigator and coworkers have found that many cancer-derived mutations in human ARF exon 2 disrupt its normal nucleolar localization and impair its ability to block nuclear export of MDM2 and P53 (Zhang et al., 1999b) providing a molecular mechanism underlying ARF-mediated p53 stabilization and activation and underscoring the function of ARF in tumor suppression. The preliminary results presented in this proposal identify two previously unrecognized functions of ARF: that ARF induces an S-phase arrest independent of p53 and that the apoptotic response to ARF can be antagonized by functional retinoblastoma (Rb) protein. The later finding suggests the possibility that ARF may selectively target cells with altered Rb function for apoptotic cell death while sparing normal cells. The goals of this proposal are to further define ARF induced apoptosis, p53 independent functions of ARF, and to determine the possible utility of ARF gene therapy for the treatment of oral SCC.

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

- **Project Title: BEHAVIOR MODIFICATION, DENTISTS AND ORAL CANCER CONTROL**

  Principal Investigator & Institution: Silverman, Sol Jr.; Professor of Oral Medicine; American Dental Association 211 E Chicago Ave Chicago, Il 60611

  Timing: Fiscal Year 2002; Project Start 12-AUG-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): The hypothesis for this proposal is that the professional behavior of dentists can be modified by strengthening continuing education in **oral cancer** through a focus on prevention and early detection. The long-range goals are to increase the number of dentists who counsel at-risk patients about tobacco cessation, consistent with Healthy People 2010 objective 3-10c; and to increase the proportion of oral cancers detected at the earliest stage, consistent with Healthy People 2010 objective 21-6. Our project focuses on **oral cancer** prevention education for practicing dentists in the United States. Key components of **oral cancer** prevention include risk assessment and risk reduction for tobacco and alcohol use, chemoprevention, early detection and diagnosis. Based on these key components, a standardized continuing education course has been developed and will be presented within each of the ten U.S. Department of Health and Human Service regions. Outcomes assessment methodology has been designed and will be implemented. Prevention and early detection are the focus of this project because despite advances in **oral cancer** treatment, only about half of all persons diagnosed with **oral cancer** survive more than five years. Data indicate that the majority of at-risk Americans does not benefit from **oral cancer** screening from their primary care professionals. Survival rates for those with **oral cancer** has not significantly changed in the past 20 years, and it has worsened for African American males. The first activity for this fiveyear proposal is a workshop to standardize a continuing education program, with input from **oral cancer** and tobacco cessation experts and an ADA ad hoe advisory committee. A second workshop will be

scheduled to complete the continuing education program, facilitate course coordinator calibration and finalize the outcomes assessment process. Continuing education programs will be conducted nationwide and learning outcomes will be assessed over the fiveyear period. This project will also explore potential for use of the standardized continuing education program for other health care professionals, e.g., dental hygienists, nurse practitioners and primary care physicians.

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

- **Project Title: BIOLOGY OF HEADPIN (A NOVEL SERPIN) IN ORAL CANCER**

  Principal Investigator & Institution: Clayman, Gary L.; Associate Professor; Head and Neck Surgery; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

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

  Summary: Squamous cell carcinoma (SCC) of the oral cavity is a debilitating and often fatal disease afflicting approximately 30,000 individuals annually in the United States and is a major health problem worldwide. To better understand the molecular biology governing the invasive and aggressive behavior of these tumors, differences in gene expression have been studied between non-malignant oral mucosa and SCC derived from the oral cavity. Using differential display reverse transcription-based PCR, a novel serine proteinase inhibitor (serpin) was cloned, called headpin, that is down regulated in SCC biopsies and in 50 percent of established head and neck squamous cell carcinoma (HNSCC) tumor lines. Headpin was mapped to a serpin cluster on chromosome 18q21, which is a region that often exhibits loss of heterozygosity in head and neck cancers. Purified and functional recombinant human headpin (rHeadpin) has been generated and kinetic analysis indicates it is a bona fide suicide-inhibitor of both cathepsin L (catL) and cathepsin K (catK). Immunohistochemistry using a highly specific mAb raised against headpin has confirmed that the protein is abundant in non-malignant oral epithelium and lost or down-regulated in primary and metastatic SCC from the oral cavity. Based on the current body of literature linking expression of catL to progression of tumors, the implicit role of catK in degrading bone extracellular matrix, and the ability of headpin to inhibit both of these enzymes, suggest that loss of headpin protein expression from oral SCCs contributes to their aggressive clinical behavior. To test this hypothesis, the full target spectrum of proteinases inhibited by headpin will be assessed, while investigating the in vitro and in vivo consequences of headpin re-expression in tumors, define the mechanism(s) of headpin loss in tumor specimens, and analyze the predictive clinical SIGNIFICANCE of headpin expression in archival specimens from patients with oral SCC. Progress in this area could lead to development of new molecular based targets for the management of **oral cancer.**

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

- **Project Title: CADHERIN-MEDIATED REGULATION OF MMPS IN ORAL CANCER**

  Principal Investigator & Institution: Munshi, Hidayatullah G.; Robert H. Lurie Comprehensive Cancer Center; Northwestern University Office of Sponsored Research Chicago, Il 60611

  Timing: Fiscal Year 2003; Project Start 11-SEP-2003; Project End 31-AUG-2008

  Summary: (provided by applicant): The invasive behavior of oral squamous cell carcinoma (OSCC) requires coordinated cellular events including degradation of the extracellular matrix (ECM) and the acquisition of motility. Altered expression of

cadherins, transmembrane proteins that promote cell-cell contacts, has been associated with progression of OSCC. In many tumors, loss of E-cadherin or aberrant expression of N-cadherin has been shown to correlate with increased invasive behavior. Production of ECM degrading proteases, for example matrix metalloproteinases (MMPs), is also an early event in the malignant progression. In OSCC, a correlation between enhanced expression of MMP-2 (gelatinase A), MMP-9 (gelatinase B), membrane-type 1 MMP (MT1-MMP) and tumor progression has been described. Our data demonstrate that E-cadherin can regulate the expression of MMP-2 and MMP-9. Moreover, we have shown that disruption of cell-cell adhesions can induce MMP-dependent cellular invasion. Furthermore, our preliminary data demonstrate the involvement of phosphatidylinositol 3-kinase (PI3-kinase) in the E-cadherin-mediated regulation of MMPs. Based on these results, it is the working hypothesis of this proposal that a functional link between cell-cell adhesion and proteolysis regulates OSCC invasive behavior. Specifically, we propose that cadherin engagement modulates MMP expression and consequently controls cell motility and invasion. To test this hypothesis, we will assess the role of E- and N-cadherin in the regulation of MMP expression. Immunohistochemical and biochemical analysis of tumor tissues will be employed to evaluate the expression patterns of E- and N-cadherins, and MMPs. The biochemical pathways that are involved in the regulation of MMPs by E- and N-cadherin will then be evaluated. The long-term goal of the proposed research is to provide a more detailed understanding of the functional link between cell-cell adhesion and proteolysis and the contribution of this interplay to regulation of metastasis.

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

- **Project Title: CADHERINS IN ORAL SQUAMOUS CELL CARCINOMAS**

  Principal Investigator & Institution: Johnson, Keith R.; Professor; Oral Biology; University of Nebraska Medical Center Omaha, Ne 681987835

  Timing: Fiscal Year 2003; Project Start 01-APR-1998; Project End 31-JAN-2008

  Summary: (provided by applicant): Cadherins are the transmembrane component of the adherence junction, a structure that may appear at first glance to be a static structure. Nevertheless, we know that cells must be able to adjust the strength of cellular adhesions in order to respond to their environment. We have shown that N-cadherin expression in oral squamous epithelial cells produces a cell with increased motility and invasion. Our hypothesis is that cells obtain signals when they make contact via cadherins and that the signals an oral squamous epithelial cell obtains by making contact via N-cadherin differs from the signal the same cell obtains by making contact via-cadherin. The signals cells obtain through contact with one another allow them to modify their behavior. Our goal is to understand the signals epithelial cells receive through N-cadherin particularly when they inappropriately express this cadherin, and why these signals differ from those the same cell gets from Cadherin. Signaling through cadherins has been difficult to study because there is no obvious way to" activate" the signal. Thus, for this application we have generated a unique activatable form of N-cadherin and propose to use this cadherin to investigate signals downstream of cadherin contact. A second goal is to determine if N-cadherin expression in oral epithelium is sufficient to produce a tumor or if it modifies the behavior of cells that are already tumor cells. To address this question we have generated a transgenic mouse model for **oral cancer.** Thus, our specific aims for this proposal are: 1) to understand cadherin-mediated cellular signaling; and 2) to understand the role N-cadherin plays in oral squamous cell carcinoma progression.

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

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

  Principal Investigator & Institution: Hinds, Philip W.; Associate Professor; New England Medical Center Hospitals 750 Washington St Boston, Ma 021111533

  Timing: Fiscal Year 2004; Project Start 01-APR-2004; Project End 28-FEB-2009

  Summary: (provided by applicant): Head and neck cancer is believed to originate via a multi-step process that involves the activation of oncogenes and inactivation of tumor suppressor genes, however, the specific pattern of progression and the necessary genetic alterations have not been delineated. Although treatment advances have been made in the last 30 years, little or no survival improvement has been obtained. Identifying the specific genes or proteins involved in transformation of a normal cell to a malignant cell, and the particular sequence of these genes or proteins, is necessary for the development of early detection methods, the formulation of new treatment strategies, and the prediction of patient outcome. While studies on oral tumorigenesis are specifically beneficial to head and neck cancer patients, such studies are likely to also aid the understanding of multi-step carcinogenesis in general. To translate these advantages into procedures that may be beneficial to **oral cancer** patients, the basic molecular changes involved in **oral cancer** development must be understood. To this end we investigated the mechanism of cell cycle dysregulation in **oral cancer** development. As with most human tumors, the common tumor suppressor p53 (but not its regulator pl4ARF) and the pRb pathway are disrupted in **oral cancer** cells. Most interestingly, we found that the pRb regulator cdk6 is preferentially hyperactivated in **oral cancer** cells by a variety of mechanisms, while the related kinase cdk4 is active at levels similar to those observed in primary cells. These data complement a number of studies in our labs and others that indicate that cdk4 and cdk6 are not equivalent in their ability to induce proliferation in all cell types and may have non-overlapping roles in tumorigenesis. Further, inhibition of both kinases by p 16INK4a can lead to a senescent state in **oral cancer** cell lines, indicating that continued activity of cdk4, cdk6 or both is required for tumor cell proliferation. In order to better understand the roles of these pRb pathway regulators and the process of cell cycle dysregulation in general in **oral cancer,** we propose three specific aims: (1) construct and deconstruct **oral cancer** cells by manipulating the activity of cell cycle regulators in normal oral epithelial cells and **oral cancer** cells respectively. This will test suspected targets for antiproliferative agents in **oral cancer** cells and will elucidate the consequences of dysregulation of known cell cycle regulators. (2) Reversibly inhibit cdk4, cdk6 or both in order to induce senescence and apoptosis in **oral cancer** cells and thus validate them as targets for therapy. (3) Determine the biological activity of CLLL7, a novel cdk4/cdk6 interacting protein encoded by a gene on chromosome 13.

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

- **Project Title: CELL CYCLE REGULATORS OF ORAL CANCER**

  Principal Investigator & Institution: Rheinwald, James G.; Associate Professor and Head; Oral Pathology; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-APR-1998; Project End 31-MAR-2004

  Summary: The objective of this Program Project is to unite a network of scientific investigators who are focusing on the molecular biology of the cell cycle in order to understand the mechanisms of oral carcinogenesis. This proposal consists of six highly interdependent research projects and cores, connected both scientifically and technically. The central theme uniting the three research projects is the perturbation of

key cell cycle regulators in the genesis of **oral cancer.** These key regulators as well as a novel cell cycle regulator have been identified by this research group. Findings from the research projects will be validated by collaborative efforts of the Cell Culture Core and the Tissue Bank and Pathology Core. This program project will support and promote synergistic interactions among the cores and research projects that will speed up the investigations of the process central to the development of oral cancer: cell cycle control. There are three research projects in this **oral cancer** program project: "HPV and Cell Cycle Dysregulation in Oral Cancer" will study the role of human papillomavirus (HPV), the p53 and pRB pathways, and the cell cycle regulator cdk6 in **oral cancer.** "Cyclin D1 and a Genetic Model of Oral Carcinogenesis" will investigate the genetic basis of proliferation and transformation of oral keratinocytes by the aberrant expression of the G1- specific cyclin D1 oncogene in a transgenic mouse model. "Cell cycle Biology of doc-1" tests a putative tumor suppressor gene doc-1 as a regulator of the cell cycle. Three Core Facilities have been created to support the scientific projects. The Administrative Core, in addition to its managerial function, serves the important role of facilitating electronic communication and data sharing among the investigators. The tissue Bank and Pathology Core will collect and bank human oral tumors, and will create a database to compile clinical histories, provide tissues for culturing, and perform HPV typing, in situ hybridization, and immunohistochemistry. The Cell Culture Core will generate cell cultures from normal, premalignant, and malignant human and mouse oral biopsy specimens and will construct sable transductants for the research projects. These Cores will also validate conclusions from the research projects in human **oral cancer** tissues.

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

- **Project Title: CELL SURFACE MARKER AND HOMING TARGET FOR ORAL SCC**

  Principal Investigator & Institution: Sauk, John J.; Professor and Chair; Oral & Maxillofacial Pathology; University of Maryland Balt Prof School Baltimore, Md 21201

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

  Summary: This revised proposal has as an objective the development of a novel therapy for well-differentiated oral squamous carcinoma based on targeting the expression of an endoplasmic reticulum resident protein that is uniquely expressed on the cell surface of well-differentiated carcinomas. Well-differentiated oral squamous cell carcinomas like other well-differentiated carcinomas are difficult to treat because of their low mitotic indices and proliferation rates. However, these well- differentiated neoplasms are known to possess and express an endoplasmic reticulum (ER) collagen chaperone, Hsp47. Although Hsp47 specifically binds procollagen in the ER, in malignancy the protein escapes ER retention to be expressed on the cell surface. We hypothesize that the specific peptide binding characteristics of this protein and unique location in malignancy provides a marker that may serve as a target to which drugs or contrast agents may be directed for chemotherapy or imaging. This hypothesis will be tested through the accomplishment of three specific aims. These include: (1) Expand the repertoire of Hsp47-binding peptides by utilizing random peptide libraries and two-hybrid screening of random displayed peptides with Hsp47 as a bait protein; (2) Determine the availability and fate of Hsp47 binding peptides on the cell surface of epidermoid carcinoma cells in culture and in solid tumors; and (3). Determine the efficacy of Hsp47-binding peptides and Hsp47 monoclonal antibodies in homing chemotherapeutic drugs to tumor sites in oral squamous carcinoma xenografts. To accomplish these aims we have assembled a collaborative team of pathologists, molecular biologists, oncologists, and experts in developmental therapeutics that

encompass the University of Maryland's Schools of Dentistry, Medicine and The Greenbaum Cancer Center. The ultimate success of this proposal will be determined by the impact that such an approach has on reducing the morbidity and mortality of **oral cancer.**

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

- **Project Title: CHARACTERIZATION OF THE 11Q13 AMPLICON IN ORAL CANCER**

  Principal Investigator & Institution: Gollin, Susanne M.; Professor; Human Genetics; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): Gene amplification, the generation of extra copies of a gene(s), is a common and critically important genetic defect in **oral cancer** (OSCC) cells. Amplification of chromosomal band 11q13, which harbors the cyclin D1 gene (CCND1) and other genes, appears to be a relatively early event in oral carcinogenesis, occurs in -45% of oral cancers, and is an indicator of poor prognosis. The mechanism underlying gene amplification has been largely unexplored in **oral cancer** and consequently, is not well understood. Therefore, a new approach is indicated. Based on our recent studies of **oral cancer** cells, we posit that 11q13 amplification in **oral cancer** occurs by breakage-fusion-bridge (BFB) cycles. We observed a predictable pattern of organization, an "amplification fingerprint" consistent with BFB cycles, characterized by an inverted duplication chromosome pattern at 11 qI 3, with genes from the segment just distal to the proximal chromosomal breakpoint duplicated and flanking both sides of the amplified genes in the amplicon. In addition, we observed amplified CCND1 in anaphase bridges between nascent **oral cancer** cells. To test our hypothesis, we will carry out three Specific Aims. 1. To use our novel quantitative PCR technique (quantitative microsatellite analysis, QuMA) to prepare a high-resolution copy number map of the 11q13 amplicon in OSCC cells and primary tumors, define the minimal amplified region and the genes located therein, and determine whether breakpoints are clustered at "hotspots." To identify BAC clones that span the amplicon breakpoints and validate our QuMA data using fluorescence in situ hybridization (FISH), revealing the structural organization of the amplicon and whether it fits the BFB model or an alternative model. 2. To use FISH, to show that the 11 qi 3 amplicon is localized to anaphase bridges. 3. To use Northern Blots and TaqMan quantitative RT-PCR to determine transcription patterns and the expression level of genes and novel ESTs in and around the amplicon in OSCC cells and tumors. Our data suggest that the most highly amplified segment includes expressed new genes, with CCND1 amplified to a lesser extent. The results of this study may lead to targeted methods for prevention, early detection, therapy, and/or eradication of cells harboring gene amplification.

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

- **Project Title: CHEMOPREVENTION OF ORAL CANCER WITH BBIC**

  Principal Investigator & Institution: Meyskens, Frank L.; Professor of Medicine; Medicine; University of California Irvine Irvine, Ca 926977600

  Timing: Fiscal Year 2003; Project Start 14-MAR-1997; Project End 31-AUG-2008

  Summary: (provided by applicant): The long term objective of this proposal is to determine whether Bowman-Birk Inhibitor (BBI) Concentrate (C), a protease inhibitor extracted from soybeans, can cause regression of oral leukoplakia and whether certain candidate intermediate marker endpoints can predict response by serving as a surrogate

for oral leukoplakia. The ultimate goal of this research is to prevent human cancer. The specific aims are: (1) To conduct a placebo-controlled, double-blind and randomized 6 month phase lib cancer control chemoprevention trial of BBIC in patients with oral leukoplakia. (a) To determine the clinical and histologic response rate of oral leukoplakia to BBIC. (b) To serially measure the effect of BBIC on intermediate marker endpoints (IME). 1) In oral mucosal cells the level of proteolytic activity (PA) and levels of erb-B2 (neu), retinoic acid receptor beta (RAR-beta), bcl-2, and mutant p53 protein will be measured. 2) In tissue biopsies of oral leukoplakia lesions the latter four proteins above will also be measured by immunohistochemistry. 3) In serum, the levels of the protein, neu, will be serially measured. (c) To correlate the clinical and histologic responses of oral leukoplakia to the effect on cellular levels of PA, erb-B2 (neu), RAR-beta, bcl-2, and mutant p53 expression, and serum levels of neu. (d) To determine the individual and group side-effects to BBIC. (2) To follow long term (one year) those patients who achieve a PR or CR afterthe initial 6 months trial Based on the phase Ila and early phase lib results we estimate that about 25-35% of patients completing the 6 months of BBIC will fall in this category. The same parameters outlined for specific aim 1 will be measured. Particular attention will be paid to adherence and toxicity as we eventually wish to use BBIC in the long term setting of second malignancy prevention. All aspects of these phase II IME trials will be carefully monitored for compliance, safety, and toxicity by continuous local evaluation by our NCI-approved Data Safety and Monitoring Board (DSMB) and in concert with the NCI. The results from these studies should provide a substantial biologic and therapeutic rationale for a large Phase III randomized risk reduction trial of head and neck cancer as well as provide impetus for further exploration of these non-toxic group of compounds as chemopreventive agents in humans.

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

- **Project Title: CHROMOSOME 18 TUMOR SUPPRESSOR GENES IN ORAL CANCER**

  Principal Investigator & Institution: Carey, Thomas E.; Professor; Otolaryngology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2002; Project Start 15-SEP-1998; Project End 30-JUN-2004

  Summary: Squamous cell carcinoma (SCC) of oral cavity is a devastating and deadly disease. At present, there are few definitive indicators for predicting outcome and determining the clinical management other than tumor state and lymph node involvement. Studies over the past two decades have shown that gene defects underlie cancer development and progression, and play a critical role in defining the natural history and biological behavior of cancers. The Principal Investigator has shown that losses affecting the long arm of chromosome 18 (18q) occur in 55-60 percent of oral SCC. The preliminary data indicate that 18q loss is associated with poor prognosis and death from cancer in head and neck SCCs. Moreover, loss of heterozygosity (LOH) on 18q is associated with progression in individual patients. If the Principal Investigator can identify the basis for these findings, then genetic markers could be used in selecting high-risk patients for more aggressive therapy, and spare low risk patients from unnecessary treatment morbidity. Chromosomal regions frequently affected by LOH are thought to indicate the presence of a tumor suppressor gene (TSG) within the affected region. Three candidate TSGs have been identified on 18q; DCC (deleted in colon cancer), DPC4 (deleted in pancreatic cancer), and MADR2 (mad related gene 2). The goals of the application are: to establish the smallest region of loss on 18q in oral SCC, to

test the hypothesis that one or more TSGs within the smallest region of loss on 18q is associated with tumor progression; to test the hypothesis that restoration of the affected TSG will affect tumor growth or invasive behavior; and using markers identified in Aim 1 and the tissue specimens from a large, controlled, randomized treatment trial for SCC, test the hypothesis that 18q LOH is associated with survival and/or response to therapy. From these studies, the Principal Investigator expects to further define chromosome 18q alterations as an important feature of biologically advanced disease and to develop the knowledge for designing new strategies to counter the effect of tumor suppressor gene inactivation.

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- **Project Title: CLONAL CHANGES IN ORAL LESIONS OF HIGH-RISK PATIENTS**

  Principal Investigator & Institution: Rosin, Miriam P.; Professor; British Columbia Cancer Research Centre 601 W 10Th Ave Vancouver,

  Timing: Fiscal Year 2003; Project Start 24-SEP-1999; Project End 29-FEB-2008

  Summary: (provided by applicant): Survival rates for **oral cancer** patients have remained unchanged in the past several decades largely because of diagnosis at late stage and local recurrence after treatment. In retrospective studies, patterns of loss of heterozygosity (LOH) have been associated with risk of progression of oral premalignant lesions to cancer and disease recurrence. The objective of the current proposal is to evaluate the prognostic value of specific LOH patterns in combination with clinical and histological features to predict outcome for oral lesions within a longitudinal study. We have used the unique medical infrastructure in British Columbia to establish one of the largest cohort studies of precancer and cancer patients in order to systematically follow changes in clinical, pathological and molecular parameters over time. The proposed grant renewal will extend the follow-up time of the established cohort and will accrue additional patients to 200 **oral cancer** patients and 200 patients with primary oral dysplasia. It will also fund the collection of tissue samples (biopsies, scrapes, brushings) and the analysis of allelic loss in these specimens. This extension will allow for better longitudinal modeling of risk patterns, including temporal changes of clinical, pathological and molecular markers, and will provide a multi-faceted risk model with clinical application that can be used to manage oral lesions and cancers.

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

- **Project Title: CONTRAST ENHANCED SPECTROSCOPIC DETECTION OF ORAL CANCER**

  Principal Investigator & Institution: Motamedi, Massoud; Professor; Biomedical Engineering Center; University of Texas Medical Br Galveston 301 University Blvd Galveston, Tx 77555

  Timing: Fiscal Year 2002; Project Start 01-SEP-2001; Project End 31-AUG-2003

  Summary: (Provided by Applicant): Each year about 31,000 Americans develop **oral cancer.** Squamous cell carcinoma accounts for 95 percent of all malignant oral lesions Oral squamous cell carcinoma is a condition that will kill approximately half of patients afflicted within five years of diagnosis. Early diagnosis is stressed, because this could increase the survival rate from 50 percent to about 80 percent. Contrast enhanced diagnostic applications of fluorescence spectroscopy may offer an effective means for early, non-invasive and rapid detection of epithelial neoplastic transformation. Our goal is to develop a unique spectroscopic contrast agent that can be applied topically for early detection of epithelial neoplasm using fluorescence imaging. Underlying our aims

are the hypotheses that spectral information from contrast-enhanced fluorescence images of oral lesions can be used as a reliable approach toward accurate and early non-invasive detection of pre-malignant and malignant lesions in the oral cavity. This revised proposal will focus on the development and testing of topical application of newly developed Lanthanide Chelate-based contrast agent to induce selective accumulation of a fluorescing dye in malignant transformed epithelial tissue for the purpose of early lesion detection. Our preliminary work has shown: (1) promising correlation between the spectral information observed in contrast-enhanced fluorescence and pathological state of the lesion in the early stage of development, and (2) the ability of malignant oral lesions to selectively accumulate the contrast agent as compared to benign lesions or normal tissue. We propose to synthesize a new contrast agent that can be excited in the region of 3 10-330 nm and perform cellular and in vivo studies to; (1) optimize the chemical structure and spectroscopic properties of the dye for safe and practical applications, (2) better understand the cellular and morphological basis for the observed selective uptake of the dye by pre-malignant and malignant oral tissues, and (3) examine the diagnostic power of the proposed contrast enhanced approach as compared to other techniques as well as histopathlogical findings in a series of pre-clinical animal studies. The knowledge gained from this study may lead to the development of a simple, inexpensive and non-invasive diagnostic tool for detection and screening of **oral cancer** in a dentists office, guiding the biopsy and follow up of suspicious oral lesions by otolaryngologists and oral surgeons.

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

- **Project Title: CORE --BIOSTATISTICS**

  Principal Investigator & Institution: Goldberg, Judith D.; Professor and Director, Biostatistics; New York University 15 Washington Place New York, Ny 10003

  Timing: Fiscal Year 2002

  Summary: The Biostatistics Core, directed by Judith D. Goldberg, Sc.D., Professor and Director of the Biostatistics Division at New York University School of Medicine, will provide statistical leadership to the Disparities Center. In particular, the Core provides collaboration in various aspects of the component projects including study design and planning, data collection and processing, data analysis, and manuscript. The primary research activities of the Core will serve as a resource for research design and statistical collaboration in design and planning of 2-3 pilot studies each year as well as for those studies that are in development for outside funding. The Core will provide full statistical collaboration for the additional project to be developed. The Core will provide a data repository for all projects involved in the Disparities Center and for all Pilot Studies that are funded through the Center. As part of this activity, the Core staff will coordinate the development of standards for documentation and databases for central archiving. For those projects in the Disparities Center with external statistical staffing and support, the Core will provide consultation and collaboration as required to ensure that the resulting data can be integrated and incorporated into the Center database archives. Specific Aims: 1. To provide statistical leadership to the NYU **Oral Cancer** RAAHP Center in the review and oversight of Projects 1-5 and the development of pilot projects, new projects, and development of ancillary projects for external funding. 2. To provide statistical collaboration for Project #3, **Oral Cancer** Detection: and Emerging Technologies [D. Sirois, P.I.] in all aspects of study design, data collection and management, analysis and reporting of results. 3. To develop and maintain the archival databases for all projects in the NYU **Oral Cancer** RAAHP Center. 4. To provide leadership for the coordination of statistical activities for all projects in this Center.

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

- **Project Title: CORE--INFORMATICS**

  Principal Investigator & Institution: Schleyer, Titus K.; Associate Professor & Director; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002

  Summary: The purpose of the informatics core is four-fold: (1) establish a research collaboratory, i.e. an electronic infrastructure that makes it easy for participants to work together remotely, for the NYU **Oral Cancer** RAAHP Center; (2) describe and analyze the collaborative processes within the Center; (3) disseminate Center results to interested audiences; and (4) investigate the feasibility of improving **oral cancer** diagnosis and management practices using information technology-based interventions. While the vision of research collaboratories supported by information technology has been articulated numerous times, it has been implemented and evaluated only rarely in biomedical research. The first goal of this project is to support our multi-institutional, multi- disciplinary and evaluated only rarely in biomedical research. The first goal of this project is to support our multi-institutional, multi- disciplinary and collaborative Center using collaborative work and knowledge management technologies. The project will first determine detailed required for the collaborative infrastructure and gather baseline participant, task, and interaction data. The collaborative infrastructure will be designed and implemented using commercial off-the-shelf software for applications such as Web-based workspaces; discussion lists; newsgroups; online, real-time collaboration; automatic notifications; and possibly Internet-based videoconferencing. After implementation and training, utilization data and user feedback will be collected in order to refine and evaluate the infrastructure. Collecting and analyzing interaction and utilization data will support our second goal. and help us understand how large, distributed research collaborations work. Our third goal is to disseminate NYU **Oral Cancer** RAAHP Center research results to the larger biomedical community and other stakeholders. The Web and the Internet will be the main avenues for dissemination. We will build on a differentiated understanding of what information the Center's audiences need, and how they will use it. A major goal is to create a "virtual community" centered on the NYU **Oral Cancer** RAAHP Center Project to enable shared vision of knowledge creation, development and dissemination diagnosis and management of **oral cancer** both for the practitioner as well as the patient. We anticipate that this project will not only lend significant support to the objectives of the NYU **Oral Cancer** RAAHP Center, but also help gain new insights in how large scale collaborative research projects can be supported with information technology, which opportunities or needs exist for further development of tools and applications, and which informatics-related variables can positively or negatively affect project outcomes.

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

- **Project Title: CORE--TISSUE BANK AND PATHOLOGY**

  Principal Investigator & Institution: Regezi, Joseph A.; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002

  Summary: The Tissue Bank and Pathology Core will have several functions that directly support the research investigators in this program project. Collection, storage, and cataloging of biopsies and surgical tissue specimens from oral cancers and precancers will be an essential goal; this will include the handling of specimens from animal

models. Research investigators on the four major projects and the pilot projects will be provided frozen and paraffin-embedded tissue sections from oral cancerous and precancerous lesions as needed. A substantial numb3er (>3000) of archived and frozen biopsy specimens already have been formally organized as part of existing tissue bank for the UCSF **Oral Cancer** Research Center. Specimen information has been stored in an Access database. This database will be maintained to manage all data related to patients and clinical samples. Within the Tissue Bank, diagnostic groups include hyperplasia, hyperkeratosis, dysplasia, carcinoma in situs, verrucous carcinoma, and invasive squamous cell carcinoma, and invasive squamous cell carcinomas, and include several cohorts of SCC that are of biologic, etiologic, and/or pathogenetic significance, such as patients who have serial biopsies from a single oral region, patients in age group <35 years, and patients with oral dysplasias that progressed to SCC and others in which the dysplasia did not transform to SCC. New fresh and fixed specimens will be received from oral and surgical pathology with the assistance of personnel in the UCSF Cancer Center. Implementation of a universal surgical consent form will allow us to link fresh surgical specimens with patients through either medical chart review or the UCSF Cancer Registry. The Stomatology Clinical Center will continue to be valuable source of unfixed precancerous lesions. Outcome information on archived surgical specimens will continue to be added to the database through the cooperation of the UCSF Cancer Registry. Technical and consultative services in biostatistics, histopathology and immunohistochemistry will be provided to all investigators.

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- **Project Title: CYCLIN B-1 AS A TUMOR-SPECIFIC ANTIGEN IN ORAL CARCINOMA**

  Principal Investigator & Institution: Finn, Olivera J.; Professor and Chair; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 01-SEP-1997; Project End 31-AUG-2007

  Summary: (provided by applicant) For active specific immunotherapy to become a reality, tumor specific antigens must be identified. A new antigen discovery system was used based on in vitro grown human dendritic cells presenting peptides purified by HPLC from class I molecules of human tumors to healthy naive CD8+ and CD4+ T cells. They identified several immunostimulatory peptides and determined they were derived from cycling B1 protein. They also found cyclin B1 specific T cells in patients with head and neck cancer whose tumors overexpressed this protein. Further studies showed that cyclin B1 is overexpressed in a large number of human tumors, including those of the head and neck, and that this overexpression is a result of in activation of p53 function. Based on these results, they hypothesize that cyclin B1 may be a good target of an immune response in **oral cancer** and that cyclin B1 protein and peptides derived from it would be good candidates for **oral cancer** vaccines. They propose to test this hypothesis by conducting in vitro and pre-clinical studies in vivo in mouse models. In specific aim 1, they will use recombinant cyclin B1 protein to evaluate its potential to elicit not only CTL responses but also helper T cell responses. In vitro priming will be employed using dendrite cells loaded with the whole protein or individual peptides to generate T cells specific for this antigen and to identify as large a repertoire as possible of cyclin B1 peptides stimulatory to both CD8+ and CD4+ cells. In specific aim 2, they will test the potential of cyclin B1 to be a tumor rejection antigen in vivo. They will utilize the p53 knockout mouse as a model of cancer prevention and cancer therapy of spontaneous tumors though vaccination with cyclin B1. They will also employ a transplantable tumor model of a mouse squamous cell carcinoma that grows in the oral cavity.

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- **Project Title: DEVELOPMENT OF P53-BASED VACCINES FOR ORAL CANCER**

  Principal Investigator & Institution: Deleo, Albert B.; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 01-SEP-1997; Project End 31-AUG-2007

  Summary: (provided by applicant) Nearly 50 percent of oral carcinomas contain p53 mutations, making mutant p53 peptides attractive candidates for use in cancer vaccines. The probability is greater, however, that tumors will present wild-type sequence (wt) peptides derived from mutant p53 rather than mutant peptides. Our research is guided by the hypothesis that the effectiveness of vaccines targeting wt p53 epitopes will be influenced by (1) the ability of a patient's tumor to present wt p53 epitopes for immune recognition and (2) the ability of the patient's T-cells to respond to these epitopes. Our ongoing analysis of these factors, which focuses on the first of four CTL-defined wt p53 epitopes identified, p53, indicates that: 1) nature or site of an alteration in p53 influences processing and presentation of this epitope and, perhaps, other epitopes as well; 2) only a third of PBMC of either normal donors or patients responded ex vivo to this epitope; and 3) tumors of "responsive" patients had little/no potential to present wt p53 epitopes, suggesting that the outgrowth of "epitope-loss" tumors might have occurred in these patients. At the same time, a consensus is developing that multiple epitope-based vaccines may be required for tumor rejection. The identification of five T-cell defined wt p53 epitopes for vaccine use, including a DR4-restricted, Th-dedined wt p53 epitope that we recently identified, raises issues about how best to construct p53-based vaccines. The specific aims of this project focus on these issues and are aimed at determining ex vivo: 1) the responsiveness of HLA-A2+ and/or HLA-DR4+ patients to the identified class I and class II HLA-restricted wt p53 epitopes, 2) ability of patient?s tumors to present these epitopes based on a comparative analysis of p53 expressed in established cell lines with p53 expressed in patients' tumors, and 3) evaluate the efficacy of DC-based vaccines employing various combinations and sources of wt p53 epitopes in the induction of T cells recognizing CTL.

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

- **Project Title: DNA-BASED VACCINE FOR TREATMENT OF ORAL CARCINOMA**

  Principal Investigator & Institution: Cohen, Edward P.; Professor and Senior Attending Physician; Microbiology and Immunology; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2003; Project Start 15-JUL-2003; Project End 31-MAY-2007

  Summary: Vaccine development for oral carcinoma is the current major research objective of my laboratory. The long-term objective is to develop a vaccine that can be used in the overall management of patients with squamous cell carcinoma of the head and neck (SCCHN). The vaccination strategy combines known requirements for generation of a robust anti tumor immune response--antigen presentation, allogeneic stimulation and the secretion of immune-augmenting cytokines. The vaccine is prepared by transfer of DNA from squamous carcinoma cells into a highly immunogenic syngeneic/allogeneic cell line in which genes specifying tumor associated antigens (TAAs) are expressed. The recipient cells are modified in advance of DNA-transfer to secrete cytokines. This type of vaccine is based on the principle that TAAs are the products of mutant and dysregulated genes in cancer cells and that transfer of tumor-DNA into recipient cells results in stable integration and long-term expression of the

genes specifying TAAs. Prior published data in mice indicate that immunization with transfected cells induced strong anti tumor immune responses, immunological memory and prolongation of survival. Our recent studies (PNAS, 99: 9415-9420, 2002) confirm the immunogenic properties of recipient cells transfected with DNA from human oral carcinomas. This type of vaccine has a number of advantages, including the selection of immunogenic recipient cells, in which the transferred DNA is replicated. Thus, the vaccine can be prepared with DNA derived from small amounts of tumor tissue. Further studies in a mouse model of oral carcinoma are now required to define the mechanisms of the immunotherapeutic effects of the vaccine and to optimize this promising strategy. Using murine antigen presenting cells transfected with DNA from squamous carcinomas, the minimum amount of tumor tissue required to prepare an effective vaccine and the cell types mediating tumor rejection will be determined. The transfected cell-population will be enriched for cells that express TAAs, to increase the therapeutic potential of the vaccine. Its possible toxic effects will be evaluated. These studies will provide insights into the mechanism of tumor rejection and guidelines for optimization of the vaccination strategy. It is expected that development of an effective vaccine to be used alone or in combination with conventional therapy will expand the future therapeutic options available for patients with **oral cancer.**

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- **Project Title: EFFICACY OF BUPROPION FOR TREATING SPIT TOBACCO USERS**

  Principal Investigator & Institution: Dale, Lowell C.; Mayo Clinic Rochester 200 1St St Sw Rochester, Mn 55905

  Timing: Fiscal Year 2002; Project Start 01-MAY-2002; Project End 30-APR-2006

  Summary: Although overall rates of cigarette smoking have declined over the past 40 years, the use of spit tobacco (ST) has tripled. The use of ST can lead to nicotine addiction and physical dependence. ST use is known to increase the risk of periodontal disease and **oral cancer.** Moreover, ST use increases the risk for cancer of the esophagus, larynx, stomach and pancreas and the risk of cardiovascular disease. Effective interventions are needed to assist ST users to stop. Bupropion, a monocyclic anti-depressant that inhibits the neuronal re-uptake of norepinephrine and dopamine and may also selectively inhibit neuronal nicotinic receptors, has demonstrated efficacy for smoking cessation. In a placebo-controlled pilot study, we have shown possible treatment effects of sustained release bupropion (SR) in ST user. Our aims are: 1) To evaluate the efficacy of a 12-week course of bupropion SR rates of abstinence from all tobacco use; 2) To evaluate the efficacy of a 12-week course of bupropion SR compared to placebo on the end of treatment and 12- month rates of abstinence from all tobacco use; 2) To evaluate the efficacy of a 12-week course of bupropion SR compare to placebo on the end of treatment and 12-month rates of abstinence from ST; 3) To determine what baseline characteristics in addition to medication assignment are associated with abstinence from all tobacco and from ST, at the end of treatment and at 12 months; 4) To determine the association between baseline urine tobacco alkaloids with self-reported tobacco use behavior and level of nicotine dependence assessed using the Fagerstrom Tolerance Questionnaire modified for ST users; 6) To determine if ST users successful in abstaining from ST switch to a nicotine-replacement product or a different tobacco product (cigarettes, pipe, or cigars). In a randomized, double-blind, placebo-controlled trial, we will compare bupropion SR to placebo in 320 regular users of ST. Active or placebo bupropion will be taken for a total of 12 consecutive weeks starting one week before the target quit date. Behavioral intervention will be provided for all subjects.

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

- **Project Title: EPIDEMIOLOGY OF GENETIC SUSCEPTIBILITY TO ORAL CANCER**

  Principal Investigator & Institution: Nazar-Stewart, Valle; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002

  Summary: This abstract is not available.

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

- **Project Title: ETHNOPHARMACOLOGICAL STUDIES IN ORAL MEDICINE**

  Principal Investigator & Institution: Colvard, Michael D.; Oral Med and Diagnostic Scis; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2002; Project Start 01-MAR-2002; Project End 28-FEB-2005

  Summary: (Provided by applicant): Aphthous ulcers and oral pain are considered the most frequent oral ulcerative pathologies of the human species. Oral dermatological conditions, **oral cancer** and xerostomia are significant related oral pathologies and these conditions also produce significant pain and ulcerative conditions within the oral cavity. Few scientific studies exist which survey, identify and assess, in controlled formats, the efficacy of the various phytomedicines, which are used by humans throughout the planet, for the myriad pain and pathological conditions of the oral cavity. Minimal scientific data are available which identifies the medicinally active compounds and histopathological effects of phytomedicines used as treatments for oral pain, ulcer and cancer pathologies. This proposed project intends to observe, survey and identify, the ethno-pharmaceutical oral medicine practices and oral phytomedicinal preparations used by the indigenous peoples and populations of Costa Rica. Initial data will be gathered via a literature- and field-based survey of ethno-pharmaceutial practices of Costa Rican and United States citizens for cancer, ulcerative and pain conditions of the oral cavity. Survey data will provide guidance for the collection and cataloguing of the targeted plant species used during the practice of oral medicine in Costa Rica and the United States. Identified plant materials will be collected, taxonomically identified, extracted, the extracts tested in oral related affections, such as pain, inflammation, cancerous growth, and salivation. An Agreement will be set up between the University of Illinois at Chicago and the Universidad Latina of Costa Rica, to access Costa Rican genetic resources for this proposed study. Active samples will be recollected for fractionation and isolation studies. Promising constituent compounds will be subjected to in vivo and in vitro testing against epidermal keratinocytes cell lines, in mouse tail-flick and cytotoxic assessments to determine efficacy, safety, and potential as analgesic, anesthetic, anti-inflammatory, anti-cancer and anti-xerostomia (sialogogue) drugs. The proposal will form the basis of a program aimed at the discovery and development of botanically derived oral medications for non-microbial originating oral diseases and conditions.

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

- **Project Title: ETIOLOGY AND PREVENTION OF ORAL CANCER**

  Principal Investigator & Institution: El-Bayoumy, Karam E.; Director of Research; Institute for Cancer Prevention 1 Dana Rd Valhalla, Ny 10595

  Timing: Fiscal Year 2003; Project Start 01-MAY-2003; Project End 30-APR-2008

  Summary: (provided by applicant): A model of progression of head and neck sqiamous cell carcinoma (HNSCC) in humans has been described which includes up-regulation of cyclin D1, activation of Stat-3, and expression of high levels of cyclooxygenase-2 (COX-

2). Mutations and inactivation of p53 and other tumor suppressor genes (e.g. Rb, p16) have also been observed. Primary prevention, e.g., cessation of tobacco use, moderation of alcohol consumption, and increased intake of fruits and vegetables appears unattainable for a significant fraction of the population. Thus, other approaches such as chemoprevention are being explored. We have reported that selenium, as 1,4-phenylenebis(methylene)selenocyanate (p-XSC), inhibited tongue tumors of rats treated with 4-nitroquinoline-N-oxide (NQO). p-XSC also leads to growth inhibition and/or apoptosis in cultured human oral carcinoma cells, inhibits the formation of benzo[a]pyrene (B[a]P)-DNA adducts in the mouse tongue, and therefore has the potential of inhibiting B[a]P-induced tongue tumorigenesis. Based on these previous studies we hypothesize thatp-XSC inhibits tumorigenesis by multiple mechanisms including inhibition of DNA damage and cell proliferation, as well as induction of apoptosis in premalignant and transformed cells. To test our hypothesis we propose the following specific aims, Aim 1: To elucidate the mechanism of inhibition of NQO-induced tongue tumorigenesis by p-XSC. During tumor induction we will determine the effect of-XSC on: a) NQO-induced DNA damage; b) NQO-induced mutagenesis in vivo (in the lacI rat); c) NQO-induced (i) cell proliferation, (ii) apoptosis and (iii) proteins involved in cell cycle, cell proliferation, and apoptosis that have been implicated in the development of HNSCC (cyclin D1, Stat-3, COX-2, p16, pRb and p53). Changes in global gene expression will also be examined using eDNA microarray analysis; Aim 2: To determine the effect of p-XSC on tongue tumor induction by B[a]P in mice and on endpoints described in Aim 1; and Aim 3: To determine the effect of NQO or B[a]P, and p-XSC individually and in combination on certain of the biochemical, molecular and cellular events described in Aim 1 using cultures of normal cells, leukoplakia, and squamous cell carcinoma. To our knowledge, this application is the first to determine whether a tobacco smoke carcinogen (B[a]P) which induces tongue tumors in the mouse, alters those genes that are known to be involved in HNSCC and thus provides important leads toward the etiology of **oral cancer.** The long-term applications of this project may lead to strategies for the prevention and control of HNSCC. By identifying critical intervention targets in tongue tumorigenesis, it should be possible to minimize the gap between basic research and clinical application, and lead to translational clinical interventions.

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- **Project Title: ETIOLOGY OF KARYOTYPIC DEFECTS IN ORAL CANCER**

  Principal Investigator & Institution: Saunders, William S.; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002

  Summary: This abstract is not available.

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

- **Project Title: FLORIDA MODEL FOR ORAL CANCER CONTROL, PHASE I**

  Principal Investigator & Institution: Tomar, Scott L.; Professor; Operative Dentistry; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-AUG-2004

  Summary: (provided by applicant): In 1994-98, Florida had the 2nd highest crude mortality rate and the 5th highest age-adjusted mortality rate for oral and pharyngeal cancer. The specific aims of this proposed study are to: (1) Perform an epidemiologic assessment of **oral cancer** in the State of Florida; (2) Assess the level of knowledge,

opinions, and the prevention and early detection activities of healthcare providers in Florida about these cancers; (3) Assess the level of knowledge, opinions, and behaviors of a general population sample of adults in Florida regarding **oral cancer;** (4) Assess the educational resources for health care providers in the state of Florida for **oral cancer** prevention; and (5) Build an organizational infrastructure in Florida to facilitate community- based interventions for **oral cancer** prevention and control. We will use data from Florida's Cancer Data System and state vital statistics datasets to provide a detailed analysis of the incidence, mortality, survival, and stage distribution at time of diagnosis by age, sex, race, ethnicity, and geographic region. Principles of social marketing will be applied to assess the knowledge, attitudes, practices, facilitators, and barriers for **oral cancer** prevention among representative samples of Florida's general dentists, primary care physicians, nurse practitioners, and dental hygienists. We will conduct a telephone-based survey using a random digit dial (RDD) sample of adults aged 40 years and older to assess their knowledge, attitudes, practices, facilitators, and barriers for **oral cancer** prevention. Patients diagnosed with **oral cancer** at the University of Florida Shands Medical Center, the University of Miami / Jackson Memorial Medical Center, and the V.A. Medical Center in Gainesville will be interviewed to determine their diagnosis history and to identify potential targets to facilitate earlier cancer detection. We will create an inventory of available professional education resources for **oral cancer** in Florida. As part of the Florida Comprehensive Cancer Control Initiative, this study will convene representatives of a wide range of professional and voluntary organizations, public and private agencies, educational institutions, and community-based organizations to develop a plan to enhance statewide **oral cancer** control.

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- **Project Title: FLUORESCENCE SPECTROSCOPY TO DETECT ORAL NEOPLASIA**

  Principal Investigator & Institution: Gillenwater, Ann M.; Head and Neck Surgery; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

  Timing: Fiscal Year 2003; Project Start 15-MAY-2003; Project End 30-APR-2007

  Summary: (provided by applicant): **Oral cancer** is a major health problem worldwide. Patients with early disease have better chances for cure and functional outcome, yet most patients present with advanced tumors. Early detection improves outcomes for **oral cancer** patients. The goal of this proposal is to develop a new technology, fluorescence spectroscopy, for non-invasive, early detection of oral cavity neoplasia and assessment of molecular changes associated with oral carcinogenesis. We will test the hypothesis that changes in biochemistry and tissue morphology produced during carcinogenesis result in alterations in the optical properties of oral mucosa. In Aim 1, we will develop diagnostic algorithms based on results of clinical trials using fluorescence and reflectance spectroscopy, and determine the sensitivity and specificity to non-invasively identify and distinguish dysplasia and early carcinoma from benign lesions and normal mucosa. We will obtain fluorescence and reflectance spectra at four different source-detector separations which sample information from different depths spanning the epithelium and superficial stroma. In Aim 2, we will investigate the biological basis for changes in fluorescence spectra of inflammatory and neoplastic lesions using short-term culture of human oral tissue. Vital microscopy using widefield Transverse slices of normal and abnormal tissue will be maintained in culture for examination with autofluorescence microscopy. We will compare the pattern of autofluorescence of normal, dysplastic and cancerous oral mucosa; changes will be related to those measured in vivo using fluorescence spectroscopy. We will explore which chromophores are responsible for oral mucosa fluorescence by comparing

autofluorescence patterns to immunohistochemical patterns of fluorophores, including collagen crosslinks, NADH, FAD, cytokeratins and porphyrin, and absorbing and scattering chromophores such as hemoglobin. With this information, we will evaluate the potential of fluorescence spectroscopy as an intermediate endpoint biomarker of cancer progression. In Specific Aim 3, we will develop mathematical models to describe the fluorescence properties of oral tissue, to extract the relative contributions of principle chromophores modulated with neoplasia. We will use parameters extracted from this model to develop diagnostic algorithms based directly on alterations in tissue biochemistry and morphology that can be probed using fluorescence. Successful completion of this research program will provide a clinical tool that could dramatically improve early detection and monitoring of oral neoplasia. Technology to non-invasively assess molecular changes in oral mucosa could augment clinical and translational research of genetic mechanisms involved in carcinogenesis and treatment of oral neoplasia.

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

- **Project Title: GENERAL CLINICAL RESEARCH CENTER-FORSYTH DENTAL INSTIT**

  Principal Investigator & Institution: Flier, Jeffrey S.; Professor; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

  Timing: Fiscal Year 2003; Project Start 01-DEC-1977; Project End 30-NOV-2004

  Summary: (provided by applicant): The BIDMC's GCRC proposes to form a satellite with the Forsyth Dental Institute (FDI), a world class center for clinical investigation of oral disease. This proposal describes a spectrum of investigations involving treatment of periodontal diseases, development of a vaccine for dental caries, testing of mercury amalgam toxicity and investigation of **oral cancer.** Sixteen projects are described that will be conducted at the Satellite Center that include microbiology, microbial genomics, microbial taxonomy, immunology and toxicology as these studies relate to conditions of oral health and disease and microbial biofilms. The proposed Satellite Center will include a Dental Clinic Core, a Laboratory Core and Biostatistics/Informatics support. Specific areas of investigation in this application include: 1) comparison of conventional and antibacterial_supplemented treatments of periodontal disease; 2) investigation of means to prevent periodontal disease; 3) studies on familial distribution of oral bacteria; 4) studies of oral bacteria as examples of naturally occurring biofilms; 5) studies of oral bacteria that penetrate cells; 6) studies of the ways in which early lesions of periodontal disease are initiated; 7) investigation of the microbiology associated with **oral cancer;** 8) studies that contribute to the development of a dental caries vaccine; 9) investigation of the potential toxicity of mercury amalgams; and 10) studies of the uncultivable bacteria of the oral cavity with planned development of a microbial microarray for oral bacteria identification. In addition to the planned studies as outlined above, a strategy to create bi_directional linkage between parent and satellite GCRC's is described in which a dental facility will be established at the BIDMC GCRC to be staffed by Forsyth personnel. Through this facility, it is envisioned that future studies on the oral health effects of systemic disease, and the converse, effects of systemic disease on oral health will be investigated. It is also stressed that this facility will encourage closer affiliation between the Joslin Diabetes Center (JDC) Satellite and the Forsyth Satellite. It is envisioned that this proposal will expand the research horizon of the FDI and contribute new technology to the research of the parent.

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- **Project Title: GENETIC ALTERATIONS AS DIAGNOSTIC AND PROGNOSTIC BIOMARK**

  Principal Investigator & Institution: Koch, Wayne M.; Professor; Otolaryn & Head & Neck Surgery; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2002; Project Start 01-SEP-1999; Project End 31-AUG-2004

  Summary: Recent investigation into the molecular mechanisms of malignant transformation and behavior promises to yield real improvements in the management of **oral cancer.** A spectrum of genetic alterations in squamous cell carcinoma (SCC) of the upper aerodigestive tract has been described targeting the p53, p16, PTEN, Cyclin D1 and RB genes. Specific areas of chromosomal loss have been mapped as well, for which the target genes are unknown. Efforts to apply this knowledge in a variety of clinical settings have already begun. Translational research uncovers phenotypic correlates of genetic changes in order to better understand their mechanism of action. Genetic alterations may also serve as biomarkers for detection of cancer cells and for prognostication. Early detection of cancer and accurate prediction of the response of individual tumors to specific therapeutic options would be invaluable for the management of disease. This proposal seeks to expand previous translational research in three ways. First, it will investigate the utility of genetic markers to augment routine histologic evaluation. Mutations of p53 will be used to map the extent of disease in surgical resection margins and the results correlated with local recurrence and survival. Second, the spectrum of genetic alterations in well defined groups of patients will be catalogued and correlations sought with clinical outcome and epidemiological factors. This work will attempt to identify useful prognostic markers that can direct therapeutic decisions, as well as to focus future research efforts on markers of particular phenotypic significance. The third aim is to validate a new molecular strategy for early detection of oral SCC. A panel of microsatellite markers with a high propensity for shifts in **oral cancer** will be tested in order to demonstrate its specificity for cancer and sensitivity for detection of minimal disease. DNA from exfoliated cells from the oral cavities of cancer patients and controls will be examined for tumor-specific shifts not present in germline DNA from peripheral blood lymphocytes. This approach will also be applied for surveillance of patients after curative therapy is complete. Through these three translational strategies, it is likely that valuable benefits will accrue both for understanding the basic behavior of oral SCC, and for the management of patients with this devastating disease.

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- **Project Title: GENETIC DETERMINANTS OF MULTISTEP ORAL TUMORIGENESIS**

  Principal Investigator & Institution: Hittelman, Walter N.; Professor of Medicine; Experimental Therapeutics; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

  Timing: Fiscal Year 2004; Project Start 01-SEP-1999; Project End 30-NOV-2006

  Summary: Despite notable advances in early diagnosis and local disease control, oral carcinoma remains a significant public health problem worldwide. Over the past thirty years, while the cancer incidence rates have increased among men and women, limited improvement of the cure and five-year survival rates has been achieved through classical multimodal therapeutic approaches, encouraging the development of innovative strategies. The rational development of novel approaches for the prevention, early detection, and effective treatment of oral carcinoma is critically dependent on a

better understanding of the molecular and cellular mechanisms specific biomarkers for cancer risk assessment, early detection underlying the tumorigenesis process in the oral cavity. This knowledge will lead to the identification of specific biomarkers for cancer risk assessment, early detection of disease, response to primary or secondary intervention, and prognostic evaluation of the disease. Moreover, the identification of the key biologic pathways in the tumorigenesis process will lead to the development of new, targeted interventional approaches. Molecular cytogenetic analyses of oral cavity tumors have uncovered a number of recurrent genetic events. While a limited number of candidate genes have been identified, little is known about their function during oral tumorigenesis. Chromosome 1lq13 gene amplification is observed in 30-50% of oral cancers and may involve several genes potentially important for creating the malignant phenotype. The goal of this project is to determine the etiology, timing, and functional consequences of chromosome 11ql 3 amplification during the multistep, oral tumorigenesis process. The working hypothesis is that different genetic events associated with oral tumorigenesis interact in a synergistic fashion to drive the accumulation of the functional pathways necessary for malignant evolution. Characterizing the evolving tissue at critical times of genetic alteration will permit a better understanding of the functional consequences of these interactive genetic events in oral malignancy. The following Specific Aims are proposed: Specific Aim 1: Determine the frequency and functional consequences of chromosome 1l ql 3 gene amplification during the multistep process. Specific Aim 2: Determine the functional significance of cyclin D 1 alterations for oral tumorigenesis. Specific Aim 3: Determine the role of EMS 1 alterations during the multistep process The in vivo model system for these studies will be human oral tumor resection specimens exhibiting contiguous histologic evidence of a transition from normal epithelium through premalignant regions to invasive disease. Using in situ approaches (in situ hybridization, microdissection and PCR, and immunohistochemistry), sequential genetic and phenotypic events (e.g., genomic instability, gene amplification, dysregulated proliferation, altered migration) will be characterized during the multistep process. New hypotheses derived from observations in the in vivo model system will be tested in an in vitro, two-dimensional tissue culture model where candidate gene expression can be regulated and its functional consequences characterized spatially and quantitatively in cell outgrowths. The elucidation of the pathways and forces that drive the multistep process in the oral cavity will allow a better understanding of the biological underpinnings of **oral cancer** development and will lead to the development of new approaches to reduce the morbidity and mortality of **oral cancer.**

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- **Project Title: GENETIC EPIDEMIOLOGY OF ORAL PREMALIGNANCIES AND CANCER**

  Principal Investigator & Institution: Zavras, Athanasios I.; Oral Health Policy & Epidem; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-MAY-1999; Project End 30-APR-2004

  Summary: The purpose of the proposed 5-year career development award is to provide training in translational, patient oriented research at the postdoctoral level and to prepare the applicant for a leadership role in the fields of clinical research and molecular epidemiology. It is anticipated that the phased development plan will provide new and enhanced multidisciplinary skills in patient-oriented research, clinical trials, pharmacoepidemiology, molecular biology and statistical genetics, which will be later applied to the study of disease etiology and control. One of the strengths of the

proposed development plan is the participation and commitment of four mentors, whose diverse and unique talents will influense the training of the applicant. Institutional support by Harvard School of Dental Medicine (responsible for training in cancer genetics), Harvard School of Public Health (pharmacoepidemiology and statistical genetics), the Massachusetts General Hospital Cancer Center (hands-on training in ethics and clinical trials) and Quintiles Corporation (training in clinical trials management, regulatory process and Good Clinical Practices) will ensure a plethora of educational resources and opportunities. This blend of academia, healthcare and research industry will provide for the specific skills required to a career devoted to clinical trials and epidemiolocic studies that utilize state-of-the-art molecular methods and findings. In his research, the investigator will directly interact with human subjects in an effort to identify environmental and genetic risk factors related to oral premalignancies. A case-control study will be conducted to investigate the association between oral premalignant lesions, genetic susceptibility markers and life-style risk factors (diet, alcohol and tobacco use) in greeks, a population who has traditionally exhibited very low **oral cancer** prevalence rates. Specifically, the investigators will study the effects of tobacco, alcohol, diet and polymorphisms at the Glutathione-S-Transerase T1 (GST-T) gene and Alcohol Dehydrogenase 3 (ADH3) gene. Impairment of an individual's ability to metabolize carcinogens properly may increase their bioavailability, and thus, inrease the probability of genetic damage of cell-cycle control regulators. An additional hypothesis to be evaluated is that p53 tumor suppressor gene mutations are more frequent in the lesions of patients with the GST-TO genotype than the GST-T1 genotype. Apart from contributing to the current body of knowledge about disease etiology, the proposed international collaborative investigation will provide the framework upon which the investigator will prepare for an independent research career.

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- **Project Title: GENOMIC SCANNING IN ORAL CANCER**

  Principal Investigator & Institution: Plass, Christoph; Associate Professor, Department of Medic; Medical Microbiol & Immunology; Ohio State University 1960 Kenny Road Columbus, Oh 43210

  Timing: Fiscal Year 2002; Project Start 01-APR-2000; Project End 31-MAR-2005

  Summary: Head and Neck cancers (HNC) are the sixth most common cancer in the world, and therefore are a major public health concern. It is now well- established that cancer is a genetic disease at the cellular level. Genetic alterations include the activation of oncogenes and inactivation of tumor suppressor genes. Although substantial progress has been made, still relatively little is known about the genetic mechanisms involved in initiation, progression, and recurrence of these cancers. It is now well accepted that epigenetic alterations (DNA methylation) as well as genetic changes are important for the development of cancer. The importance of DNA methylation in progression of HNCs is not completely understood. To gain a better understanding of the genetic and epigenetic events associated with these events in head and neck squamous cell carcinomas (HNSCC), we propose to identify novel oncogenes and candidate tumor suppressor genes. Our hypothesis is that tumorigenesis of HNSCC is associated with epigenetic changes e.g. promoter methylation, which results in specific changes at the RNA level. We are planning to use the Restriction Landmark Genomic Scanning (RLGS) method which is uniquely suited to identify altered DNA methylation patterns as well as DNA amplification. The goals are: (1) to use RLGS to identify novel amplified sequences and tumor suppressor candidate regions based on altered DNA methylation pattern; (2) the construction of an AscI-EcoRV arrayed library to facilitate the cloning.

(3) The cloning of candidate cancer genes will focus on those areas that are altered at high frequency in the tumors. Candidate oncogenes will be identified in chromosomal regions with high incidences of LOH and/pr DNA methylation. (4) The final goal is the establishment of suitable diagnostic biomarkers, which can be used for rapid identification of HNSCC-specific alterations.

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- **Project Title: HARVARD COLLABORATIVE ORAL CANCER STUDY**

  Principal Investigator & Institution: Kelsey, Karl T.; Professor; Cancer Cell Biology; Harvard University (Sch of Public Hlth) Public Health Campus Boston, Ma 02115

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

  Summary: The epidemiology of **oral cancer** has clearly demonstrated that its principal etiology is smoking and alcohol consumption, with over 75% of all **oral cancer** in the United States attributable to these two avoidable risk factors. At the same time, only a relatively small proportion of exposed individuals develop this disease. Elucidation of the factors that contribute to susceptibility to this disease will be crucial in developing novel intervention and prevention strategies. The role genetic susceptibility plays in explaining variation in the patterns of occurrence of exposure-related cancers is advancing rapidly. Much of the research has focused on lung cancer and genes which code for enzymes that either activate or inactivate xenobiotic compounds. Since the enzymes are involved inactivation and deactivation of tobacco and alcohol-related carcinogens, it has been hypothesized that they may influence cancer susceptibility. Polymorphisms in many of these genes have been identified and associated with an increased risk for lung cancer. In addition these genes appear to further alter cancer risk by level of cigarette smoking. Since tobacco carcinogens are clearly associated with **oral cancer** carcinogenesis, investigation into the role that genetic susceptibility has in **oral cancer** development is warranted. We propose a case-control molecular epidemiologic study in the greater Boston metropolitan region to investigate the role that genetic polymorphisms in metabolic enzymes have in the development of **oral cancer.** This project will focus on the relationship between **oral cancer,** the established risk factors, and diet. Speciflcally, we will investigate the association between **oral cancer,** smoking levels, alcohol ingestion, diet, and the presence of specific genetic polymorphisms of metabolic enzymes. We will establish a DNA bank, including obtaining paraffin blocks of tumors for future studies of somatic genetic alterations, and estimate the prevalence if genetic polymorphisms in two cytochrome P450 genes (CYPL4I and CYP2E 1), three glutathione 5-transferases (GSTMI, GS7TI, GSTP 1), the alcohol dehydrogenase type 3 (ADH3), and the methylenetetrahydrofolate reductase (MTHFR) gene. Previous associations of these polymorphisms with lung cancer or colon cancer are not readily generalizable to **oral cancer** without additional works such as we propose here. These finding should lead to an improved characterization of high risk individuals for whom aggressive preventive measures may be targeted. Our DNA bank and comprehensive epidemiologic approach will also provide an invaluable resource for continuing studies of the molecular and genetic epidemiology of **oral cancer.**

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- **Project Title: HEAD /NECK TUMORIGENESIS--CELLULAR DETERMINANTS /PREVENTION IMPLICATIONS**

  Principal Investigator & Institution: Hittleman, Walter N.; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

Timing: Fiscal Year 2002

Summary: Aerodigestive tract tumors have been hypothesized to represent a "field cancerization" process whereby a whole field is exposed to carcinogenic insult, accumulates genetic damage, and is at increased risk for proceeding through a multistep process of tumor development. The purpose of this proposal is to examine the hypothesis of "field cancerization" at the cellular and molecular levels to identify probes which can be used to characterize the multistep tumorigenesis process in the aerodigestive tract. The information gained from these initial studies will then be utilized to assess risk of malignancy in the aerodigestive tract (in individuals at risk for tumor development) as well as to determine the effect of chemoproventive treatment on these cellular parameters. Using surgically resected tumor and normal tissue obtained from individuals with primary head and neck tumors and premalignant lesions (leukoplakia), we propose to identify cytogenetic, immunocytochemical, and molecular markers that can be utilized to identify genotypic and phenotypic changes associated with tumorigenesis. We will then examine adjacent and distant "normal" tissue, in and out of the field at risk, for the degree of genetic alteration as well as for the degree of dysregulation of proliferation and differentiation (i.e. characterization of the field). Hypothetically, one would expect that individuals with head and neck primaries who exhibit increased genetic and phenotypic alterations in their normal tissue would be at increased risk for the development of a second primary. Similarly, those individuals exhibiting increased alterations in premalignant tissue (e.g. leukoplakia) might be expected to be at increased risk for developing **oral cancer.** These hypotheses will be tested first in a retrospective fashion by examining archival tumor and normal tissue specimens of individuals previously resected for primary head and neck tumors who have or have not subsequently developed a second primary. During the fourth and fifth years, the informative immunocytochemical and molecular probes will be utilized to examine tissues obtained prospectively from patients entered at M.D. Anderson Cancer Center onto the clinical protocols described in Projects 1 and 3 to determine the validity of the findings obtained from retrospective studies as well as to determine the effect of chemopreventive treatment on the expression of these markers in the tissue at risk.

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- **Project Title: HERPES SIMPLEX VIRUS IN THE TREATMENT OF ORAL CANCER**

  Principal Investigator & Institution: Shillitoe, Edward J.; Professor and Chairman; Microbiology and Immunology; Upstate Medical University Research Administration Syracuse, Ny 13210

  Timing: Fiscal Year 2002; Project Start 01-APR-2000; Project End 31-MAR-2005

  Summary: We will develop new strains of Herpes simplex virus type-1 (HSV- 1) for use in the treatment of **oral cancer.** HSV- 1 has potential as a therapeutic tool for **oral cancer** since it infects oral epithelium as its natural host tissue, is highly cytotoxic, and spreads rapidly from one cell to another. The only disadvantage of HSV-1 is that it can spread to the nervous system, causing paralysis and death. To prevent this, we will develop a new strain of the virus whose replication is limited to **oral cancer** cells. This will be done by removing a promoter that controls expression of an essential viral gene, and replacing it with a promoter that is active in **oral cancer** cells but not in nervous- system cells. We will increase the anti-tumor effect of the virus by adding a gene for a cytokine. This will increase the local immune response to the infected tumor. We will then make the anti-tumor effect even stronger by exploiting the anti-tumor bystander effect that occurs when ganciclovir is activated by HSV-1. We expect that the triple combination of a tumor- restricted virus, enhanced local immune response, and anti-tumor bystander

effect will be more effective in treatment of an experimental model of **oral cancer** than other treatments, and could lead to human trials in the future.

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- **Project Title: HPV AND MRPS IN ORAL CANCER PATHOGENESIS**

  Principal Investigator & Institution: Palefsky, Joel M.; Professor of Medicine; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002

  Summary: The molecular pathogenesis of **oral cancer** remains poorly understood. A substantial proportion of oral dysplasias and cancers, but not all, are associated with human papillomavirus (HPV) infection. A better understanding of the mechanisms underlying HPV+ and HPV-oral disease incidence and progression is needed to develop new approaches to this highly lethal disease. The focus of this project is on the role of two novel cellular proteins, macrophage inhibitory factor-related protein (MRP)-8 and MRP14 in the pathogenesis of **oral cancer.** MRP8 and MRP14 are members of the factor-related protein (MRP)-8 and MRP14 in the pathogenesis of **oral cancer.** MRP8 and MRP14 are members of the S-100 calcium binding protein family. They have been shown to have multiple intracellular and extracellular functions in white blood cells, but their biology in normal and neoplastic oral epithelium has not yet been studied. MRP8 and MRP14 may regulate intracellular calcium levels and play a role in calcium-dependent signaling pathways in both MRP14 may regulate intracellular calcium levels and play a role in calcium-dependent signaling pathways in both HPV+ and HPV-cells. In HPV+ cells, the MRP8/14 may regulate intracellular calcium levels and play a role in calcium-dependent signaling pathways in both HPV+ and HPV- cells. In HPV+ cells, the MRP8/14 complex may inhibit casein kinase II-mediated phosphorylation of the HPV E7 oncoprotein thereby attenuating its function. We have shown that MRP8 and MRPP14 levels vary considerably depending on the stage of oral disease. In normal epithelium, MRP8 and 14 expression are low, but are highly up-regulated in low-grade dysplasia. However, high-grade dysplasia and cancers are associated with loss of expression of MRP8 and/or MRP14. We hypothesize that MRP8 and MRP14 inhibit cell growth through a variety of mechanisms and that up-regulation of MRP8 AND mrp14 represents a cellular response to events initiating low-grade dysplasia, such as HPV infection. We also hypothesize that loss of expression of MRP8 and/or MRP14 represents a step in oral disease progression. Accordingly, we have four specific aims: 1) To analyze expression of MRP8, MRP14 and effect of MRP proteins on HPV+ and HPV-oral epithelial cell lines; 3) To determine the effects of the MRP8/14 complex on the phosphorylation and function of the HPV E7 protein; and 4) To study the effects of the MRP8/14 complex on HPV+ and HPV-oral cancer cell growth in the nude mouse model. This project will advance our understanding of the role of MRP8 AND mrp14 in oral dysplasia and cancer if our hypotheses are confirmed, manipulation of MRP expression in oral dysplasia and cancer may represent a novel therapeutic approach to treatment of these diseases.

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

- **Project Title: HPV, GENETIC INSTABILITY & ORAL CANCER**

  Principal Investigator & Institution: Park, No-Hee; Professor; Dental Research Institute; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 30-JUN-2006

Summary: (Provided by Applicant) Frequent infection with human papillomavirus (HPV) in the oral cavity has been noted in HIV immunocompromised children and adults. HIV-infected individuals are more susceptible to infection with multiple HPV subtypes, including types 16 and 18. These "high risk" HPVs that are closely associated with development of malignant oral cancer: the viral DNA is frequently found in **oral cancer** cells and tissue. Moreover, transfection of normal human oral keratinocyte (NHOK) cells with cloned "high risk" HPV genome immortalizes these cells, which can convert to fully transformed cells when exposed to chemical carcinogens. Since (1) the same chemical carcinogens cannot transform NHOK cells and (2) the loss of genomic integrity is the hallmark of neoplastic cells, "high risk" HPV must play a critical role in the malignant transformation of NHOK cells by disrupting cells' ability to maintain genomic integrity. Genomic integrity is maintained by constant repair of DNA damage; thus, disturbance of DNA repair results in mutations, which ultimately induces malignant transformation of cells. The central hypothesis of the project is that infection of NHOK cells with "high risk" HPV oncogenes disrupts DNA repair; and that inhibition of HPV oncogene expression allows pre-neoplastic human oral epithelial cells expressing high risk" HPV oncogenes to regain their DNA repair activities and genomic integrity. To test this hypothesis, the applicants propose the following specific aims: (1) to determine the basal and genotoxic agent-induced DNA repair activities of NHOK cells, HOK cells transfected with the HPV-16 genome, and pre-neoplastic oral epithelial cells (derived from lesion biopsies) expressing "high risk" HPV; (2) to investigate the effects of HPV-16 oncogenes on basal and genotoxic agent-induced DNA repair activities of NHOK cells; and (3) to study the effect of "high risk" HPV ribozymes on DNA repair activities and mutation frequency (and rate) of hypoxanthine phosphoribosyl transferase (hprt) gene of pre-neoplastic and neoplastic human oral epithelial cells (expressing "high risk" HPV) derived from lesion biopsies. The applicants expect to answer the following questions: Does "high risk" HPV disrupt the repair of DNA damage in NHOK cells? If so, which DNA repair process is impaired? Are viral oncogenes responsible for such disruption? If so, is the inactivation of p53 or pRB by HPV oncogenes solely responsible for the disruption? Do pre-neoplastic or neoplastic cells (expressing "high risk" HPV) derived from human oral lesion biopsies have the same spectrum of DNA repair defects as NHOK cells transfected with "high risk" HPV genome? Does the disruption of viral oncogene transcripts restore the DNA repair activites and genomic integrity of HPV-immortalized HOK cells, pre-neoplastic and neoplastic human oral epithelial cells (from lesion biopsies) expressing "high risk" HPV oncogenes?

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- **Project Title: IDENTIFICATION OF GREEN TEA POLYPHENOL-TARGETED GENES**

  Principal Investigator & Institution: Hsu, Stephen D.; Oral Biol/Maxillofacial Path; Medical College of Georgia 1120 15Th St Augusta, Ga 30912

  Timing: Fiscal Year 2003; Project Start 12-JUN-2003; Project End 31-MAY-2005

  Summary: (provided by applicant): Green tea polyphenols appear to be chemopreventive against certain cancers, including **oral cancer;** but how cancer cells succumb while normal cells survive this polyphenol exposure is not known. Lack of this information prevented clinical uses of polyphenols for **oral cancer** chemoprevention or treatment. The long-term goal of this investigation is to elucidate the signal pathways and mechanisms by which green tea polyphenols differentially target normal and malignant cells to direct protective or apoptotic effects. Preliminary data from our

laboratories have demonstrated that normal epithelial cells express p57 (KIP2) in response to green tea polyphenols in a dose- and time-dependent manner. We propose a novel concept, that green tea polyphenols are able to activate two pathways: 1) a p57-mediated survival pathway, and/or 2) a caspase 3-dependent apoptosis pathway. The hypotheses to be tested is that p57 induction by green tea polyphenols in normal epithelial cells may serve an anti-apoptotic function, absence of the p57 response in malignant cells may result in induction of caspase 3-dependent apoptosis. The immediate goal of this proposal is to identify the survival or apoptotic genes that are regulated by green tea polyphenols. In this proposed project, the survival/apoptosis gene expression profile will be determined following green tea polyphenol exposure, in normal human epidermal keratinocytes and in human oral squamous cell carcinoma cells. Specifically, the levels of p57 expression induced by the most potent green tea polyphenol, (-)- epigallocatechin-3-gallate (EGCG), in normal human epithelial cells will be determined. Using RT-PCR, mRNA stability assay, Northern and Western blot analyses, the relationship between transcription/translation levels of p57 induction and the time/dose of EGCG will be established. The RNA samples at specific time points will be subjeted to gene array analysis and profiling. Not only will the expression profile of those genes that are either activated or suppressed by EGCG in normal or tumor cells, but promising cellular targets for future chemotherapeutic intervention may be identified. Data generated from this proposal may reveal novel drug targets for treatment of head and neck cancer.

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

- **Project Title: INACTIVATION OF CYTOTOXIC EFFECTORS IN ORAL CARCINOMAS**

  Principal Investigator & Institution: Jewett, Anahid; Assistant Professor; Dental Research Institute; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2002; Project Start 01-JUN-2001; Project End 31-MAY-2004

  Summary: The long-term objective of this application is to determine whether the initiation and progression of oral carcinomas in vivo is due to the induction of functional inactivation and cell death of Natural Killer cells. Human carcinomas of the head and neck and the oral cavity induce the least detectable cell-mediated anti-tumor immune responses, and decreased frequencies of proliferating lymphocytes have been observed in the peripheral blood and tumor tissue of **oral cancer** patients. More importantly, regressing oral tumors contain significantly larger numbers of functional NK cells when compared to those associated with primary tumors. Thus, the central hypothesis is that the initiation of NK cell apoptotic signaling by factors secreted from the NK cells or elaborated by **oral cancer** cells during their interaction will result in the inactivation of NK cell cytotoxic function, thereby enhancing the survival of oral carcinoma cells. To delineate the mechanisms by which Natural Killer cells lose their cytotoxic function and undergo apoptotic cell death in the presence of **oral cancer** cells, the following will be examined: 1. The role of oral tumor cell induced TNF-alpha release from NK cells in the absence of IFN-gamma secretion in inactivation and cell death of NK cells. There are also plans to study the effect of oral tumor cells on inhibition of TNF receptor associated protein (TRAFs) and NFkappaB functions in NK cells. 2. The effect of oral tumor cell elaborated TGF-beta on the inhibition of NFkappaB activity in NK cells, and subsequent induction of NK cell inactivation and cell death. 3. The roles of oral tumor cell induced stress related c-jun N-terminal kinase (JNK) and protein tyrosine phosphatase 1C (PTP1C) signaling in NK cells and in the regulation of TNF-alpha and

NFkappaB and induction of NK cell inactivation and cell death by oral carcinoma cells. 4. The differential effects of sensitive and resistant oral carcinoma cells on NK cell inactivation and cell death. 5. The effect of patient derived oral tumor cells in NK cell inactivation and cell death. Using both in vitro established oral tumor lines and in vivo studies utilizing tumor tissues and immune cells from individuals with cancer of the oral cavity, the exact mechanisms by which oral carcinoma cells exert an immunosuppressive effect on NK cells will be examined. Understanding the mechanisms by which NK cells become functionally inactivated and undergo cell death will enable design strategies to reverse such inactivation and ensure effective immunity against oral tumor cells.

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- **Project Title: INDIVIDUAL PREDOCTORAL DENTAL SCIENTIST FELLOWSHIP**

  Principal Investigator & Institution: Gu, Ying; Oral Biology and Pathology; State University New York Stony Brook Stony Brook, Ny 11794

  Timing: Fiscal Year 2002; Project Start 10-MAR-2002

  Summary: The general research goal is to study the therapeutic potential, and mechanisms of action, of tetracyclines(TCs) in protecting extracellular matrix(ECM) and preventing cancer metastasis. My particular interest is in TCs newly discovered ability to suppress the matrix metalloproteinases activity and to prevent angiogenesis. The long-term goal of this research is to demonstrate that TCs, including chemically modified tetracyclines (CMTs) which are devoid antimicrobial properties, can prevent pathologic ECM breakdown. We specifically propose to study the ability of a special formulated non-antimicrobial TC(CMT-3) to inhibit connective tissue breakdown in a tumor cell culture system. A complete interstitial ECM, which is well established in Dr.Simon's lab, will be employed to characterize the tumor cell-mediated ECM degradation. Our preliminary results have demonstrated that tumor proteinases (matrix metalloproteinases and one specific tumor serine proteinase, tumor-associated trypsin) both contributed to the high ECM degradative activities of a human colon carcinoma cell line, COLO 205. We then intend to use COLO 205 as a model system to study the ability and the mechanisms of CMT-3 in protecting ECM from breakdown through its inhibitory effect on tumor enzymes. The ultimate goal is to connect the effect of CMTs on this cancer cell model system to **oral cancer** and select one or more CMTs for use in preliminary human clinical trial.

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

- **Project Title: INDIVIDUAL PREDOCTORAL DENTAL SCIENTIST FELLOWSHIP**

  Principal Investigator & Institution: Kibbey, Megan M.; Pharmacology; Medical University of South Carolina 171 Ashley Ave Charleston, Sc 29425

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 29-SEP-2007

  Summary: (provided by applicant): Oral and oropharyngeal squamous cell carcinomas (OSCC) account for nearly 8,000 deaths a year nationally, with South Carolina ranking the highest of the fifty states in **oral cancer** mortality. Significantly, the survival rate of 51% has not changed over the past thirty years. Because the mortality of OSCC directly relates to the stage of diagnosis, early detection techniques and targeted therapy are clearly needed for enhanced survival rates. A strong correlation exists between the IGF system and cancer; individuals with the highest serum levels of insulin-like growth factor-1 (IGF-1) have the highest incidence of prostate and breast cancer. IGF-1 and IGF-2 mediate their tumorigenic effects through activation of the IGF-1 receptor (IGF-1R).

The IGFs also bind with high affinity to a family of soluble proteins known as the IGF binding proteins (IGFBPs), which reduce the bioavailability of the IGFs by sequestering them from the IGF-1R. The IGFBPs are natural inhibitors of the IGF system. As such, they are presently the only known IGF antagonists. Preliminary data suggest that the IGF system may be a target for therapeutics and prevention of OSCC. Our working hypothesis is that the amplification of the IGF system causing the overexpression of IGF-1R, IGF-1 or IGF-2, plays a central role in the molecular pathogenesis of OSCC. To test our hypothesis the following Specific Aims have been formulated: Specific Aim 1: Examine the expression of the IGF system components in model OSCC cell lines and human OSCC tissue, and Specific Aim 2: Determine the role of the C-terminus of lGFBP-2 in IGF binding.

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- **Project Title: INTERACTION OF UPA/R AND INTEGRINS IN ORAL CANCER**

  Principal Investigator & Institution: Stack, Mary S.; Associate Professor; Obstetrics and Gynecology; Northwestern University Office of Sponsored Research Chicago, Il 60611

  Timing: Fiscal Year 2002; Project Start 01-JUN-2001; Project End 31-MAY-2005

  Summary: (Adapted from the investigator's abstract) The invasive behavior of oral carcinoma requires coordinated cellular events including basement membrane attachment and detachment, extracellular matrix (ECM) proteolysis, and acquisition of motility. Altered expression of matrix binding integrins is associated with oral carcinoma progression. Integrins can promote an hierarchy of cellular responses dictated by the physical nature of the integrin engagement, thereby transducing distinct signals from the ECM. Production of two distinct classes of ECM-degrading proteinases, plasminogen activators (PA) and matrix metalloproteinases (MMP) is also in early event in malignant progression. The correlation between enhanced expression of the serine proteinase urinary-type PA (uPA or urokinase), MMP-9 (gelatinase B) and tumor progression is well described. Binding of urinary type-PA (uPA) o its cellular receptor (uPAR) leads to enhanced pericellular plasmin formation, which in turn directly degrades ECIV giycoproteins and activates selected MMPs such as MMP-9. Moreover, uPAJR may also regulate invasive behavior via novel, proteinase-independent mechanisms, by modifying integrin adhesive functions and modulating integrin signaling pathways. Our data demonstrate that a3b1 integrin aggregation alters expression of both uPA and MMP-9. Further, a3bl integrin aggregation induces uPA/R/a3b 1 integrin association and MAP kinase (MAPK) activation, resulting in enhance(proteinase transcription Based on these results, it is the working hypothesis of this proposal that a functional link between adhesion and proteolysis regulates oral carcinoma invasive behavior. Specifically we propose a multi-functional interaction of the uPA/R system with carcinoma cell integrins, such that integrin-in edited adhesion modulates cellular, iPA expression, while subsequent uPA/uPAR/integrin interactions in turn regulate downstream adhesive events that control proteinase expression, proliferation, adhesion and motility. To test this hypothesis, we will assess the specific physical parameters of a3b1 integrin engagement that control proteinase induction. The ability of uPAIR to modulate a3b1 signaling and modify proteinase expression and proliferation will then be analyzed. Immunohistochemical and biochemical analysis of normal and tumor tissues will be employed to evaluate integrin, proteinase, and MAPK expression and activity. The functional contribution of induced proteinases to the cellular invasive phenotype will then be evaluated. The long term goal of the proposed research is to provide a more detailed understanding of the functional link between

adhesion and proteolysis and the con tribution of this in terplay to regulation of metastasis.

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

- **Project Title: JUNCTIONS, CYTOSKELETON & MATRIX OF THE ORAL EPITHELIUM**

  Principal Investigator & Institution: Jones, Jonathan C.; Professor; Cell and Molecular Biology; Northwestern University Office of Sponsored Research Chicago, Il 60611

  Timing: Fiscal Year 2002; Project Start 01-AUG-1997; Project End 28-FEB-2007

  Summary: (provided by the applicant) Approximately 90 percent of oral cancers are squamous cell carcinomas originating from the oral epithelium. It is the sixth most prevalent solid tumor worldwide. The development and progression of **oral cancer** involves alterations in cell-cell junctions, cell-matrix adhesion sites and their associated cytoskeleton elements. The molecular bases of these alterations has been and continues to be the focus of this program project. The overall goal of the fourprojects and cores is to gain new insight into how the extracellular matrix influences cell behavior, how the functions of extracellular matrix elements are modified post-translationally by specific proteolytic events, how cytoskeleton changes impact cell motility and organization and how intercellular junction assembly/disassembly is regulated in normal and tumor epithelial cells. This proposal details the continuation of a concentrated and multidisciplinary set of studies by an interactive team of investigators at Northwestern University Medical School. The four component projects are highly interdependent. The subproject, "Laminin-5 and hemidesmosomes in oral epithelial cells" will study the molecular mechanisms underpinning the way matrix impacts cell adhesion and motility of **oral cancer** cells via the activity of their cell surface components. The subproject, "Cell adhesion and proteolytic potential in oral squamous cell carcinoma" will focus on the molecular mechanisms regulating metastasis-associated proteinases and the structural consequences of matrix degradation by cancer cells.The subproject, "Cytoskeletal-cell surface interaction in oral epithelial cells" will test the hypothesis that changes in expression of intermediate filament proteins regulates cell migration and tumor cell metastasis. The subproject, "Regulation of cell-cell junction structure and dynamics in oral tumor cell migration" will investigate the role of reversible modulation in cadherin-based cell-cell adhesion in oral cell migration that occurs during tumor progression. These multidisciplinary studies will provide precise information about the dissemination of cancer cells in this devastating cancer.

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- **Project Title: MICHIGAN ORAL CANCER PREVENTION NETWORK**

  Principal Investigator & Institution: Ismail, Amid I.; Professor; Cariology/Restor Sci/Endod; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-AUG-2004

  Summary: (provided by applicant): The Michigan **Oral Cancer** Prevention Network (MOCPN) will be established in response to RFA number DE-00-005 to promote the early detection of **oral cancer** and its prevention through organized community and provider-oriented programs and research. The MOCPN will be formed through collaboration between the Michigan Department of Community Health and the School of Dentistry, University of Michigan. The MOCPN will include the following additional partners: Michigan Tobacco Reduction Coalitions; Michigan Cancer Consortium;

Michigan Primary Care Association; Federally-Qualified Health Centers; Tobacco Free Michigan Action Coalition; Michigan Association of Health Plans; Voices of Detroit Initiative (VODI); community-based dental clinics; Michigan Dental Association; Michigan Dental Hygienists Association; Schools of Dentistry at the University of Michigan and University of Detroit-Mercy, and Departments of Otolaryngology, University of Michigan and the Henry Ford Health System. During Phase I, the network members, using the Planned Approach to Community Health (PATCH) model will consider focusing on two communities: 1) members associated with the partners including primary and dental care providers in 130 clinics or health centers and 2) residents of Wayne, Macomb, and Oakland counties who have the highest incidence and mortality rates of **oral cancer** in Michigan. The network will assess the **oral cancer** screening practices of primary care providers and survey current activities in the areas of tobacco cessation and reduction of heavy use of alcohol. The MOCPN Will survey primary care providers and all members of the partnering agencies, coalitions, and consortia for their knowledge and practices on **oral cancer** detection and prevention. The MOCPN will seek funding to disseminate and evaluate the CD- ROM training program that is being developed for the VODI with funding from the HRSA/CAP grant. The MOCPN will also develop a web-based database to collect information on screened patients and track their final diagnosis and treatment. The database will be accessible to primary care providers, specialists, and hospitals providing care for patients with potentially cancerous oral lesions. The MOCPN will survey the curricula of dental, medical and nursing schools in the state, and provide expertise to include information and training on **oral cancer** screening and prevention. By the end of the 3rd year, or earlier, the MOPCN would be ready to plan and implement community-based intervention studies.

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- **Project Title: MMP-2 IN PERIODONTAL DISEASE AND ORAL CANCER**

  Principal Investigator & Institution: Steffensen, Bjorn; Associate Professor; Periodontics; University of Texas Hlth Sci Ctr San Ant 7703 Floyd Curl Dr San Antonio, Tx 78229

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-MAY-2006

  Summary: MMP-2 is a member of the family of matrix metalloproteinases (MMPs), which together cleave a broad range of tissue components. While this property of the MMPs is a beneficial feature of normal development and tissue adaptation, uncontrolled MMP-2 activity has been strongly associated with inflammatory diseases, such as periodontal disease and arthritis, and tumor expansion and metastasis. This application is designed to develop compounds, which specifically inhibit MMP-2 activity. Since cleavage of molecules by MMP-2 occurs only if there is binding between the enzyme and substrate molecules, the specific mechanism by which MMP-2 binds its main collagen substrates will be investigated. In a collaborative effort, molecular biology and protein structural analysis methods will be applied to first identify specific MMP-2 binding sites on collagen by screening a random peptide library and mapping the functional peptide sequences on collagen. To identify the precise collagen binding site residues on MMP-2, nuclear magnetic resonance studies will be used to analyze the MMP-2 collagen binding domain (CBD) complexed with synthetic peptides, which mimic the CBD binding sites on collagen. The specificity of the identified sites and amino acids will be tested in competitive ligand binding assays and by analyzing the effects of site-specific mutations in the CBD. Once the precise binding sites on both collagen and MMP-2 are defined, small molecules will be developed that can inhibit the full-length native MMP-2 activity by competing for substrate binding and by

substituting binding site residues on the CBD. This will be accomplished in both MMP-2 ligand binding and activity assays, and in experiments with MMP-2 expressing cells. The proposed studies should define the specific binding site interactions between MMP-2 and its main collagen substrate and explore a new strategy to inhibit MMP-2 in inflammatory diseases and cancer based on competition for substrate binding.

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- **Project Title: MOLEC. PROFILING OF ORAL CANCER AGGRESSIVENESS/OUTCOME**

  Principal Investigator & Institution: Ziober, Barry L.; Otorhinolaryngology Head & Neck Surgery; University of Pennsylvania 3451 Walnut Street Philadelphia, Pa 19104

  Timing: Fiscal Year 2004; Project Start 01-MAR-2004; Project End 28-FEB-2006

  Summary: (provided by applicant): Oral squamous cell carcinomas (OSCC) represent the 6th most common cancer in the United States and are associated with low survival and high morbidity. Unfortunately, the 50% survival rate of patients with OSCC has not improved in the last 20 years. Furthermore, aggressive treatment of OSCC is disfiguring and can lead to long-term functional problems. One approach to reducing morbidity and mortality in OSCC patients is to accurately predict which tumors will be aggressive. The current staging system is inadequate in predicting tumor aggressiveness and patient outcome because of the wide variation in tumor behavior. This heterogeneity in tumor behavior is believed to reflect differences in the underlying gene expression profiles of individual cancers. Recently, gene expression profiling has identified tumor aggressiveness signatures and predictors of patient outcome in breast cancer, lung cancer, prostate cancer, etc. An aggressiveness signature and outcome predictor has not been described for OSCC. This R21 proposal will test the hypothesis that gene expression profiling using high-density microarrays will identify a gene signature for OSCC tumor aggressiveness and a molecular predictor for patient outcome. This hypothesis will be explored using three specific aims. 1.) Obtain gene expression profiles using paired normal and OSCC specimens from our Head and Neck Tumor Bank. 2.) Identify a molecular signature for OSCC aggressiveness and a predictor for patient outcome. 3.) Validate the molecular signatures with an independent sample of patients. This study will involve collaborations between investigators with expertise in microarrays, tumor biology, statistics, medicine, pathology, and bioinformatics. The data from this work will serve as preliminary data in R01/R33 applications testing the clinical utility of customized OSCC aggressiveness and patient outcome arrays as well as applications directed at understanding OSCC cancer biology and the development of new OSCC therapies. The unique molecular signature for OSCC tumor aggressiveness and the predictor of patient outcome established from this work has the enormous potential to reduce OSCC patient mortality and morbidity.

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

- **Project Title: MOLECULAR EVENTS IN ORAL CANCER PROGRESSION/PREVENTION**

  Principal Investigator & Institution: Stoner, Gary D.; Professor and Chairman; Medicine Administrtation; Ohio State University 1960 Kenny Road Columbus, Oh 43210

  Timing: Fiscal Year 2002; Project Start 15-SEP-1998; Project End 30-JUN-2003

  Summary: The goals of the **Oral Cancer** Research Program (OCRPP) at The Ohio State University are to: 1) enhance and facilitate investigations of those interactions between human cells of the oral cavity and tobacco by- products that lead to adverse biological

responses; 2) coordinate activities that will utilize the information obtained from these interactions, at malignant oral lesions; and, 3) promote and develop research that will determine the efficacy of control and intervention strategies. Established investigators in the **Oral Cancer** Research Program Project "Molecular Events in the Progress/Prevention of Oral Cancer" are concentrating their efforts in five major areas of research (Research Projects) to address this central theme. Research Project 1 (Carcinogen/Oxidant Synergism in **Oral Cancer** Initiation is focussing on initiating events in **oral cancer.** They will determine the metabolic fate of tobacco-associated carcinogens (TAC) in oral mucosal cells and how the metabolism of these compounds may be modified by ethanol. Project 1 will also explore the ability of oral mucosal cells to respond to physiologically relevant concentrations of reactive oxygen species. The genetic events leading to the establishment of premalignant and malignant lesions will be studied by Research Projects 2 and 3. Research Project 2 (Role of G/1 Phase Regulatory Genes and Identification of Differentially Expressed Novel Genes in Premalignant Oral Lesions) will evaluate those genes more closely associated with aberrant cell proliferation. Research Project 3 (Inactivation of the TGF-beta Receptor Complex in **Oral Cancer** Development) will study the loss of control of cell cycle proliferation by evaluating the effect of gene alterations (mutations, deletions, methylation) on the TGF-beta receptor complex (i.e., protein binding, kinase activity, and modification of specific downstream substrates). Research Project 4 (Molecular Mechanisms in Conversion of Cells in Oral Tissues from Normal to Premalignant and from Premalignant to Malignant) will explore those conditions involved in the transformation of normal cells into premalignant cells by TACs and the conversion of premalignant oral dysplasias into squamous cell carcinomas. In concert with Research Projects 2 and 3, the cells transformed in vitro by TAC, or concerted to malignancy by TAC, will be examined to determine if the same changes occur in cell cycle regulatory genes and the TGFbeta receptor complex as are found in premalignant and malignant tissues form patients. The rationale for the studies in Research Projects 1, 2, 3, and 4 is to provide information on those premalignant to the malignant stage. This information will be employed by Research Project 3 (Chemoprevention of Premalignant and Malignant Oral Tumors) which will develop strategies for intervention and preventive measures whereby the cytotoxic or genetic damage manifested by tobacco-related products is inhibited or modified and progression of dysplastic lesions to malignancy is prevented. This involves both natural and synthetic chemicals that affect the activation and detoxification of TAC and that interact with and modify the function of critical cellular genes or gene products that are responsible for the generation and maintenance of premalignant dysplasias and the conversion of these dysplasia into malignant oral cancers. In summary, the major thrust of the Program Project is to investigate the multiple genetic pathways in the loss of regulatory control of cell proliferation, differentiation, and apoptosis. With this information, we should be able to determine which chemopreventative agents will best intervene in the early stages of the cascade of events leading to **oral cancer** and by understanding the nature of the molecular changes occurring in the early stages of disease, we can develop strategies directed towards the modulation of those events that are specifically involved in the process.

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- **Project Title: MOLECULAR MECHANISMS OF ORAL CANCER DEVELOPMENT**

  Principal Investigator & Institution: Weghorst, Christopher M.; Associate Profesor; Environmental Health Sciences; Ohio State University 1960 Kenny Road Columbus, Oh 43210

  Timing: Fiscal Year 2002; Project Start 01-JUN-1998; Project End 31-MAY-2004

Summary: The objective of this R29 proposal is to understand what role inactivation of the p16 tumor suppressor gene plays in the multi-stage development of oral cancers, with an emphasis on premalignant lesions. The studies described herein address the hypothesis that a subset of the genetic changes commonly present in end-stage oral squamous cell carcinomas (SCC) will have already occurred in premalignant (leukoplakia, erythroplakia and proliferative verrucous leukoplakia) lesions. The p16 gene has previously been shown to be inactivated through a variety of mechanisms in 80 percent of SCC of the head and neck. In contrast, a critical evaluation of the role of p16 inactivation in premalignant oral lesions has yet to be explored. Therefore, we will focus our studies on this critical cell cycle regulatory gene in premalignant cells. The experimental approach involves a combination of genetic and biochemical methodologies. Studies in Specific Aim 1 are designed to determine the incidence and mechanism of p16 inactivation (including deletions, insertions, single nucleotide substitutions, and gene hypermethylation events) in premalignant oral lesions. Secondary to our evaluation of premalignant lesions, SCC will be screened for p16 mutations in an effort to identify a larger number of missense mutations for subsequent studies in Specific Aims 2 and 3. Once identified, premalignant and malignant oral lesions exhibiting p16 mutations will be assessed at the level p16 transcription and translation for altered p16 expression compared to patient-matched normal tissues (Specific Aim 2). These expression studies will be performed as a means of determining a precise level of p16 deregulation. In addition, specific P16 mutant proteins will be evaluated in Specific Aim 3 for their degree of biologic activity compared to the wild-type P16 protein. Mutant P16 proteins will be constructed by site-directed mutagenesis and evaluated for their ability to bind to CDK4 and inhibit CDK4 kinase activity in vitro. The in vivo functional activity of specific mutant P16 proteins will also be evaluated indirectly by determining the levels of phosphorylated and unphosphorylated RB proteins in samples derived from individual premalignant and malignant oral lesions. Overall, it is anticipated that the results from these studies will not only broaden our understanding of the molecular mechanisms of **oral cancer** development, but may also aid in the identification of specific causative agents, intermediate endpoint biomarkers, and the development of successful intervention strategies which target premalignant disease.

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- **Project Title: MOLECULAR PREDICTORS OF ORAL CANCER DEVELOPMENT**

  Principal Investigator & Institution: Jordan, Richard C.; Associate Professor; Stomatology; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 03-JUN-2002; Project End 31-MAR-2004

  Summary: (provided by applicant) Despite improvements in the management of oral squamous cell carcinoma (SCC), the 5-year survival rate has remained disappointingly low, at about 40%, for the past several decades. Therefore, this indicates the need for new strategies to improve outcome. One such strategy is to better understand the earliest forms of oral SCC, in the precancerous stage, with the long-term aim of preventing the progression to fully developed disease. Oral epithelial dysplasia is the single most important risk factor for **oral cancer;** however, only about 20% of all patients with epithelial dysplasia will ever progress to malignancy. Presently, for the individual patient with dysplasia, no reliable biomarkers have been discovered that indicate increased risk of progression to oral SCC. Our long-term goal is to identify molecular biomarkers that will predict oral SCC development. The objectives of this proposed

research are to determine the mRNA expression levels of specific novel biomarkers, identified in our microarray studies of oral SCC, in routinely processed biopsies of oral precancers and to determine if these changes are associated with the progression to **oral cancer.** The central hypothesis is that analysis of gene expression of specific biomarkers can be used to distinguish which oral premalignancies will progress to cancer from those which will not. The rationale for the proposed research is that by studying oral precancers, where it is known which progressed to oral SCC, critical genetic events necessary for **oral cancer** development can be established. This phased application will be significant because it will provide new molecular insights into the development of **oral cancer** and it will identify potential new targets for screening and therapeutic intervention. In the R21 phase, we will establish a reliable, quantitative PCR method for gene expression in routinely processed oral biopsies. Specific Aim 1: To optimize quantitative real-time PCR for the analysis of gene expression in laser microdissected (LCM) routinely processed oral biopsies. Specific Aim 2: To establish the quantitative requirement for LCM-generated RNA for real-time PCR. In the R33 phase, we will apply this technology to conduct a large-scale, molecular epidemiological study of specific novel biomarkers, identified in our microarray studies of **oral cancer,** in a cohort of 96 patients with oral precancer who have been followed for several years and where it is known which patient developed **oral cancer** and which did not. Specific Aim 1: To determine if oral cancer-associated biomarkers are overexpressed in LCM-oral epithelial dysplasias and oral SCC using real-time PCR. Specific Aim 2: To determine if specific biomarkers can be used to predict **oral cancer** development in patients with oral precancer.

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

- **Project Title: MOLECULAR PREDICTORS OF ORAL PREMALIGNANCY PROGRESSION**

  Principal Investigator & Institution: Wong, David T.; Professor & Chair; Diagnostic & Surgical Sciences; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2002; Project Start 11-FEB-2002; Project End 31-JAN-2004

  Summary: Oral cavity cancer is the 6th most common cancer in the United States. Pathogenesis of this cancer includes specific features of histopathological and molecular progression from normal to premalignant to tumor. Yet the molecular basis of this solid tumor is not well understood. Only 18 percent of oral premalignancies progress to cancer. The ability to predict the malignant progression of oral premalignancies will reduce the mortality and restricts the morbidity of this cancer since it is readily accessible for examination. This Exploratory Project is a sequential series of studies to test the hypothesis that broad gene expression monitoring using high-density microarrays offers the potential to identify genes in the malignant progression of oral premalignancies. Three Specific Aims are in place to test this hypothesis. Specific Aim 1 is to obtain gene expression profiles for 12,000 genes on progressing and non-progressing human oral premalignancies. Specific Aim 2 is to use bioinformatics tools to generate an "Oral Premalignancy Progression Predictor Gene" set (OPPPG). Specific Aim 3 is to validate the OPPPG set on an independent sample set. The proposed work is based on a history of successful collaborations amongst the investigators who are at the forefront of the respective fields. The outcome of this application will be unique and highly relevant molecular resources capable of predicting of oral premalignancy progression. In addition to understanding the biology and pathogenesis of this cancer, the generated results will serve as basis of future clinical and translational applications

such as diagnostics, molecular epidemiology and treatment outcome monitoring of **oral cancer** patients (R33 and RO1).

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

- **Project Title: MOLECULAR PROGRESSION MODEL FOR HNSCC**

  Principal Investigator & Institution: Sidransky, David; Professor; Otolaryn & Head & Neck Surgery; Johns Hopkins University 3400 N Charles St Baltimore, Md 21218

  Timing: Fiscal Year 2004; Project Start 01-APR-1998; Project End 28-FEB-2009

  Summary: (provided by applicant): We have described a preliminary genetic progression model that describes the timing of specific genetic events in head and neck squamous cell carcinoma progression. This model has included the nature and timing of loss and amplification at specific chromosomal loci that contain putative tumor suppressor genes and proto-oncogenes, respectively. Specific tumor suppressor genes, including p14 and p16, and proto-oncogenes, including p63, have been identified as critical in **oral cancer** development. This study builds upon the foundation of this prior model by identifying specific, ordered transcriptional alterations in order to establish a transcriptional progression model of **oral cancer.** The transcriptome of oral SCC described by this model will be correlated with DNA based SNP analysis to map and identify putative oncogenes and tumor suppressor genes. Specific attention will be directed at identification of early transcriptional and genetic alterations. These early molecular events will be identified and developed as targets for early detection and staging approaches, with emphasis on molecular detection strategies amenable to rapid, automated application.

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

- **Project Title: NEOADJUVANT THERAPY OF OR CANCER BY INHIBITING NF-KAPPAB**

  Principal Investigator & Institution: Wang, Cun-Yu; Associate Professor; Biologic & Materials Sciences; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

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

  Summary: Oral cancer typically presents as a very malignant tumor. More than 90 percent of oral cancers are squamous cell carcinoma which also is one of the most common malignant types occurring lung, skin, and ovary. At advanced stage, p53 is mutated in about 60 percent of tumors and the effectiveness of chemotherapy and radiotherapy has been very disappointing. Therefore, improving the efficacy of these therapies has become an urgent topic for both clinical oncologists and basic scientists. There is increasing evidence that apoptosis plays a critical role in the response to chemotherapy and radiotherapy. Resistance to apoptosis is likely to serve as a primary mechanism whereby tumor cells are able to escape chemo- and radio-therapy killing. Recently, this laboratory has observed that the transcription factor NF-kappaB is activated by several chemotherapeutic compounds and ionizing irradiation, and inhibition of NF-kappaB enhanced the apoptotic response of these stimuli in human fibrosarcoma model system in vitro and in vivo. The specific aims proposed in this application are the following: 1). Determine whether chemotherapy and radiotherapy activate NF- kappaB in oral squamous cell carcinoma and whether inhibition of NF-kappaB potentiates apoptosis of oral SCC induced by these therapies in vitro. 2). Explore the molecular mechanisms involved in NF-kappaB suppression of cancer therapy-mediated apoptosis. The role of NF-kappaB-induced genes c-IAP1 and 2 will be

examined. 3). Determine whether inhibition of NF-kappaB as a neoadjuvant will enhance the efficacy of **oral cancer** therapy in a nude mouse model. We will utilize adenovirus-mediated delivery of super-repressor-IkappaBalpha and proteasome inhibitors to block the activation of NF-kappaB in vivo and determine whether these approaches will effectively inhibit the tumor growth in vivo. 4). Identify chemo- and radio-resistant genes by genetic screening. By using a unique cell line HT1080I cells that is sensitive to cancer therapy-induced apoptosis, efforts will be made to identify chemo- and radio-resistant genes from oral squamous cell carcinoma utilizing retroviral cDNA-based functional cloning. These studies will uncover the genetic mechanism of **oral cancer** resistance to cancer therapy and have an important implication in improving the efficacy of **oral cancer** therapy.

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

- **Project Title: NEOVASCULAR REGRESSION FOR ORAL CANCER THERAPY**

  Principal Investigator & Institution: Nor, Jacques E.; Cariology/Restor Sci/Endod; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

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

  Summary: (provided by applicant): One person dies every 30 minutes in the U.S. as a consequence of head and neck cancer. Solid tumor growth is dependent on the ability of tumor cells to recruit and sustain their own microvascular network. Therefore, targeted disruption of the tumor vasculature might be beneficial for the treatment of patients with **oral cancer.** The broad long-term goals of this research are to understand the biology of microvessel regression and to develop antiangiogenic strategies for **oral cancer.** The objectives of this application are to study the process of caspase mediated disruption of human microvessels in vitro and in vivo, and to examine the effect of the disruption of the tumor neovascular network on oral tumor growth. Dimerization of caspase-9, an apical protease of the apoptotic pathway, activates an irreversible signaling pathway that results in cell death. To perform the studies proposed here. An inducible artificial death switch (iCapase-9) has been as engineered and characterized; it consisted of the catalytic domain of caspase-9 fused to an FKBP-based dimerizer domain. Microvascular endothelial cells stably transduced with iCaspase-9 will be plated in collagen matrices to study molecular mechanisms of capillary tube disruption in vitro. Human microvessels will be engineered in immunodeficient mice with endothelial cells expressing iCaspase-9 to study the biology of microvessel regression in vivo. There are also plans to design and characterize a targeted adenoviral vector to deliver iCaspase-9 specifically to the tumor endothelium. Tumor neovascular endothelial cells express specific markers (alpha vBeta2 and KDR), which are expressed in low levels, or not expressed by endothelial cells of mature blood vessels. The approach will target the adenoviruses to tumor neovessels by: 1) enhancing the tropism of the vector with the incorporation of the RGD-4C peptide (shown to bind to alpha v Beta3 and to home specifically to tumor neovessels into the adenoviral fiber protein; and 2) by driving the expression of iCaspase-9 with domains of the promoter and enhancer of KDR (shown to be preferentially expressed in tumor neovessels). This research will enhance the understanding of the biology of neovascular regression, and will investigate a novel anti-angiogenic strategy based on targeted delivery and controlled activation of a pro-apoptotic caspase in the endothelium of oral tumors.

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

- **Project Title: NEW YORK STATE ORAL CANCER CONTROL PARTNERSHIP**

  Principal Investigator & Institution: Kumar, Jayanth V.; Assistant Director; New York State Dept of Health Rensselaer, Ny 12144

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-AUG-2004

  Summary: (provided by applicant): **Oral cancer** is a significant problem in New York State. During the period 1993-1997, there was an annual average of 1889 cases of oral and pharyngeal cancers. Trends in morbidity and mortality show only a modest change in the past twenty years. The proportion of oral cancers diagnosed in early stages range from a low of 27 percent among black males to a high of 49 percent among white females. New York has a diverse population and more than 3 million adults are engaged in high-risk behaviors. The objectives of this proposal are to plan and develop an organizational infrastructure, conduct needs assessment, and guide the development of interventions for the prevention and early detection of **oral cancer** in New York State. We will develop a unique private-public partnership with representatives from many different organizations. A steering committee consisting of the State Health Department, New York University College of Dentistry (NYUCD), American Cancer Society, Schuyler Center for Analysis and Advocacy, Memorial Sloan Kettering Cancer Center, a patient support organization (Support for People with Oral, Head and Neck Cancer), The New York State Task Force on Immigrant Health and several other organizations will guide the needs assessment, development of the partnership, and assessment of the type and appropriateness of interventions. We will use the planning model developed by Green and Kreuter to conduct the needs assessment. During the first phase of the project, the activities will focus on analysis of data on incidence and mortality of oral cancers. Surveys of the public and professionals will be conducted to assess knowledge, opinions and behaviors. The New York State Cancer Registry will be used to examine the county specific rates and map the cases. The BRFSS data will be used to assess the knowledge, opinion and behavior of the public. Also, four separate surveys of approximately 1000 health care professionals (physicians, dentists, nurse practitioners/physician assistants, and dental hygienists) will be conducted. Another survey of approximately 700 health educators will be conducted to assess their knowledge, opinion, and the type of educational materials used. In addition, focus groups and interviews will provide insight into the opportunities and barriers for designing interventions. We will also prepare two case studies of **oral cancer** patients. During the second phase of the project, NYUCD will take the lead in developing, implementing and evaluating interventions.

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- **Project Title: NORTH CAROLINA NEEDS ASSESSMENT FOR ORAL CANCER CONTROL**

  Principal Investigator & Institution: Patton, Lauren L.; Associate Professor; Dental Ecology; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 01-SEP-2001; Project End 31-AUG-2004

  Summary: (provided by applicant): Most oral and pharyngeal cancers (OPC are preventable, and many are curable when diagnosed at an early stage. North Carolina (NC) is the 11th most populous state and ranks 13th in age-adjusted mortality rate for OPCs. In NC, African Americans carry a disproportionate burden of this malignancy and are twice as likely to be diagnosed with regional or distant spread OPC as whites. Because tobacco and alcohol use are responsible for most oral cancers, and because the

disease can be detected and treated at an early stage, it should be possible to develop and implement public health interventions that will impact this disease. However, since states may differ in the epidemiology of **oral cancer,** the public's exposure to risk factors and its awareness of the disease, health providers' knowledge, opinions, and practices regarding the disease, and the resources available for preventing and controlling the disease, state-specific plans are needed. In this project, NC OPC surveillance data will be used to characterize features of the state's OPC burden. Phone surveys of the general adult population will identify levels of public awareness about OPC risks, risk prevention, signs and symptoms, and access to care. Health care provider surveys and focus groups will identify how attitudes, knowledge and behavior regarding OPC prevention and early detection affect diagnosis stage. Patients newly diagnosed with OPC will be interviewed to document and characterize events leading to their diagnosis. An advisory committee will review research findings and guide development of statewide intervention. The hypothesis for this NC application is that by gaining state-specific information through needs assessments and by creating an organizational infrastructure responsible for developing, implementing, and evaluating a statewide plan for promoting the prevention and early detection of **oral cancer,** the incidence and mortality rates for OPC in NC, particularly among minorities, can be reduced.

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

- **Project Title: NOVEL APPROACHES TO DETECT VIRUS-CANCER ASSOCIATIONS**

  Principal Investigator & Institution: Ahlquist, Paul G.; Professor; Inst for Molecular Virology; University of Wisconsin Madison 750 University Ave Madison, Wi 53706

  Timing: Fiscal Year 2002; Project Start 01-MAY-2002; Project End 30-APR-2006

  Summary: (provided by applicant): Viruses are established, causal factors in 15%-20% of human cancers and are widely suspected to be involved in more. The long-range goals of this project are to develop methods to simultaneously screen tumor and other tissue samples for the genomes or partial genomes of many viruses, to use these methods to test for novel virus-cancer associations, and to determine their statistical and clinical significance. In particular, this highly collaborative proposal describes how a new, uniquely flexible, maskless photolithography technology will be used to produce and refine high density oligonucleotide microarrays able to sensitively detect all genes or transcripts of all known human tumor viruses. For comparison, arrays of PCR-amplified viral probes spotted on glass slides will also be tested. Additional experiments will systematically optimize extraction and amplification methods for specific, sensitive, and robust detection of viral RNA and DNA sequences at low copy number in clinical tissue samples. The resulting tools and methodology will be applied to relevant clinical samples to test and resolve the emerging connections of two well- characterized human tumor viruses, human papilloamavirus (HPV) and Epstein- Barr virus (EBV), with oral cancers and breast cancers, respectively, and to compare the microarray results with other state-of-the-art virus detection methods applied to the same tissue samples. These studies will provide proof- of-principle tests of microarray use in detecting and characterizing viral contributions to cancer and address significant, current issues in the viral etiology of specific tumors. Simultaneous microarray screening for many viruses o viral genotypes amplifies the power of etiologic and diagnostic studies on precious tissue samples, offers the potential to discover unsuspected virus-cancer links, and allows profiling expression of viral and selected cell genes to provide the molecular signatures of a tumor and to evaluate the potential contribution of the virus to that

tumor. The methods developed also will be applicable to probe for virus involvement in other chronic or acute disorders.

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

- **Project Title: NOVEL OPTICAL PROBE FOR ORAL AND DENTAL TISSUE SCREENING**

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

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

  Summary: Currently under development is a novel optical probe for non-invasive characterization and monitoring of the biochemical and morphological changes in oral cavity epithelium leading to dysplasia and ultimately to invasive squamous cell carcinoma. Oral squamous cell carcinoma is a condition, which will kill approximately half of patients afflicted within five years of diagnosis and may leave surviving patients with severe aesthetic or functional compromises. Approximately 31,000 Americans develop **oral cancer** each year. **Oral cancer** progresses through a series of morphologic changes, which, if detected and treated early, can vastly improve prognosis and survival. Clinicians in the oral and Dental fields play an important role in early detection of **oral cancer,** and the current application seeks to develop a tool to aid these clinicians in accurate screening and diagnosis. During a previous Phase 1 SBIR effort, a fluorescence image guided optical coherence tomography (FIG-OCT) probe, capable of simultaneously acquiring and co-registering tissue autofluorescence and optical coherence tomography (OCT) images, was designed and built. Fluorescence imaging provides a highly sensitive and rapid means for oral cavity screening, while the ability of OCT to elucidate high-resolution sub-surface morphological features leads to a superior diagnostic technique with higher specificity than autofluorescence imaging alone. In a hamster model of **oral cancer,** it was successfully demonstrated that FIG-OCT resulted in a rapid and accurate technique for **oral cancer** screening. The current Phase 1 application presents plan to adapt this instrument into a form, which can be used, for preliminary clinical investigation in humans. PROPOSED COMMERCIAL APPLICATION: NOT AVAILABLE

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

- **Project Title: NYU ORAL CANCER RAAHP CENTER**

  Principal Investigator & Institution: Katz, Ralph V.; Professor and Chair; Basic Science and Craniofacial Biology; New York University 15 Washington Place New York, Ny 10003

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-JUL-2008

  Summary: This proposed NYU **Oral Cancer** Research for Adolescent and Adult Health Promotion (RAAHP) Center is a P50 Center which was designed in response to the NIDCR request for applications for Centers for Research to Reduce Oral Health Disparities (RFA:DE-99-003). The overall goal of this proposed NY **Oral Cancer** RAAHP Center is to conduct studies and promote activities that will reduce oral disparities in the United States. While **oral cancer** occurs in all segments of the U.S. population, **oral cancer** rates (both incidence and mortality) are highest among minority populations, especially in African Americans and in Hispanics. Specifically, this proposed Center will, as stated in the RFA, support research "that will lead to an understanding of the factors associated with health disparities as well as to the support and development, testing and evaluation of interventions designed to reduce [oral cancer] disparities". The

Specific Aims of the overall Center are: 1) to conduct a set of five major studies, as fully described in this grant application; 2) to design and conduct a sixth major study on **oral cancer** in the theme of this Center; 3.) to stimulate and support the design, writing and submission of Developmental 'Spin-Off'; 4.) to stimulate and support the development, selection, funding and implementation of two types of pilot research studies: bioethics and scientific pilot studies; 5.) to maintain three Cores (Administrative, Informatics, and Biostatistics) that will support the scientific activities of all the investigators in this proposed Center; 6) to develop and implement a full set of intra-Center research training and career development activities which focus on creating opportunities for scientists from underrepresented groups within the scientific workforce; 7) to participate fully in inter-Center national research and training networks; 8) to serve as an intellectual and administrative nidus to stimulate **oral cancer** research interests, discussions, and planning sessions among Center participants as well as among other cancer research colleagues; and 9) to provide information and findings on **oral cancer** to community involved health service units.

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- **Project Title: ODC-AZ AS A TUMOR SUPPRESSOR BY DNA DEMETHYLATION**

  Principal Investigator & Institution: Tsuji, Takanori; Ctr/Biochem/Biophys Scis & Med; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

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

  Summary: (provided by applicant): This is a four-year proposal to examine novel anti-tumor activities of ornithine decarboxylase-antizyme (ODC-Az) in carcinogenesis by a DNA demethylation mechanism. ODC-Az is an intracellular inhibitory molecule of ornithine decarboxylase (ODC) enzyme activity that causes polyamine depletion, which is, implicated in anti-proliferation and differentiation. Expression of ODC-Az is, significantly reduced in animal and human **oral cancer** cells compared with normal counterparts. Forced-expression of the ODC-Az gene in **oral cancer** cells altered malignant phenotype by re-activation of genes involved in tumor suppression. Several genes up regulated by ODC-Az are known to be silenced in tumor cells owing to aberrant hypermethylation of the promoter region. Based on this evidence, this application proposes experiments to test the following hypotheses; 1) ODC-Az re-activates tumor suppression-related genes silenced in tumor cells by DNA aberrant hypermethylation, 2) ODC-Az is a potential physiological tumor suppressor molecule. This proposal is design to utilize newly developed strategies, such as cDNA arrays, genetically engineered animal of cancer models and protein transduction systems. This is a novel and promising pathway to counter the deregulated growth and differentiation as well as the silencing mechanism of tumor suppressor genes in cancer cells. The mechanism, by which the regulatory genes involved in normal function of growth invasion and metastasis may become affected by DNA methylation, will be, investigated in the proposed studies. There are two Specific Aims in this proposal: 1) To elucidate the gene expression profile regulated by ODC-Az in human head and neck cancer and 2) To validate ODC-Az as a physiological tumor suppressor molecule. The long-term goal of this project is to determine if ODC-Az could be use therapeutically as a physiological growth suppressor, inducer of terminal differentiation, and inducer of DNA demethylation for reactivation of tumor suppressor genes in the treatment of patients with cancer.

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

- **Project Title: ORAL CANCER CENTER**

  Principal Investigator & Institution: Myers, Eugene N.; Professor, Chairman; Otolaryngology; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 01-AUG-1999; Project End 31-JUL-2004

  Summary: This is an application to establish an **Oral Cancer** Center at the University of Pittsburgh within the overall program of the Comprehensive Oral Health Research Center of Discovery The University of Pittsburgh already has in place substantial resources, capabilities, innovative research and clinical activities with direct relevance to cancer of the oral cavity, which includes the School of Medicine, the School of Dental Medicine, the Graduate School of Public Health, the University of Pittsburgh Medical Center Health System, and the University of Pittsburgh Cancer Institute. Using these resources. the proposed **Oral Cancer** Center will focus research and clinical efforts on **oral cancer** and will aim to develop a broad-based comprehensive program integrating biomedical, behavioral, social and clinical services as well as basic re research in **oral cancer.** The overall objectives of the Center are to coordinate and encourage multi-disciplinary collaborations within a large pool of existing expertise in **oral cancer.** Improvement in the clinical care of patients with oral cavity cancer is highly dependent upon scientific investigations and on rapid translation of research findings into novel clinical trials to improve the cure rate in oral cavity cancer. The **Oral Cancer** Center will foster basic and clinical research, as exemplified by the four major programs. Molecular Carcinogenesis and Cell Biology. Oral Immunology; Prevention and Control; and Clinical Investigations, which will encompass the scope of research at the Center. Within the programs are five research and one pilot proposals included in this application. Fie Cores will provide support for the Center's research and clinical activities. To ensure the availability of high quality preention, control, early detection, and education programs in **oral cancer** in Western Pennsylvania, the **Oral Cancer** Center will implement and expand community outreach activities and develop methods to improve education of health care professionals. Increased awareness of risk factors for **oral cancer** among health care providers and the public are likely to make an impact on prevention and early detection of oral cavity cancer. The overall goal of the **Oral Cancer** Center at the University of Pittsburgh is to make a substantial impact on decreasing morbidity and mortality from oral cavity cancer in Western Pennsylvania.

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

- **Project Title: ORAL CANCER DETECTION: CURRENT/EMERGING TECHNIQUES**

  Principal Investigator & Institution: Sirois, David A.; New York University 15 Washington Place New York, Ny 10003

  Timing: Fiscal Year 2002

  Summary: The stage of cancer at the time of treatment is the most important factor affecting treatment outcome: early diagnosis is associated with more than a 75% 5-year survival rate whereas lite diagnosis is associated with less than a 25% 5 year survival. While survival rates for many cancers have improved during the past twenty years, the survival rate for **oral cancer** has remained unchanged because most cases are diagnosed at advanced stages. The natural history of **oral cancer** is such that the asymptomatic, pre-malignant lesion can be identified long before malignant transformation if individuals are properly evaluated and adequate assessment technology exists to support the diagnostic process. The unaided clinical examination alone is inadequate for detecting **oral cancer,** when performed by experienced clinicians, and ultimately will

require adjuvant assessment tests to improve early detection. As recommended in Objective 9.6 of Healthy People 2010 earlier detection is essential to improve treatment outcomes for **oral cancer.** Earlier detection will require technologies that improve visualization of, or surveillance for, early mucosal changes associated with dysplasia or malignancy, combine with diagnostic tests which accurately characterize the malignancy potential. This project will systematically examine selected current and/or emerging technologies to determine their utility and optimal application, along or in combination, to reliability detect oral cancer/pre-cancer at its earliest stage by applying the tests to low-risk, high-risk and known **oral cancer** lesions. Unlike previous studiers this project allow every subject and lesion to be exposed to every assessment test, with specific attention to populations with varying risk for **oral cancer** and to the intended use of a test as a screening, surveillance adjuvant or definitive diagnostic tool. The inclusion in this study of emerging technologies will facilities the analytical validation of tests which could revolutionize the detection and diagnosis of **oral cancer.** It is expected that insights gained from this study will be hypothesis-provoking, leading to new ideas about biomarkers for **oral cancer** and their exploitation for the prevention, early detection and treatment of **oral cancer.**

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

- **Project Title: ORAL CANCER PREVENTION AND DETECTION: THE ILLINOIS MODEL**

  Principal Investigator & Institution: Warnecke, Richard B.; Professor and Director; Surgery; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2002; Project Start 01-SEP-2001; Project End 31-AUG-2004

  Summary: (provided by applicant): This proposal responds to RFA DE-00-005, "State Models for **Oral Cancer** Prevention and Early Detection." The overall objective is to develop a statewide model for implementing **oral cancer** prevention and early detection in Illinois. We propose to: 1) develop an enduring statewide alliance for **oral cancer** prevention and early detection initiatives and 2) complete both state- wide and community epidemiological needs assessments. The statewide partnership will provide leadership, support, and coordination to build the program in collaboration with an existing network of 96 local health departments (LHDs), located throughout Illinois. Working through LHDs to ensure participation by key organizations and individuals at the local level, the statewide partnership will facilitate and coordinate access to and efficient use of available resources and the existing planning infrastructure beginning at the state level and then with each participating LHD. In Illinois, LHDs have capacity for local planning to meet local needs. They most often are the lead implementation sites for public health service delivery. LHD staff are most knowledgeable about the health needs of their communities and, hence, are the most effective channels for local program planning and implementation. As part of a larger planning effort the Division of Oral Health (DOH), Illinois Department of Public Health initiated an Oral Health Needs Assessment and Planning Program (OHNAPP) using the "Seven-Step" planning model devised by the Association of State and Territorial Dental Directors which will be employed in this project as well. Participation in IPLAN and OHNAPP has provided LHDs with training, technical assistance, data and quality assurance mechanisms to help determine oral health status and plan comprehensive programs that meet community oral health needs. Oral and pharyngeal cancer is one of six priority areas identified by those communities who have completed the OHNAPP assessment. This project will extend that aspect of the plan more broadly across Illinois. The ultimate outcome of the process will be the development and implementation of appropriate

statewide and community-specific intervention strategies that will enable the state to meet the two primary objectives related to **oral cancer** defined by the Healthy People 2010 initiative: Increase the proportion of adults who, in the past 12 months, report having had an examination to detect oral and pharyngeal cancer and increase the proportion of oral and pharyngeal cancers detected at the earliest stage.

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

- **Project Title: ORAL CANCER: MOLECULAR PROFILES & CLINICAL OUTCOMES**

  Principal Investigator & Institution: Chen, Chu; Associate Member; Fred Hutchinson Cancer Research Center Box 19024, 1100 Fairview Ave N Seattle, Wa 98109

  Timing: Fiscal Year 2003; Project Start 16-JUN-2003; Project End 31-MAY-2008

  Summary: (provided by applicant): Oral and oropharyngeal squamous cell carcinoma (OSCC) is the 6th most frequently diagnosed cancer worldwide. In the U.S., approximately 30,300 new cases were diagnosed in 1999. The 5-year survival of patients with OSCC -about 50%- has not improved in the past two decades. Survivors often suffer orofacial dysfunction, disfigurement, and psychological stress. A major impediment to the effective management of OSCC patients is our limited ability to predict the natural history of individual lesions. While prognosis is to some extent correlated with anatomic site, tumor thickness, tumor grade, and lymph node involvement, there is much unexplained variability in the clinical course of OSCC patients. Physicians cannot reliably identify those patients (within a given tumor site, stage, grade, etc) who might benefit most from specific diagnostic and/or therapeutic interventions, such as screening for occult metastasis, or offering particularly aggressive surgical or radiation therapy. Studying tumor characteristics via examination of genomic scale gene expression may improve our understanding of tumor behavior. Our goals in this study are to determine whether: 1) The prognosis of OSCC patients is associated with tumor gene expression profiles; 2) OSCC tumor characteristics known to be related to patient outcome - such as stage and nodal status - are associated with tumor gene expression profiles; and 3) Tumor gene expression differs among invasive OSCC, pre-neoplastic oral squamous cell lesions, and normal oral tissue. We will enroll patients who are newly diagnosed with invasive OSCC or oral dysplasia, and patients with no current or past history of these conditions, at the University of Washington Medical Center and its two other affiliated medical centers. At the time of diagnosis, we will obtain from each patient fresh tissue from biopsies and resections and baseline demographic and baseline lifestyle information through an in-person interview. Patients will be followed prospectively to identify clinical outcomes through review of medical records, patient interviews, and linkage to the National Death Index and Social Security Death Index. We will identify genes whose expression profiles are associated with clinical and pathological endpoints of interest by 1) interrogating pathologically verified OSCC tumor tissues, dysplastic lesions, and normal tissues using Affymetrix U133A oligonucleotide arrays for 12,000 genes; 2) analyzing the array data with a modified linear regression model and Bonferroni correction while adjusting for demographic, lifestyle, and comorbidity variables; and 3) confirming gene expression by SYBR (r) Green I quantitative RT-PCR/melting point dissociation curve analyses. The results of this study have the potential to influence clinical care of **oral cancer** and oral dysplasia in that the molecular signatures we identify may permit physicians to 1) screen oral lesions and surgical margins of tumors for malignancy, 2) screen OSCC patients with negative cervical nodes for occult metastasis, and 3) identify patients with potentially poorer outcome who might benefit from more aggressive treatments. This study may also uncover genes and pathways that are important for **oral cancer** development, and

potential molecular targets for chemoprevention and therapeutics. As such, this proposal is highly responsive to the recommendations made by the NCI Head and Neck Cancer 1999 Priority Setting Workshop (http://www.nci.nih.gov/disease-initiative/headneckcancer).

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

- **Project Title: ORAL MUCOSA MICROBIOTA IN HEALTH, CANCER & MUCOSITIS**

  Principal Investigator & Institution: Mager, Donna L.; Forsyth Institute Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-MAR-2000; Project End 28-FEB-2005

  Summary: The composition and role of the microbiota of oral mucous membranes in both health and lesions of the soft tissues are not well understood. Preliminary data from systemically healthy subjects show that significant differences exist in bacterial composition on different mucous membranes within the same subject. This suggests that different surfaces represent different habitats that favor colonization by different microorganisms. Early indications also suggest differences between the microbiotas of soft tissues in periodontally healthy and periodontally diseased subjects. It is likely that pathologic changes in the oral mucous membranes will favor colonization by different organisms than those found on healthy soft tissue. This study proposes to comprehensively examine the microbiota of different oral mucous membranes in health and disease using checkerboard DNA-DNA hybridization. Specific Aims are 1. To compare the microbial composition of samples from 8 different oral mucous membrane sites with that found in saliva, supra and sub-gingival plaque in subjects stratified according to periodontal status (health or disease) and smoking status (current or never). 2. To compare the microbiota found in **oral cancer** lesions with that found on healthy soft tissues in the same subjects and systemically healthy subjects. 3. To examine changes in the mucous membrane microbiota during and after a standard protocol of chemotherapy and radiation therapy. Subjects will be followed for five years. A cross-sectional study of four groups of 25 systematically healthy subjects will be done at Forsyth Dental Center. Subjects will be selected based on smoking history and periodontal disease status. Samples will be taken from the dorsum, lateral and ventral surfaces of the tongue, floor of mouth, cheek, hard palate, vestibule/lip, attached gingiva and saliva as well as supra and subgingival plaque of the mesial aspect of each tooth in each subject. Each sample will be tested for its content of 40 bacterial species using checkerboard DNA-DNA hybridization. Comparisons will be made for each species among sample location, disease status and smoking history. A longitudinal study of 50 **oral cancer** patients is proposed of the Dana Farber Cancer Institute. Samples from the cancer lesion, the mucosal surfaces, saliva, supra and subgingival plaque will be taken and evaluate for their content of 40 bacterial species at baseline, during and after a standard protocol of combined-chemotherapy and radiation therapy. Comparisons will be made at baseline between microbial species on cancer lesions and healthy surfaces. Mucositis will be scored and salivary function tested. Cultural techniques, PCR and cloning will also be used to seek organisms that were not in the standard battery of probes. The data from the proposed studies should help to clarify the ecological relationships between oral bacterial species and the habitats that they colonize. In addition, the studies should indicate if the microbiota on cancerous lesions differs from that on healthy mucous membranes. Detection on unusual microbial shifts in mucositis might suggest possible routes to minimizing this condition.

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

- **Project Title: OXIDATIVE DNA DAMAGE, DNA REPAIR AND ORAL CANCER**

  Principal Investigator & Institution: Fan, Chun-Yang; Pathology; University of Arkansas Med Scis Ltl Rock Little Rock, Ar 72205

  Timing: Fiscal Year 2002; Project Start 01-SEP-2001; Project End 31-AUG-2006

  Summary: (provided by applicant): Cigarette smoking is the major known head and neck cancer risk factor and represents the single leading preventable cause of death in the United States. Tobacco enhances the production of reactive oxygen species (ROS) in cells, resulting in the generation of oxidative lesions in DNA, such as strand breaks and oxidative DNA base lesions. Among various oxidative DNA lesions, 8-hydroxyguanine (8-OH-G) is by far the most abundant. If not sufficiently repaired, 8-OH-G can cause mutation by mispairing with adenine, yielding G:C to T:A transversion upon DNA replication. The human gene responsible for the repair of this specific DNA lesion was recently cloned and named human 8-oxoguanine DNA glycosylase (hOGG1). The hOGG1 gene is implicated in the carcinogenesis of head and neck squamous cell carcinoma (HNSCC) for several reasons. 1) The hOGG1 gene is located at 3p25, a chromosomal region with frequent allelic loss in HNSCC. 2) Yeast with mutations in this gene produce a mutator phenotype with accumulation of G:C to T:A transversions. 3) Studies of p53 mutations in HNSCC-related tumors showed a bias in favor of G:C to T:A transversions, as indeed would be expected if hOGG1 repair function was disabled. 4) The hOGG1 gene is amenable to the proposed study because of availability of its complete genomic DNA sequence, intragenic single nucleotide polymorphism (SNP) sites, and antibodies to the gene product. We hypothesize that hOGG1 inactivation promotes the development of oral SCC and this hypothesis will be tested by the following three specific aims. 1) Determine the frequency of loss of heterozygosity (LOH) in the hOGG1 gene. 2) Characterize the hOGG1 protein expression patterns in normal and neoplastic squamous mucosa. 3) Explore the genetic or epigenetic mechanisms of hOGG1 inactivation by identifying somatic mutations or promoter methylation in the oral SCC cases with evidence of LOH or lack of protein expression of hOGG1. The role of hOGG1 inactivation has never been previously examined in oral SCC. This study will help to determine whether hOGG1 can be used as a genetic marker for early detection, prognostic prediction, and a potential target for gene therapy in oral SCC. By obtaining a K award, the PI will have the opportunity to develop skills for patient- oriented research under the direction of basic and clinical science mentors.

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

- **Project Title: P12DOC-1 & CDK2 IN CELL CYCLE CONTROL & ORAL CANCER**

  Principal Investigator & Institution: Hu, Miaofen G.; Orak Medicine Infection and Immunity; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

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

  Summary: Cell cycle dysregulation is a central mechanism in carcinogenesis. Oncogenes and tumor suppressors exert their ultimate mode of action by impinging at strategic points in the cell cycle. Tumor-associated genes interact with key cell cycle regulators in tumor promotion and tumor suppression. The proposed fellowship training provides opportunities for the applicant to examine the molecular, biological, and functional interactions of a recently identified growth suppressor protein, p12(DOC-1), and the cell cycle regulator cyclin-dependent kinase 2 (CDK2), in cell cycle control and oral carcinogenesis. p12(DOC-1) is a growth suppressor identified by differential gene expression screening between normal and malignant oral keratinocytes. p12(DOC-1)

negatively regulates DNA replication by associating and mediating phosphorylation of the catalytic subunit of DNA-polymerase alpha/primase (DNA-PP), implicated in the termination mechanism of DNA replication at the end of S phase. Data will be presented to show that p12(DOC-1) interacts with CDK2, a regulator of G1/S transition, S phase progression and DNA replication. We hypothesize that p12(DOC- 1) interacts with CDK2 in cell cycle control and tumor suppression. This hypothesis will be tested by the following three specific aims: 1. to examine the molecular interactions of p12(DOC-1) with CDK2; 2. to examine the interactions of p12(DOC-1) with CDK2 in cell cycle control and 3. to examine the interactions of p12(DOC-1) with CDK2 in **oral cancer.** The outcome of the proposed work will advance our understanding of cell cycle control and oral carcinogenesis by examining mechanisms of interactions of a novel cell cycle regulator p12(DOC-1) with the well- studied S phase regulator, CDK2.

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- **Project Title: PAPILLOMAVIRUS ONCOGENES AND ORAL CANCER**

  Principal Investigator & Institution: Bagchi, Srilata; Molecular Biol/Oral Diseases; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2002; Project Start 01-AUG-1998; Project End 31-JUL-2004

  Summary: Despite significant advances in surgery, radiation therapy and chemotherapy, the survival rates for **oral cancer** have not improved significantly over the past 30 years. Furthermore, ulceration, lack of salivary function, difficulties in chewing and eating are some of the significant side effects associated with current therapies. Development of new therapeutic approaches requires identification of agents that will affect growth of cancer cells without destroying adjacent healthy tissues. The long-term goal of this proposal is to develop a genetically altered protein which will inhibit growth of HPV-associated **oral cancer** cells without affecting growth of normal cells. Studies from several laboratories have shown that about 40 percent of oral cancers are linked to HPV infections. The expression of the E7 oncoprotein encoded by HPV is critical for development and maintenance of the HPV-associated cancers. Previous studies have also shown that an inhibiting E7 expression blocks growth of HPV-transformed oral keratinocytes. This proposal is based on our observations that the HPV oncoprotein E7 functionally associates with the S4 subunit of the 26S proteasome and induces a proteolytic degradation of the Rb tumor suppressor protein. We will investigate the hypothesis that inhibition of the E7/S4 interaction will block Rb-degradation and E7's ability to transform oral keratinocytes. The specific aims are to: 1) establish the role of the S4 in E7-induced immortalization of oral keratinocytes. 2) identify the minimal S4-peptide sequence that binds and inhibits function of E7. 3) generate a genetically altered S4 protein that will sequester E7 into a non-functional complex and will inhibit growth of HPV-transformed keratinocytes. The proposed studies will (1) elucidate the role of S4 in HPV-associated oral cancers and (2) generate S4-specific reagents that will be valuable in therapeutic interventions of oral cancers.

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

- **Project Title: PATHWAYS AND MECHANISMS CONTROLLING EARLY ORAL NEOPLASIA**

  Principal Investigator & Institution: Garlick, Jonathan A.; Assistant Professor; Oral Biology and Pathology; State University New York Stony Brook Stony Brook, Ny 11794

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

Summary: (Adapted from the Investigator's Abstract): **Oral cancer** begins as a premalignant lesion in which a small nest of dysplastic cells expands while in contact with normal cells. During the recent grant period, unique models were developed which mimic the human mucosal and cutaneous microenvironment in premalignant disease and which showed that direct cell-to-cell contact between neighboring keratinocytes is crucial in controlling the development of invasive cancer from a premalignant lesion. It is known that loss of cell-cell contact mediated by intercellular adhesion is a central factor leading to the progression of advanced cancer and metastasis. However, the role of changes in intercellular adhesion in progression of early neoplasia in stratified epithelium is not clear. The objective of this application is to discover the intercellular pathways, which direct this, control it, or cause it to be lost. Because cadherins and catenins integrate cell adhesion with growth signaling they are excellent molecular candidates to regulate cell-cell interactions in premalignant disease. The experimental plan in this proposal is to perturb cadherins and catenins models of premalignancy and to monitor intraepithelial tumor cell expansion in vitro and invasion in vivo. The Principal Investigator hypothesizes that cadherin/catenin-mediated cell-cell interactions can control premalignancy and that changes in adhesions can activate pathways leading to cancer. He will test if overexpression of E-cadherin (Aim 1) or overexpression of alpha-catenin (Aim 2) will increase adherens junctions and limit neoplastic progression. The Principal Investigator will then determine if decreased adhesive interactions will trigger cancer progression by overexpressing dominant negative forms of E-cadherin (Aim 3) and desmosomal cadherins (Aim 4) to disrupt adherens junctions and desmosomes, respectively. He will test his hypotheses in tissue models, which mimic premalignant human stratified epithelium. Adenoviral vectors will be used to express these exogenous genes in short-term, in vitro studies and retroviral vectors will be used for long-term, in vivo studies using our novel human skin/nude mouse chimera. He expects to find cadherin-catenin-mediated pathways and mechanisms that will drive or arrest early neoplastic progression. This insight will be an important step towards finding new therapies to block premalignant disease progression and prevent cancer.

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- **Project Title: PREVALENCE OF HPV IN THE ORAL CAVITY OF HIV+ INDIVIDUALS**

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

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

  Summary: (provided by applicant): Human immunodeficiency virus (HIV) has infected over 33 million people worldwide leading to immune suppression from the selective depletion of CD4+ T cells. This lack of immunity results in numerous opportunistic infections with over 50% of the HIV-infected individuals developing pathology involving the oral cavity. Among the pathogens responsible for oral disease in HIV+ patients is the mucosatropic human papillomavirus (HPV). Although HPV cannot be routinely cultured, it is the most common viral sexually transmitted disease. HPV is the etiologic agent of oral and genital warts, focal epithelial hyperplasia, and a large proportion of cervical, anogenital, and oral squamous cell carcinomas. HIV co-infection leads to increased rate of HPV genital infection, increased HPV persistence, and increased rates of HPV-related pathology (cervical or anal dysplasia), which is more difficult to treat. Similarly, preliminary studies indicate that HIV co-infection leads to increases in the prevalence of oral HPV and HPV-related oral pathology including **oral**

cancer. Surprisingly, treatment of HIV with highly active anti-retroviral therapy (HAART) has led to increases in apparent HPV-related oral warts. These warts have been large, painful, and difficult to treat. Continued use of HAART for the HIV+ patient may lead to substantial increases in the incidence of oral warts and other HPV-related oral pathology such as squamous cell carcinomas. The studies to date have been limited by the lack of or the restrictive scope of the molecular techniques used to detect HPV infection. Thus, little is known about the prevalence, site of infection and natural history of oral HPV infection. A better understanding of oral HPV infection particularly in the HIV+ co-infected individual is of paramount importance in order to prevent HPV-related oral pathology. Preliminary data demonstrates the ability to detect oral HPV infection utilizing consensus PCR primer sets that were developed for detection of genital HPV. These techniques can be extended to detect oral HPV types. We hypothesize that a high throughput PCR-based method for detecting oral HPV types can be developed and utilized to determine the prevalence and site of oral HPV infection in a cohort of HIV+ individuals

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- **Project Title: PROGRESSION OF METASTASIS OF ORAL TONGUE CANCER**

  Principal Investigator & Institution: Myers, Jeffrey N.; Associate Professor; Head and Neck Surgery; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

  Timing: Fiscal Year 2003; Project Start 10-MAY-2003; Project End 30-APR-2008

  Summary: (provided by applicant): Current theories of tumor progression postulate that normal epithelial cells need to acquire mechanisms to evade apoptosis and acquire several other essential biologic properties in order to progress to invasive and metastatic tumors. Programmed cell death after detachment from the basement membrane is known as an oikis. The central hypothesis is of this application is that evasion of anoikis is associated with local tumor progression, and metastasis of squamous cell carcinoma of the oral cavity (SCCOC). Four individual inter-related hypotheses would be evaluated in four separate Aims. The first hypothesis is that anoikis-resistance is necessary but not sufficient for tumor progression, including local growth as well as regional and distant metastases. To demonstrate that anoikis-resistance is associated with disease progression, we will investigate the growth of human SCCOC cell lines in an orthotopic, nude mouse model that we have developed. Human SCCOC cell lines and anoikis resistant cells that have been selected in vitro will be injected into the tongues of nude mice, and these mice will be examined for tumor growth, length of survival and the presence of regional nodal and distant metastases. Conversely, we will demonstrate the anoikis resistance of cell lines that we have derived from in vivo orthotopic selection of regional and distant metastases by quantitation of their survival in suspension culture. The second hypothesis guiding the next Aim of this application is that the pro-survival signals mediating anoikis resistance are not constitutive but rather are induced by the process of cell detachment data to date, suggest that this is due to the induction of apoptosis suppression that is far downstream, as we have found that cell detachment induces resistance to multiple forms of apoptosis induction by both the extrinsic and intrinsic pathways. The third hypothesis is that the BiR containing proteins c-IAP-2, survivin, and XIAP are mediating the detachment-induced survival in the face of multiple forms of apoptotic signaling. This hypothesis will be tested by increasing and decreasing expression or activity of either of these two regulatory molecules in5cell lines and examining the resultant cell lines for their anoikis resistance in vitro and their tumorigenicity and metastatic potential in vivo. The final hypothesis is that expression

of the downstream apoptotic regulatory molecules c-IAP-2, survivin, and XIAP is associated with tumor progression and metastasis in human SCCOC and in an orthotopic model of **oral cancer.** To demonstrate that these apoptotic regulatory molecules are expressed in human SCCOT tumors and that their expression is linked with poorer clinic pathologic outcomes, archival human SCCOT tumor will be evaluated for expression of these apoptotic regulatory molecules by in situ hybridization and immunhistochemistry. It is anticipated that high expression of apoptotic inhibitory molecules in tumor specimens from patients with poor clinicopathologic outcomes will provide insight into the potential roles of the IAPsas prognostic indicators and/or therapeutic targets. Further support for these roles of IAPs will result from demonstration that increased expression of these molecules leads to more aggressive tumor growth and metastasis in an orthotopic metastatic model of SCCOT.

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- **Project Title: PSYCHOSOCIAL INTERVENTION FOR ORAL CANCER PATIENTS**

  Principal Investigator & Institution: Baum, Andrew; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002

  Summary: This abstract is not available.

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

- **Project Title: PULSED DYE LASER ASSISTED CANCER CHEMOPREVENTION**

  Principal Investigator & Institution: Wang, Zhi; Associate Professor / Director; Biophysics Institute; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 02118

  Timing: Fiscal Year 2002; Project Start 21-SEP-2001; Project End 31-AUG-2004

  Summary: Oral cancer is one of the most common neoplasms, and is the culmination of the chronic disease process, carcinogenesis, after long- term exposure to some carcinogenic insults such as tobacco. Its multistep and accumulative features strongly support the rationale for prevention before invasive lesions can grow. Chemoprevention is a very promising new strategy but current strategies are very far from be satisfactory because of their significant toxicity. Anti-angiogenesis has been known as one of cornerstones for the chemoprevention. Our previous studies have indicated the effectiveness for tumor therapy of selective microvascular targeting with a 585 nn pulsed dye laser (PDL), with no damage to any neighboring tissue. The goal of this proposed study is to determine whether a PDL can catalyze the effectiveness of Retinoic Acid (RA) in cancer chemoprevention of oral dysplasia. The long-term objective of this proposal is to develop a novel treatment paradigm: laser assisted cancer chemoprevention. Using cheek pouch of a hamster model, our specific aims are to determine 1) optimal laser parameters for such selective targeting, and 2) whether PDL, when used in combination with RA, can improve the efficacy and reduce toxicity of RA by itself. To our knowledge this is the first study combining laser microvascular targeting technique with a chemopreventive agent. This proposed strategy, if successful, is very likely to lead to an alternative with higher efficacy and less toxicity than current treatment methods.

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

- **Project Title: RAP1A AND RAP1B IN THE DIAGNOSIS AND TMT - ORAL CANCER**

  Principal Investigator & Institution: D'silva, Nisha J.; Oral Medicine/Pathology/Oncology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2002; Project Start 01-JAN-2000; Project End 31-DEC-2004

  Summary: Candidate: The candidate has been involved in clinically relevant basic science research during the post-doctoral studies. This training and the candidate's understanding of confounding clinico-pathologic issues have contributed to her commitment to pursue translational research in **oral cancer.** The immediate goal is internationally renowned clinician- scientists. The long-term goal is to become an independent translational scientist capable of bridging the gap between the laboratory bench and patient care. Environment: The University of Michigan is a nurturing environment for the clinician-scientist. The Cancer Center is internationally reputed for its pioneering work in clinical and biomedical research. The developments in basic science knowledge are translated into improvements in patient care. Research Career Development Plant: The plan encompasses the 5 year award period and includes supervised basic science and translational research rotations, Head and Neck Cancer Symposia, weekly signaling, research responsibility and ethics. Research Project: The overall objective of this proposal is to enhance the understanding of the molecular choices of **oral cancer.** Rap1, a ras-like protein, will be evaluated as a predictive biomarker for malignant transformation of precancerous human oral epithelial lesions. Additionally, a rap1B, a rap1 isoform, will be assessed as a candidate protein for prognosis prediction, when used as a biomarker for metastatic potential of squamous cell carcinoma (SCC). This would allow the identification of lesions that should be treated more aggressively. The third segment involves the design of a protocol to investigate the use of rap1A in gene therapy to treat residual epithelial dysplasia or squamous cell carcinoma lesions.

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- **Project Title: RAPID IN VIVO ASSAY FOR ORAL CANCER CHEMOPREVENTION**

  Principal Investigator & Institution: Solt, Dennis B.; Associate Professor; Pathology; Northwestern University Office of Sponsored Research Chicago, Il 60611

  Timing: Fiscal Year 2002; Project Start 01-JUL-2001; Project End 31-DEC-2003

  Summary: The long range objective of this research is to develop a rapid in vivo assay for **oral cancer** chemopreventive agents(OCCAs), based on the hypothesis that effective agents(or combinations of agents) will impede or prevent **oral cancer** formation by inhibiting or blocking the induction, expansion, and persistence of the key cells and cell populations participating in each step in the carcinogenic process. In the hamster buccal pouch epithelial (HBPE) model of oral carcinogenesis, focal populations of basal cells exhibiting gamma-glutamyl transpeptidase histochemical activity(GGT foci), and patches of basal cells exhibiting nuclear p53 immunohistochemical staining (p53 foci) appear to be two such relevant populations. Specific Aim 1 is to quantify the extent to which a group of known anticarcinogens inhibit the induction of early (i.e., 4 or 10 days) GGT foci, as detected in HBPE whole mounts, when the agents are applied to the mucosal surfaces prior to and concurrent with the potent chemical carcinogens 7,12-dimethylbenz(a)anthracene(DMBA) and N-methyl-N- benzylnitrosamine(MBN). Specific Aim 2 is to quantify the extent to which three presumptive OCCAs, selected from among those shown to inhibit GGT foci induction in SA1, also inhibit the

expansion of GGT foci, during a 21-day regimen of exposure to the either DMBA or MBN,. The feasibility of identifying early p53 foci in standard sections of hamster pouch, and thus of quantifying anticarcinogen-mediated inhibition in the formation of these lesions will also be evaluated using the SA2 protocol. Specific Aim 3 will employ a complete carcinogenesis protocol to quantify the extent to which three chemopreventive agents examined in SA2, also inhibit: (1) induction of GGT foci and p53 foci(observed at 7 weeks), (2) induction of dysplastic lesions, both p53 positive and p53 negative(observed at 7 weeks), (3) induction and expansion of persistent p53 foci(observed at 12 and 21 weeks), (4) induction of persistent dysplastic lesions, both p53 positive and p53 negative(observed at 12 and 21 weeks), (5) development of dysplastic cells (including persistent dysplastic cells, and both p53 positive and p53 negative cells) detectable in cytologic smears at 12 weeks, and (6) HBPE cancer formation. (7) Anticarcinogen- mediated inhibition of forestomach papillomas will also be assessed in hamsters sacrificed at 7 weeks in the SA3 protocol. The research outlined also suggests a rational strategy for the identification of combinations of efficacious OCCAs which are likely to exhibit an additive or synergistic effect in clinical trials -specifically, combinations of agents which individually exhibit maximal inhibition of various surrogate end points of cancer relating to induction, expansion, and persistence of the key participating cell populations.

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- **Project Title: REGULATION OF HUMAN PAPILLOMAVIRUSES IN ORAL MUCOSA**

  Principal Investigator & Institution: Chen, Zhuo; None; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 01-AUG-1998; Project End 31-JUL-2004

  Summary: The candidate, Dr. Zhuo Chen, is currently a full-time research assistant professor in the Department of Basic Sciences at the University of Texas Dental Branch, which is located in the Texas Medical Center which ius the largest medical care and research complex in the world. Dr. Chen acquired excellent comprehensive training in biochemistry and molecular biology from her Ph.D and postdoctoral programs at Louisiana State University before joining the faculty, so that she is able to rapidly develop independent research programs using molecular techniques to study diseases in oral cavity. In 1996, she received an R29 (FIRST) Award from the National Cancer Institute to study the regulation of human papillomaviruses (HPV) in oral mucosa with an emphasis on regulatory mechanisms which function in tumor cells to allow the over-expression of the transforming genes of HPV. A K02 Award would provide the "chain" to help her to continue connecting her background and training in molecular biology and biochemistry to dental research, specifically to **oral cancer.** She would benefit by having additional resources and time to build a more comprehensive research program in oral carcinogenesis by combining the findings from this research with those of her other ongoing projects dealing with over-expression of oncogenes in **oral cancer.** This expanded focus will facilitate and lead to development of a proposal for funding via the RO1 mechanism. Her ultimate goal is to provide the basis for a better understanding of gene expression in oral epithelial cells and **oral cancer** cells. The proposed K02 project is based on, as well as an extension of, her R29 to further investigate why oral epithelial cells provide the unique environment for HPV-induced transformation. As the first part of this study, she has detected functionally significant mutations in the HPV long control region (LCR) isolated from **oral cancer** cells. The hypothesis is that cellular proteins or their complexes are able to act on the mutated LCR in a specific manner to

activate the transcription of the E6 and E7 oncogenes, leading to malignant transformation of epithelial cells. This work will (i) identify and characterize the major cellular protein factors and complexes that trans- regulate E6 and E7 genes from HPV-16 and -18 in both normal and malignant oral epithelial cells; (ii) determine cell-type specific interactions between the HPV LCR and major regulatory protein factors which are responsible for activation of E6 and E7 gene expression in malignant oral epithelial cells; (iii) delineate the interactions between these major factors and the LCR of HPV-16 and-18 in both normal and malignant oral epithelial cells. This project will increase our understanding of HPV gene regulation in normal and malignant oral epithelial cells. In addition, identification of cis-elements and major cellular proteins involved in HPV-related oral cancers will provide a fundamental basis by which to develop potential gene therapy strategies against cancer in the oral cavity.

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- **Project Title: REGULATION OF THE IMMORTAL PHENOTYPE IN ORAL CANCER**

  Principal Investigator & Institution: Nguyen, Dan C.; Basic Sciences; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

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

  Summary: (provided by applicant) Oral squamous cell carcinoma (SCC) is the sixth most frequent cancer worldwide with an estimated 30,000 new cases and 8,000 deaths reported in the United States each year. Many oral SCC lines are immortal in vitro, suggesting that these cells have a mechanism for maintaining chromosomal integrity. The ends of human chromosomes (telomeres) lose up to 200 base pairs of DNA per cell division due to the inability of DNA polymerase to completely replicate the chromosomal ends. Chromosomal shortening ultimately leads to senescence and cell death in normal cells. Telomerase is a ribonucleoprotein complex that synthesizes telomeric DNA onto chromosomes using its RNA component as a template. Our preliminary data have shown that all SCC lines tested expressed high levels of telomerase activity and interestingly, that induction of a key cell cycle protein Rb (retinoblastoma) downregulates telomerase activity. Based on our preliminary studies, we hypothesize that telomerase activation in **oral cancer** cells is regulated via cell cycle dependent phosphorylation of Rb and activation of E2F-1 transcription factors. In specific aim 1, we propose to determine the role of Rb in regulating telomerase activity in **oral cancer** cells. In specific aim 2, we will determine how Rb phosphorylation by cyclin dependent kinases regulates telomerase activity in **oral cancer** cells. In specific aim 3 of this proposal, we will characterize the functional domains of the transcriptional factor E2F-1 and its regulation of the telomerase promoter. These studies may lead to the development of telomerase inhibitors for **oral cancer** which do not affect non-cycling cells.

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

- **Project Title: REGULATION OF TYPE IV COLLAGENASE EXPRESSION**

  Principal Investigator & Institution: Boyd, Douglas D.; Professor; Cancer Biology; University of Texas Md Anderson Can Ctr Cancer Center Houston, Tx 77030

  Timing: Fiscal Year 2003; Project Start 01-FEB-1994; Project End 30-NOV-2007

  Summary: (provided by applicant): The 92 kDa type IV collagenase (MMP-9) contributes to the spread of **oral cancer** and understanding how its expressions regulated could ultimately yield new agents to repress its expression and diminish tumor invasiveness.

Although we previously identified multiple regulatory elements (AP-1, NF-kappaB, PEA3, Sp1) in the 670 base pair promoter, the limited number of these binding sites makes it unlikely that MMP-9 expression is solely the consequence of transactivation through these motifs. Indeed, emerging studies indicate a role for the chromatin environment (constituted by DNA wrapped around a histone core), in the regulation of gene expression. We show herein that Mtal, which promotes histone deacetylation, represses MMP-9 expression. Further, Mtal expression is undetectable in MMP-9-producing **oral cancer.** In Specific Aim 1 using genomic foot printing and chromatin immunoprecipitation assays (Chip) we will identify transcription factor-bound cis elements and acetylated histones localized at these sites in the 670 base pair MMP-9 promoter targeted by Mtal to achieve MMP-9 repression. Biological suppressors of MMP-9 expression may also provide a tool for identifying regulatory elements in the chromatinized promoter. We show herein that the metastasis suppressor gene KiSS-1 attenuates MMP-9 transcription partly by reducing NF-kappaB binding to the chromatinized promoter. Nevertheless, the degree to which NF-kappaB binding is reduced can only partly account for the diminished transcription. Therefore, in Specific Aim 2, we will identify transactivated cis elements and acetylated histones localized at these sites in the MMP-9 promoter that mediate KiSS-1-dependent repression of MMP-9.Similarly, the MEK1 inhibitor PD098059 represses MMP-9 expression and in Specific Aim 3 we will determine if the transcriptional targets of this repressor are identical to, or distinct from, those of Mtal and KiSS-1. If we determine that the transcriptional targets differ, we will determine whether combining PD098059 and KiSS-1 or Mtal proves superior to individual modalities in reducing MMP-9 expression and **oral cancer** invasiveness. Since extra-chromosomal reporters were used in our previous studies of MMP-9 transcription, regulatory elements, that depend on the chromatin environment, may have escaped detection. Thus, to identify such novel cis elements in Specific Aim 4, we will employ DNase hypersensitivity, genomic foot printing and lambdagt11 library screening to identify additional transactivators/repressors of MMP-9 expression. Ultimately, the goal of these studies is to identify new transcriptional targets in the MMP-9 promoter that allow for therapeutic intervention to repress expression of this collagenase and **oral cancer** invasiveness.

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- **Project Title: REGULATORY AND NOVEL GENES IN DEVELOPMENT OF ORAL CANCER**

  Principal Investigator & Institution: Lang, James C.; Associate Professor of Otolaryngology; Ohio State University 1960 Kenny Road Columbus, Oh 43210

  Timing: Fiscal Year 2002; Project Start 01-JUL-2001; Project End 30-JUN-2002

  Summary: This abstract is not available.

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

- **Project Title: RHOC/GALR2 IN THE METASTASIS OF OROPHARYNGEAL CANCERS**

  Principal Investigator & Institution: Henson, Bradley; Periodontics; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

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

  Summary: This proposal is submitted pursuant to the application for a Mentored Clinical Scientist Development Award by Bradley S. Henson, D.D.S. This award will enable the applicant to complete his graduate education and training in the Oral Health

Sciences Ph.D. Program at the University of Michigan School of Dentistry. The objectives of this application are to optimize current animal models of metastasis for head and neck squamous cell carcinoma (HN SCC) and investigate the role of two candidate proteins, rhoC and galanin receptor 2 (GALR2), in the spread of this disease. Last year, in the US alone, there were an estimated 30,200 newly diagnosed cases of oropharyngeal cancer [2]. Limited prognostic predictability and late detection for individual tumors, based on histopathology and existing staging protocols, results in disfiguring and debilitating surgical, chemotherapeutic and radiotherapeutic interventions. A major determinant of prognosis in HN SCC is metastatic transformation. RhoC, a member of the rho family of GTPases, has been implicated in metastatic potential in cancers of the breast and pancreas, and in malignant melanoma. It is likely that the rho GTPase family plays an important role in regulating cell movement during metastatic transformation, by configuring the actin cytoskeleton for motility through the formation of stress fibers. Rho has been shown to be downstream of galanin receptor 2 (GALR2). GALR2 binds galanin, a 30 amino acid neuropeptide, and has been implicated in small cell lung carcinoma. Overexpression or activating mutations of GALR2 may be important in the tumorigenesis of oropharyngeal SCC. Furthermore, mutations or alterations of expression of GA LR2, leading to activation of rhoC in the same tumor cell population may be an important determinant of aggressive, metastatic tumor behavior. The specific hypothesis to be investigated here is that upregulation or an activating mutation of rhoC and/or GALR2 facilitates metastasis of oropharyngeal SCC. In order to begin to address this hypothesis, we propose to: (1) investigate the role of rhoC in oropharyngeal cancer metastasis, (2.) determine whether overexpression or an activating mutation of GALR2, leads to a more aggressive, metastatic tumor phenotype and to determine if this signaling occurs via rho activation, and (3.) optimize current murine models used to study human o ropharyngeal S CC and develop primary and metastatic **oral cancer** cell lines.

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

- **Project Title: RISK OF ORAL EPITHELIAL DYSPLASIA IN PUERTO RICO**

  Principal Investigator & Institution: Morse, Douglas E.; Assistant Professor; New York University 15 Washington Place New York, Ny 10003

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2003

  Summary: Oral and pharyngeal cancer incidence in Puerto Rican males is notably higher than among white males living on the U.S. Oral epithelial dysplasia (OED) is a histopathological diagnosis characterized by cellular changes and maturational disturbances. A diagnosis of OED is significant in that it is associated with an elevated risk factors for OED, and non such studies have carried out in an Hispanic population. The primary aim of this study is to estimate the association between OED and the use of smoking tobacco and alcoholic beverages in an Hispanic population living in Puerto Rico. On an exploratory basis the proposed investigation will (a) examine the presence of a dose-response relationship as regards OED and both smoking tobacco and alcohol use, (b) test for a synergistic relationship between alcohol and smoking with regard to OED, (c) evaluate smokeless tobacco, mouthwash use and dentures and OED risk factors, (d) evaluate dietary habits as risk/protective factors for OED, and (e) examine whether polymorphisms in genes that code for enzymes active will be identified in the carcinogen activation and detoxification pathways are associated with OED. OED cases (aged 20-79) will be identified by reviewing biopsy reports generated by pathology laboratories on the Island. The control series, frequency matched 1:1 to cases on age, gender, gender, and geographic region, will consist of persons diagnosed with an

irritation fibrinoma via the same pathology laboratories. Environmental risk factor data will be obtained using a structured questionnaire. Oral cells will be obtained for DNA extraction and used in studies of genetic polymorphisms while paraffin-embedded tissue from cases and controls will be available for immunohistochemical and molecular analyses. Adjusted odds ratios will be obtained from logistic regression models. Information obtained from this study will further our understanding of the etiology of OED, provide possible explanations for the high rates of oral and pharyngeal cancer in Puerto Rico, and suggest opportunities for the primary prevention of OED and **oral cancer.**

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

- **Project Title: ROLE OF CATHEPSINS IN ORAL CANCER INVASION AND METASTASI**

  Principal Investigator & Institution: Zacharias, Wolfgang; Associate Professor; Medicine; University of Louisville University of Louisville Louisville, Ky 40292

  Timing: Fiscal Year 2002; Project Start 01-SEP-1999; Project End 31-AUG-2004

  Summary: Oral cancer is one of the 10 most frequent cancers worldwide, with an estimated 30,000 new cases being diagnosed in the U.S. every year. Histologically almost 90 percent of oral cancers are squamous cell carcinomas (SCC), which include the subtypes of verrucous carcinoma and basaloid squamous cell carcinoma. There is increasing evidence to suggest that local invasion and regional/distant metastasis of carcinomas are facilitated by increased expression and altered subcellular localization of lysosomal cathepsins B, D and L. The Hypothesis of this proposal is: Oral carcinomas with different local invasive properties and metastatic potentials possess distinct qualitative and quantitative differences in their expression patterns of cathepsin B, D and L. The inhibition of such cathepsins on the molecular level will diminish, or abolish, these malignant properties. The Specific Aims of the proposal are: Specific Aim 1: To determine the relationship of the expression patterns of cathepsins B, D, and L in oral carcinomas and their clinicopathologic parameters and histological characteristics. Specific Aim 2: To inhibit cathepsin expression in oral squamous cell carcinoma cell lines by intracellularly expressed ribozymes, and to analyze the consequences on invasive and metastatic behavior of these cells in an animal model. Specific Aim 3: To obtain overexpression of selected cathepsin proteins in transformed keratinocytes cells, and to test for induction of acquired invasive and/or metastatic phenotypes in these cells in an animal model. These experiments are designed to correlate the expression patterns of cathepsin B, D, L in **oral cancer** with the histological characteristics and clinical findings of the carcinoma subtypes. These studies will also examine the role of these enzymes in invasion and metastasis by employing ribozyme- mediated cathepsin inhibition as well as recombinant cathepsin gene expression approaches, both being applied in cell culture and in an animal model. The information correlating the functions of cathepsins B, D and L in **oral cancer** progression will be the basis for the design of therapeutic modalities to inhibit their expression, and thus cancer progression, on the molecular level.

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

- **Project Title: ROLE OF THE BCL-2 AND CASPASE FAMILY IN ACINAR APOPTOSIS**

  Principal Investigator & Institution: Quissell, David O.; Professor & Chairman; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, Co 800450508

Timing: Fiscal Year 2002

Summary: Salivary gland hypofunction is a major oral health problem that affects the quality of life for several million people in the USA. A variety of conditions can resulting in the loss of salivary acinar cell secretory function including systemic diseases such as Sjogren's Syndrome (an autoimmune disease), X-ray irradiation, cancer chemotherapy, psychological factors, malnutrition, pharmacological induced xerostomia and **oral cancer.** All of these disease conditions or treatments have the potential to alter normal salivary acinar cell homeostasis and to accelerate the entry of the salivary gland acinar cells into apoptosis. A fundamental understanding of the molecular events involved in salivary gland acinar apoptosis is required if we are to fully comprehend the specific mechanisms involved in salivary gland hypofunction. This information is also essential for the development of new treatment modalities that have the potential to block or delay the toxic effects of these various disease conditions and treatments on normal acinar cell function. The principle objective of this project is to investigate and determine at the molecular level the precise function of the two major cellular protein families that play a central role in the initiation signaling and execution of acinar cell apoptosis. The two critical regulatory protein families are the caspase and the Bcl-2 family of proteins. We will determine their level of expression, subcellular distribution, level of phosphorylation and their functional activity during t he onset and duration of acinar cell apoptosis elicited by specific apoptotic stimuli. These studies will be performed using primary cultures of rat parotid and sub-mandibular acinar cells and immortalized rat parotid and sub-mandibular acinar cell lines. The identification and characterization of these two critically important protein families will provide new basic scientific information and insights for the development of new therapeutic approaches to suppress aberrant acinar cell apoptosis, with the long term objective to improve the quality of life for millions of affected individuals.

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

- **Project Title: SEROEPIDEMIOLOGIC STUDY OF HPV AND ORAL CANCER**

  Principal Investigator & Institution: Smith, Elaine M.; Associate Professor; Epidemiology; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 24-SEP-1999; Project End 31-AUG-2004

  Summary: Evidence from our recently conducted molecular epidemiology study of **oral cancer** suggests HPV is an independent risk factor in the development of these tumors. Human papillomavirus (HPV) infection is causally associated with greater than 95 percent of carcinomas of the cervix and is often found in other genital cancers as well as in laryngeal cancers. Because of the link between HPV and these tumors, early identification of the virus may provide a crucial marker of high-risk susceptibility and for early detection. In our recent study of **oral cancer,** cancer cases were significantly more likely to be detected with HPV in cytology specimens from the oral cavity compared with those of matched healthy controls: 30 percent v. 18 percent. Over 24 percent of the cancer cases compared with only 11 percent of the controls were infected with oncogenic mucosal HPV types whereas there was no difference between cases and controls in the frequency of detecting nononcogenic-mucosal (1 percent in cases or controls) or nonmucosal types (4 percent each group). Based on the results of our current study, we propose here to focus on the association between **oral cancer** and potential molecular and genetic mechanisms that are involved in HPV-induced carcinogenesis: viral gene presence and expression, viral load, susceptibility to viral infection and/or carcinogenesis due to p53 polymorphism, and alterations in viral gene expression by mutagenesis and/or integration. The aims of this study are to: 1)

determine whether oral carcinomas harbor and express DNA genomes of oncogenic mucosal HPV types and whether HPV types/variants found in **oral cancer** biopsies match those in oral cytology specimens as potential markers in clinical screening; 2) characterize the potential influence of polymorphism in the tumor suppressor gene p53 on the susceptibility to HPV infection and/or oral carcinogenesis; and 3) evaluate the potential role of altered HPV gene expression due to mutations in the viral control region or due to viral DNA integration in the cellular genome in **oral cancer** development and progression. This study (a collaboration between clinicians, molecular epidemiologists and pathologists who are members of the U. Iowa Cancer Center) will elucidate the molecular and genetic mechanisms involved in HPV-associated carcinogenesis in the oral cavity and identify potential markers of early diagnosis and/or prognostic indicators of **oral cancer.**

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

- **Project Title: SPIT TOBACCO USE PREVENTION/CESSATION**

  Principal Investigator & Institution: Walsh, Margaret M.; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002

  Summary: Use of spit (smokeless) tobacco (ST) is increasing in prevalence among young American males, is especially prevalent among those residing in rural areas, and puts them at risk of **oral cancer,** and periodontal tissue destruction. This proposal has the following specific aims: (1) to determine the efficacy of a school-based nurse-directed, per- and dentist-assisted ST intervention program among male students in 28 high schools in rural areas of California and (2) to determine predictors of successful ST cessation among male students in rural high schools. The intervention is based on Cognitive Social Learning Theory and Diffusion of Innovation Theory and applies a public health perspective by approaching ST users in their environment and Innovation Theory and applies a public health perspective by approaching ST users in their environment and attempting to change social norms to effect behavioral change. Twenty-eight rural high schools in California will be stratified on baseline prevalence of male ST use and size of enrollment and randomly assigned within strata to either the intervention or the control group. The intervention will consists of a school advisory board; peer-led educational sessions; an oral exam and advice to quit or to stay tobacco-free by a school nurse who points out any ST-associated lesions to users by their own mouths or in photographs, provides brief cessation counseling, and facilitates three group follow-up relapse prevention sessions, conducts 1-week follow-up examines of students with ST-related oral lesions, and schedules students with persistent lesions for evaluation by a dentist; and, two follow-up telephone cells by a peer to prevent relapse. Biochemically validated self-reported quit rates and self reported initiation rates at the end of the intervention and 1 year later will be compared between groups. Baseline and follow-up questionnaire assessments of ST use will be analyzed to identify individual characteristics that are associated with quitting ST use. Results will contribute to the body of knowledge related to tobacco prevention and cessation and thereby to the primary and secondary prevention of **oral cancer** and other negative oral health effects associated with tobacco use.

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

- **Project Title: TGF-ALPHA PROCESSING IN ORAL CANCER**

  Principal Investigator & Institution: Derynck, Rik M.; Professor; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

Timing: Fiscal Year 2002

Summary: Cancer cells are subject to autocrine receptor stimulation by endogenous growth factors, and this stimulation contributes to malignant transformation and cancer development. Oral carcinoma cells often show increased (EGFR). Clinical correlation and in vitro and in vivo studies strongly suggest that increased EGFR stimulation by TGF-alpha contributes to carcinogenesis. TGF-alpha is made as a transmembrane growth factor, which undergoes regulated ectodomain cleavage or "shedding" to release soluble and diffusible TGF-alpha. Transgenic experiments suggest that this cleavage of transmembrane TGF-alpha is required for its ability to stimulate carcinoma development. TGF-alpha ectodomain shedding is mediated by TACE, a transmembrane metalloprotease, which was originally discovered for its ability to mediate TNF-alpha cleavage. The mechanisms that activate TACE and consequent TGF-alpha cleavage were unknown until recently We have recently shown that growth factors, which activate tyrosine kinase receptors, induce ectodomain shedding of TGF-alpha as well as TNF-alpha and L-selectin Growth factor-induced TGF-alpha ectodomain shedding is mediated through activation of the Erk MAP kinase pathway and does not require new protein synthesis. We have also shown that the cytoplasmic domain of TACE is phosphorylated in response to growth factor stimulation and that the cytoplasmic domain of TGF-alpha ectodomain cleavage. This proposal now builds on these findings and is aimed at characterizing the signaling mechanism(s) that lead to activation of TGF-alpha shedding and its role in oral carcinoma development. We have subdivided the proposal in four Aims. In Aim 1, we propose to characterize the growth factor-induced phosphorylation of TACE and its role in TACE activation and ectodomain shedding. In Aim 2, we propose two different approaches to identify, clone and characterize the kinase, which phosphorylates TACE and in this way activates TACE mediated shedding in response to growth factor stimulation. In Aim 3, we propose to identify and functionally characterize proteins that interact with TACE and, in this way regulate TACE activation and ectodomain shedding. Finally, in Aim 4, we will evaluate the role of TGF-alpha and its ectodomain cleavage, as a result of TACE activation and ectodomain shedding. Finally, in Aim 4, we will evaluate the role of TGF-alpha and its ectodomain cleavage, as a result of TACE activation in carcinogenesis and tumor development of oral squamous carcinoma in vivo.

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

- **Project Title: TNF A MEDITATED GENE REGULATION IN HUMAN ORAL CANCER**

  Principal Investigator & Institution: Todd, Randy C.; Assistant Professor; Oral and Maxillofacial Surgery; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

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

  Summary: This is a five-year application to support the full-time pursuit of the candidate's current research focus: understanding the molecular basis of head and neck cancer development. The candidate is currently an assistant professor of oral and maxillofacial surgery at the Harvard School of Dental Medicine. The candidate's research effort has been supported previously by an Institutional Dental Scientist Award (K16) and a Small Grant (R03), and is currently being conducted under a FIRST Award, all from the National Institute of Dental and Craniofacial Research. Funding from the proposed application will enable the candidate to pursue immediate and long-term career objectives in his overall goal toward establishing a productive career in academic dental medicine. The candidate's immediate career objectives are to pursue full-time

research to test the hypothesis that tumor necrosis factor-alpha (TNF- alpha) mediated doc-1 gene expression is a critical event lost during head and neck cancer development. Preliminary studies in the candidate's research project demonstrate TNF-alpha dramatically up-regulates doc-1 expression in malignant oral keratinocytes and ectopic expression of doc- 1 markedly elevates the fraction of cells undergoing apoptosis Therefore, studies are proposed to define the mechanism of TNF-alpha mediated doc-1 expression, verify induction of apoptosis in human malignant oral keratinocytes and explore doc-1 as a therapeutic target in human oral squamous cell carcinomas. Verification of the role of the TNF-alpha/doc- 1 pathway in apoptosis and its use as a gene therapeutic target are directions that have evolved from the candidate's FIRST Award research plan and may serve as a basis for a future R01 application. The candidate's long-term objective is to establish a productive career in academic dental medicine with a special emphasis on translating basic research in tumor biology, such as TNF-alpha/doc-1 pathway and apoptosis, towards desperately needed improvement in head and neck cancer patient care. To ensure the candidate will become an important integral part of its research and academic program, the Harvard School of Dental Medicine is uniquely qualified to support his research career development plan through a strong institutional commitment to the candidate and access to senior collaborators throughout the Harvard Medical Teaching Campus who have a similar objective: to develop a biologically-based approach to advance cancer diagnosis and treatment.

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

- **Project Title: UDPGLUCURONOSYLTRANSFERASE GENOTYPE AND ORAL CANCER RISK**

  Principal Investigator & Institution: Lazarus, Philip; Professor; Biochem and Molecular Biology; University of South Florida 4202 E Fowler Ave Tampa, Fl 33620

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

  Summary: (Adapted from the applicant's abstract): UDP glucuronosyltransferases (UGTs) may play important roles in cells as genoprotective enzymes by preventing the accumulation of carcinogenic compounds which could react with cellular macromolecules causing the oxidation of xenobiotics into active carcinogenic electrophiles. Several major tobacco procarcinogens, such as metabolites of the polycyclic aromatic hydrocarbons (PAHs) such as benzo[a]pyrene (BaP) and tobacco-specific nitrosamines (TSNAs) like 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK), are detoxified via UGT-induced glucuronidation by increasing the hydrophilicity of these agents, thus rendering them more water-soluble, more easily excreted, and less bioactive. The major goal of the proposed work is to examine detoxification by UGTs as a mechanism for differential susceptibility to **oral cancer,** specifically focusing on the glucuronidation of the major NNK metabolite, 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanol (NNAL). NNK and NNAL are considered to be major contributors to the induction of cancers of the oral cavity and lung. Large inter-individual variability in the ratio of the glucuronidated form of NNAL (NNAL-Gluc):free NNAL suggests that individuals differ greatly in their ability to glucuronidate NNK metabolites and to detoxify NNK. This is consistent with recent studies which suggest that racial differences in morbidity and mortality of lung and potentially **oral cancer** may, in part, be explained by differences in the ability of individual subjects to detoxify NNK via NNAL glucuronidation. Preliminary studies have identified at least two human UGTs (1A9 and 2B7) which possess NNAL-glucoronidating activity and demonstrate that this activity is inducible by phenobarbitol and phenolic antioxidants in rats. As the balance between metabolic activation and detoxification of carcinogens such

as NNK may be influenced by the balance of host expression of enzymes involved in tobacco carcinogen activation, the hypothesis was created that an individual's ability to glucuronidate NNAL is correlated with that individual's risk for **oral cancer** as well as for other aerodigestive tract cancers. Therefore, the objective of this proposed work is to (1) fully characterize the NNAL glucuronidation pathway in humans, (2) to elucidate, functionally assess, and determine the prevalence of potentially important genetic polymorphisms in the human UGT gene which may reflect an individual's capacity to convert NNAL to NNAL-gluc as a measure of one's ability to detoxify NNK, and (3) to examine the importance of these polymorphic genotypes in a case-control study of susceptibility to **oral cancer.** These studies may provide potentially important genetic biomarkers which may reflect upon an individual's risk for oral and potentially other tobacco-related cancers.

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

E-Journals: PubMed Central[3]

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

- **Bombesin Antagonist Prevents CO2 Laser-Induced Promotion of Oral Cancer.** by Kozacko MF, Mang TS, Schally AV, Priore RL, Liebow C.; 1996 Apr 2; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=39741
- **Chromosomal instability and cytoskeletal defects in oral cancer cells.** by Saunders WS, Shuster M, Huang X, Gharaibeh B, Enyenihi AH, Petersen I, Gollin SM.; 2000 Jan 4; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=26658
- **High-resolution mapping of the 11q13 amplicon and identification of a gene, TAOS1, that is amplified and overexpressed in oral cancer cells.** by Huang X, Gollin SM, Raja S, Godfrey TE.; 2002 Aug 20; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=123263
- **Oral cancer treatment costs in Greece and the effect of advanced disease.** by Zavras A, Andreopoulos N, Katsikeris N, Zavras D, Cartsos V, Vamvakidis A.; 2002; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=117788
- **OrCGDB: a database of genes involved in oral cancer.** by Levine AE, Steffen DL.; 2001 Jan 1; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=29839

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

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

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

- **Reduced inhibition of Candida albicans adhesion by saliva from patients receiving oral cancer therapy.** by Umazume M, Ueta E, Osaki T.; 1995 Feb; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=227962

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

- **A clinical evaluation of implants in irradiated oral cancer patients.**
  Author(s): Visch LL, van Waas MA, Schmitz PI, Levendag PC.
  Source: Journal of Dental Research. 2002 December; 81(12): 856-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12454102

- **A comparative study of normal inspection, autofluorescence and 5-ALA-induced PPIX fluorescence for oral cancer diagnosis.**
  Author(s): Betz CS, Stepp H, Janda P, Arbogast S, Grevers G, Baumgartner R, Leunig A.
  Source: International Journal of Cancer. Journal International Du Cancer. 2002 January 10; 97(2): 245-52.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11774271

- **A comprehensive review of oral cancer.**
  Author(s): Casiglia J, Woo SB.
  Source: Gen Dent. 2001 January-February; 49(1): 72-82. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12004680

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

- **A half-yearly chest radiograph for early detection of lung cancer following oral cancer.**
  Author(s): Merkx MA, Boustahji AH, Kaanders JH, Joosten F, Marres HA, Bruaset I, de Wilde PC.
  Source: International Journal of Oral and Maxillofacial Surgery. 2002 August; 31(4): 378-82.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12361070

- **A study to determine the acceptability in patients and dentists of toluidine blue in screening for oral cancer.**
  Author(s): Feaver GP, Morrison T, Humphris G.
  Source: Primary Dental Care : Journal of the Faculty of General Dental Practitioners (Uk). 1999 April; 6(2): 45-50.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11819880

- **Accumulation of mitochondrial DNA deletions in human oral tissues -- effects of betel quid chewing and oral cancer.**
  Author(s): Lee HC, Yin PH, Yu TN, Chang YD, Hsu WC, Kao SY, Chi CW, Liu TY, Wei YH.
  Source: Mutation Research. 2001 June 27; 493(1-2): 67-74.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11516716

- **Activation of p53 signalling in acetylsalicylic acid-induced apoptosis in OC2 human oral cancer cells.**
  Author(s): Ho CC, Yang XW, Lee TL, Liao PH, Yang SH, Tsai CH, Chou MY.
  Source: European Journal of Clinical Investigation. 2003 October; 33(10): 875-82.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14511359

- **Adhesive mechanisms regulating invasion and metastasis in oral cancer.**
  Author(s): Ziober BL, Silverman SS Jr, Kramer RH.
  Source: Critical Reviews in Oral Biology and Medicine : an Official Publication of the American Association of Oral Biologists. 2001; 12(6): 499-510. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11806519

- **Alcohol concentration and risk of oral cancer in Puerto Rico.**
  Author(s): Huang WY, Winn DM, Brown LM, Gridley G, Bravo-Otero E, Diehl SR, Fraumeni JF Jr, Hayes RB.
  Source: American Journal of Epidemiology. 2003 May 15; 157(10): 881-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12746240

- **Alcohol, smoking and oral cancer. A 10-year retrospective study at Base Hospital, Yaba.**
  Author(s): Adewole RA.
  Source: West Afr J Med. 2002 April-June; 21(2): 142-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12403038

- **Allelic alterations at the STR markers in the buccal tissue cells of oral cancer patients and the oral epithelial cells of healthy betel quid-chewers: an evaluation of forensic applicability.**
  Author(s): Pai CY, Hsieh LL, Tsai CW, Chiou FS, Yang CH, Hsu BD.
  Source: Forensic Science International. 2002 October 9; 129(3): 158-67.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12372686

- **Alphavbeta6-Fyn signaling promotes oral cancer progression.**
  Author(s): Li X, Yang Y, Hu Y, Dang D, Regezi J, Schmidt BL, Atakilit A, Chen B, Ellis D, Ramos DM.
  Source: The Journal of Biological Chemistry. 2003 October 24; 278(43): 41646-53. Epub 2003 August 12.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12917446

- **An evaluation of the cytotoxic effects of orthodontic bonding adhesives upon a primary human oral gingival fibroblast culture and a permanent, human oral cancer-cell line.**
  Author(s): Huang TH, Tsai CY, Chen SL, Kao CT.
  Source: Journal of Biomedical Materials Research. 2002; 63(6): 814-21.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12418029

- **An overview of the prevention of oral cancer and diagnostic markers of malignant change: 1. Prevention.**
  Author(s): Ogden GR, Macluskey M.
  Source: Dent Update. 2000 March; 27(2): 95-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11218278

- **An overview of the prevention of oral cancer and diagnostic markers of malignant change: 2. Markers of value in tumour diagnosis.**
  Author(s): Macluskey M, Ogden GR.
  Source: Dent Update. 2000 April; 27(3): 148-52. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11218286

- **Analysis of the ANA gene as a candidate for the chromosome 21q oral cancer susceptibility locus.**
  Author(s): Yamamoto N, Uzawa K, Yakushiji T, Shibahara T, Noma H, Tanzawa H.
  Source: British Journal of Cancer. 2001 March 23; 84(6): 754-9.
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  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12838890

- **U.S. dental hygienists' knowledge and opinions related to providing oral cancer examinations.**
  Author(s): Forrest JL, Drury TE, Horowitz AM.
  Source: Journal of Cancer Education : the Official Journal of the American Association for Cancer Education. 2001 Autumn; 16(3): 150-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11603878

- **Understanding the biology of oral cancer and chemoprevention.**
  Author(s): Lingen MW.
  Source: Cds Rev. 1998 May-June; 91(4): 24-8. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9760890

- **Understanding the biology of oral cancer.**
  Author(s): Das BR, Nagpal JK.
  Source: Medical Science Monitor : International Medical Journal of Experimental and Clinical Research. 2002 November; 8(11): Ra258-67. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12444391

- **Unlocking the mystery of oral cancer: HSDM student researcher finds link in chain of oral carcinogenesis.**
  Author(s): Edwards SP.
  Source: Harv Dent Bull. 2002 Fall; 10(2): 2-3. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12561774

- **Update and review: oral cancer screening.**
  Author(s): Hamilton MK, Zajack VL, Markovic N.
  Source: Pa Dent J (Harrisb). 2002 September-October; 69(5): 29-31. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12838891

- **Use of magnetic abutments for short endosseous implants following a fibula bone graft in an oral cancer patient: a case report.**
  Author(s): Ishii J, Yoshida T, Yokoo S, Komori T.
  Source: J Oral Implantol. 2003; 29(6): 289-92.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14719579

- **Use of skin and oral cancer examinations in the United States, 1998.**
  Author(s): Canto MT, Drury TF, Horowitz AM.
  Source: Preventive Medicine. 2003 September; 37(3): 278-82.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12914834

- **Use of the fixed mandibular implant in oral cancer patients: a retrospective study.**
  Author(s): August M, Bast B, Jackson M, Perrott D.
  Source: Journal of Oral and Maxillofacial Surgery : Official Journal of the American Association of Oral and Maxillofacial Surgeons. 1998 March; 56(3): 297-301.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9496839

- **Usefulness of fluorescence photography for diagnosis of oral cancer.**
  Author(s): Onizawa K, Saginoya H, Furuya Y, Yoshida H, Fukuda H.
  Source: International Journal of Oral and Maxillofacial Surgery. 1999 June; 28(3): 206-10.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10355944

- **Value of p53 expression in oral cancer and adjacent normal mucosa in relation to the occurrence of multiple primary carcinomas.**
  Author(s): Bongers V, Snow GB, van der Waal I, Braakhuis BJ.
  Source: European Journal of Cancer. Part B, Oral Oncology. 1995 November; 31B(6): 392-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8746270

- **Variable expression of cathepsin B and D correlates with highly invasive and metastatic phenotype of oral cancer.**
  Author(s): Vigneswaran N, Zhao W, Dassanayake A, Muller S, Miller DM, Zacharias W.
  Source: Human Pathology. 2000 August; 31(8): 931-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10987253

- **Views of oral cancer prevention and early detection: Maryland physicians.**
  Author(s): Canto MT, Horowitz AM, Child WL.
  Source: Oral Oncology. 2002 June; 38(4): 373-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12076702

- **Visual inspection in oral cancer screening in Cuba: a case-control study.**
  Author(s): Sankaranarayanan R, Fernandez Garrote L, Lence Anta J, Pisani P, Rodriguez Salva A.
  Source: Oral Oncology. 2002 February; 38(2): 131-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11854059

- **Visualization of metastatic lymph nodes in oral cancer by angiograms.**
  Author(s): Hata T.
  Source: The British Journal of Oral & Maxillofacial Surgery. 2000 April; 38(2): 160-1.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10864716

- **Weighing the risks and benefits of an oral cancer screening.**
  Author(s): Hicks BM, Jacks M.
  Source: Tex Dent J. 1996 June; 113(6): 45-7. Review. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9518847

CHAPTER 2. NUTRITION AND ORAL CANCER

Overview

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

Finding Nutrition Studies on Oral Cancer

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

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

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

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

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

- **Dental dateline. Oral cancer.**
  Source: Anonymous CDS-Revolume 2001 September; 94(6): 39 0091-1666
- **Oral cancer in Australia--risk factors and disease distribution.**
  Author(s): Oral and Maxillofacial Surgery, Sydney University.
  Source: Cox, S Ann-R-Australas-Coll-Dent-Surg. 2000 October; 15: 261-3 0158-1570
- **Rapid in vivo assay for topical oral cancer chemopreventive agents.**
  Author(s): Department of Pathology, Northwestern University Medical School, Chicago, IL 60611, USA.
  Source: Shabany, K Chiu, P C Raghian, A Chang, K W Solt, D B Int-J-Oncol. 2002 July; 21(1): 159-64 1019-6439

Federal Resources on Nutrition

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

- healthfinder®, HHS's gateway to health information, including diet and nutrition: **http://www.healthfinder.gov/scripts/SearchContext.asp?topic=238&page=0**
- The United States Department of Agriculture's Web site dedicated to nutrition information: **www.nutrition.gov**
- The Food and Drug Administration's Web site for federal food safety information: **www.foodsafety.gov**
- The National Action Plan on Overweight and Obesity sponsored by the United States Surgeon General: **http://www.surgeongeneral.gov/topics/obesity/**
- The Center for Food Safety and Applied Nutrition has an Internet site sponsored by the Food and Drug Administration and the Department of Health and Human Services: **http://vm.cfsan.fda.gov/**
- Center for Nutrition Policy and Promotion sponsored by the United States Department of Agriculture: **http://www.usda.gov/cnpp/**
- Food and Nutrition Information Center, National Agricultural Library sponsored by the United States Department of Agriculture: **http://www.nal.usda.gov/fnic/**
- Food and Nutrition Service sponsored by the United States Department of Agriculture: **http://www.fns.usda.gov/fns/**

Additional Web Resources

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

- AOL: **http://search.aol.com/cat.adp?id=174&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/med_nutrition.html**

- Google: **http://directory.google.com/Top/Health/Nutrition/**
- Healthnotes: **http://www.healthnotes.com/**
- Open Directory Project: **http://dmoz.org/Health/Nutrition/**
- Yahoo.com: **http://dir.yahoo.com/Health/Nutrition/**
- WebMD®Health: **http://my.webmd.com/nutrition**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**

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

- **Minerals**

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

CHAPTER 3. ALTERNATIVE MEDICINE AND ORAL CANCER

Overview

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

National Center for Complementary and Alternative Medicine

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

- **A case-control study of oral cancer in Changhua County, Taiwan.**
  Author(s): Lu CT, Yen YY, Ho CS, Ko YC, Tsai CC, Hsieh CC, Lan SJ.
  Source: Journal of Oral Pathology & Medicine : Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology. 1996 May; 25(5): 245-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8835822

- **A survey on the control of oral cancer in India.**
  Author(s): Stanley K, Stjernsward J.
  Source: Indian Journal of Cancer. 1986 June; 23(2): 105-11.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3570348

- **Accumulation of mitochondrial DNA deletions in human oral tissues -- effects of betel quid chewing and oral cancer.**

Author(s): Lee HC, Yin PH, Yu TN, Chang YD, Hsu WC, Kao SY, Chi CW, Liu TY, Wei YH.
Source: Mutation Research. 2001 June 27; 493(1-2): 67-74.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11516716

- **Adjuvant chemoprevention of experimental cancer: catechin and dietary turmeric in forestomach and oral cancer models.**
Author(s): Azuine MA, Bhide SV.
Source: Journal of Ethnopharmacology. 1994 December; 44(3): 211-7.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7898128

- **Alcohol, tobacco and paan use and understanding of oral cancer risk among Asian males in Leicester.**
Author(s): Vora AR, Yeoman CM, Hayter JP.
Source: British Dental Journal. 2000 April 22; 188(8): 444-51.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10953402

- **An epidemiologic study of 70 oral cancer cases at the Institute of Dental Medicine, Yangon, Myanmar, 1985-1988.**
Author(s): Sein K, Maung KK, Aung TH.
Source: Odontostomatol Trop. 1992 March; 15(1): 5-8.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1287609

- **Betel chewing and dietary habits of chewers without and with submucous fibrosis and with concomitant oral cancer.**
Author(s): Seedat HA, van Wyk CW.
Source: South African Medical Journal. Suid-Afrikaanse Tydskrif Vir Geneeskunde. 1988 December 3; 74(11): 572-5.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3194806

- **Betel quid and oral cancer: prospects for prevention.**
Author(s): Gupta PC.
Source: Iarc Sci Publ. 1991; (105): 466-70.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1855897

- **Betel quid chewing, cigarette smoking and alcohol consumption related to oral cancer in Taiwan.**
Author(s): Ko YC, Huang YL, Lee CH, Chen MJ, Lin LM, Tsai CC.
Source: Journal of Oral Pathology & Medicine : Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology. 1995 November; 24(10): 450-3.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8600280

- **BMI throughout life, intake of vitamin supplements and oral cancer in Spain.**
  Author(s): Nieto A, Sanchez MJ, Quintana MJ, Castellsague X, Martinez C, Munoz J, Bosch FX, Munoz N, Herrero R, Franceschi S.
  Source: Iarc Sci Publ. 2002; 156: 259-61. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12484183

- **Chemoprevention of oral cancer by green tea.**
  Author(s): Hsu SD, Singh BB, Lewis JB, Borke JL, Dickinson DP, Drake L, Caughman GB, Schuster GS.
  Source: Gen Dent. 2002 March-April; 50(2): 140-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12004708

- **Chemotherapy administered using two-route infusion of cisplatin and sodium thiosulfate and intravenous infusion of vinblastine and peplomycin in patients with oral cancer.**
  Author(s): Wada T, Harada M, Morita N, Oomata T, Koizumi T, Kawashima T, Sakamoto T.
  Source: Clinical Therapeutics. 1995 March-April; 17(2): 280-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7614528

- **Chromosomal instability and cytoskeletal defects in oral cancer cells.**
  Author(s): Saunders WS, Shuster M, Huang X, Gharaibeh B, Enyenihi AH, Petersen I, Gollin SM.
  Source: Proceedings of the National Academy of Sciences of the United States of America. 2000 January 4; 97(1): 303-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10618413

- **Cultural and dietary risk factors of oral cancer and precancer--a brief overview.**
  Author(s): Zain RB.
  Source: Oral Oncology. 2001 April; 37(3): 205-10.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11287272

- **Cytogenetic surveillance of tobacco-areca nut (mava) chewers, including patients with oral cancers and premalignant conditions.**
  Author(s): Adhvaryu SG, Dave BJ, Trivedi AH.
  Source: Mutation Research. 1991 September; 261(1): 41-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1881407

- **Dental service use and the implications for oral cancer screening in a sample of Bangladeshi adult medical care users living in Tower Hamlets, UK.**
  Author(s): Pearson N, Croucher R, Marcenes W, O'Farrell M.

Source: British Dental Journal. 1999 May 22; 186(10): 517-21.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10379085

- **Development of the Bowman-Birk inhibitor for oral cancer chemoprevention and analysis of Neu immunohistochemical staining intensity with Bowman-Birk inhibitor concentrate treatment.**
  Author(s): Armstrong WB, Wan XS, Kennedy AR, Taylor TH, Meyskens FL Jr.
  Source: The Laryngoscope. 2003 October; 113(10): 1687-702. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14520092

- **Diet and nutrition in the etiology of oral cancer.**
  Author(s): Winn DM.
  Source: The American Journal of Clinical Nutrition. 1995 February; 61(2): 437S-445S. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7840089

- **Direct cytotoxicity of garlic on human oral cancer cells.**
  Author(s): Chen JH, Lim JS, Shyu KW, Meng CL.
  Source: Zhonghua Ya Yi Xue Hui Za Zhi. 1988 March; 7(1): 13-8. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3254744

- **Dose dependant relative risk for oral cancer in tobacco chewers.**
  Author(s): Haidinger G, Hollenstein U.
  Source: European Journal of Epidemiology. 1991 January; 7(1): 93-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2026228

- **Effects of human fibroblasts on invasiveness of oral cancer cells in vitro: isolation of a chemotactic factor from human fibroblasts.**
  Author(s): Sugiura T, Shirasuna K, Hayashido Y, Sakai T, Matsuya T.
  Source: International Journal of Cancer. Journal International Du Cancer. 1996 December 11; 68(6): 774-81.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8980183

- **Elevated mutagen susceptibility in cultured lymphocytes of oral cancer patients.**
  Author(s): Trivedi AH, Bakshi SR, Jaju RJ, Dave BJ, Adhvaryu SG, Patel DD, Balar DB.
  Source: Anticancer Res. 1995 November-December; 15(6B): 2589-92.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8669829

- **Evaluation of the DNA stability of forensic markers used in betel-quid chewers' oral swab samples and oral cancerous specimens: implications for forensic application.**
  Author(s): Yang CH, Hsieh LL, Tsai CW, Chiou FS, Chou SL, Hsu BD, Pai CY.

Source: J Forensic Sci. 2003 January; 48(1): 88-92.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12570205

- **Flavopiridol, a cyclin dependent kinase (CDK) inhibitor, induces apoptosis by regulating Bcl-x in oral cancer cells.**
  Author(s): Mihara M, Shintani S, Nakashiro K, Hamakawa H.
  Source: Oral Oncology. 2003 January; 39(1): 49-55.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12457721

- **Genetic polymorphisms of CYP2E1, GSTM1, and GSTT1; environmental factors and risk of oral cancer.**
  Author(s): Hung HC, Chuang J, Chien YC, Chern HD, Chiang CP, Kuo YS, Hildesheim A, Chen CJ.
  Source: Cancer Epidemiology, Biomarkers & Prevention : a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology. 1997 November; 6(11): 901-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9367063

- **Human papillomaviruses in 91 oral cancers from Indian betel quid chewers--high prevalence and multiplicity of infections.**
  Author(s): Balaram P, Nalinakumari KR, Abraham E, Balan A, Hareendran NK, Bernard HU, Chan SY.
  Source: International Journal of Cancer. Journal International Du Cancer. 1995 May 16; 61(4): 450-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7759149

- **Induction of MDM2-P2 transcripts correlates with stabilized wild-type p53 in betel- and tobacco-related human oral cancer.**
  Author(s): Ralhan R, Sandhya A, Meera M, Bohdan W, Nootan SK.
  Source: American Journal of Pathology. 2000 August; 157(2): 587-96.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10934161

- **Inhibition of the synthesis of eicosanoid-like substances in a human oral cancer cell line by interferon-gamma and eicosapentaenoic acid.**
  Author(s): Meng CL, Yang CY, Shen KL, Wong PY, Lee HK.
  Source: Archives of Oral Biology. 1998 December; 43(12): 979-86.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9877329

- **Khat and oral cancer.**
  Author(s): Soufi HE, Kameswaran M, Malatani T.
  Source: The Journal of Laryngology and Otology. 1991 August; 105(8): 643-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1919319

- **Knowledge, attitudes and beliefs of adult South Asians living in London regarding risk factors and signs for oral cancer.**
  Author(s): Shetty KV, Johnson NW.
  Source: Community Dent Health. 1999 December; 16(4): 227-31.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10665176

- **Lack of association between p53 expression and betel nut chewing in oral cancers from Thailand.**
  Author(s): Thongsuksai P, Boonyaphiphat P.
  Source: Oral Oncology. 2001 April; 37(3): 276-81.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11287282

- **MEK inhibition enhances bleomycin A5-induced apoptosis in an oral cancer cell line: signaling mechanisms and therapeutic opportunities.**
  Author(s): Yang LC, Yang SH, Tai KW, Chou MY, Yang JJ.
  Source: Journal of Oral Pathology & Medicine : Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology. 2004 January; 33(1): 37-45.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14675139

- **Modulating effect of resveratrol and quercetin on oral cancer cell growth and proliferation.**
  Author(s): ElAttar TM, Virji AS.
  Source: Anti-Cancer Drugs. 1999 February; 10(2): 187-93.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10211549

- **Mutations in the conserved regions of p53 are infrequent in betel-associated oral cancers from Papua New Guinea.**
  Author(s): Thomas S, Brennan J, Martel G, Frazer I, Montesano R, Sidransky D, Hollstein M.
  Source: Cancer Research. 1994 July 1; 54(13): 3588-93.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8012986

- **Oral cancer and precancer related to betel and miang chewing in Thailand: a review.**
  Author(s): Reichart PA.
  Source: Journal of Oral Pathology & Medicine : Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology. 1995 July; 24(6): 241-3. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7562658

- **Oral cancer chemotherapy: the promise and the pitfalls.**
  Author(s): McLeod HL, Evans WE.

Source: Clinical Cancer Research : an Official Journal of the American Association for Cancer Research. 1999 October; 5(10): 2669-71.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10537326

- **Oral cancer in India: an epidemiologic and clinical review.**
  Author(s): Sankaranarayanan R.
  Source: Oral Surg Oral Med Oral Pathol. 1990 March; 69(3): 325-30. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2179801

- **Oral cancer in South Asia.**
  Author(s): Trivedy C, Johnson NW.
  Source: British Dental Journal. 1997 March 22; 182(6): 206.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9115834

- **Oral cancer in southern India: the influence of smoking, drinking, paan-chewing and oral hygiene.**
  Author(s): Balaram P, Sridhar H, Rajkumar T, Vaccarella S, Herrero R, Nandakumar A, Ravichandran K, Ramdas K, Sankaranarayanan R, Gajalakshmi V, Munoz N, Franceschi S.
  Source: International Journal of Cancer. Journal International Du Cancer. 2002 March 20; 98(3): 440-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11920597

- **Oral cancer patient support network.**
  Author(s): Bonner P.
  Source: Tex Dent J. 1998 June; 115(6): 65. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9667214

- **Oral lesions, genotoxicity and nitrosamines in betel quid chewers with no obvious increase in oral cancer risk.**
  Author(s): Stich HF, Rosin MP, Brunnemann KD.
  Source: Cancer Letters. 1986 April; 31(1): 15-25.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3697952

- **Paan without tobacco: an independent risk factor for oral cancer.**
  Author(s): Boucher BJ.
  Source: International Journal of Cancer. Journal International Du Cancer. 2001 February 15; 91(4): 592-3.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11251988

- **Paan without tobacco: an independent risk factor for oral cancer.**
  Author(s): Merchant A, Husain SS, Hosain M, Fikree FF, Pitiphat W, Siddiqui AR, Hayder SJ, Haider SM, Ikram M, Chuang SK, Saeed SA.

Source: International Journal of Cancer. Journal International Du Cancer. 2000 April 1; 86(1): 128-31.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10728606

- **Prognostic evaluation of preoperative thermochemoradiotherapy for N(3) cervical lymph node metastases of oral cancer.**
  Author(s): Tohnai I, Hayashi Y, Mitsudo K, Shigetomi T, Ueda M, Ishigaki T.
  Source: Oncology. 2002; 62(3): 234-40.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12065871

- **Risk assessment of tobacco, alcohol and diet in oral cancer--a case-control study.**
  Author(s): Rao DN, Ganesh B, Rao RS, Desai PB.
  Source: International Journal of Cancer. Journal International Du Cancer. 1994 August 15; 58(4): 469-73.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8056441

- **Risk factors for oral cancer in women.**
  Author(s): Kabat GC, Hebert JR, Wynder EL.
  Source: Cancer Research. 1989 May 15; 49(10): 2803-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2713863

- **Role of areca nut consumption in the cause of oral cancers. A cytogenetic assessment.**
  Author(s): Dave BJ, Trivedi AH, Adhvaryu SG.
  Source: Cancer. 1992 September 1; 70(5): 1017-23.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1515978

- **Safrole-like DNA adducts in oral tissue from oral cancer patients with a betel quid chewing history.**
  Author(s): Chen CL, Chi CW, Chang KW, Liu TY.
  Source: Carcinogenesis. 1999 December; 20(12): 2331-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10590228

- **Secretor status and oral cancer.**
  Author(s): Lamey PJ, Douglas PS, Napier SS.
  Source: The British Journal of Oral & Maxillofacial Surgery. 1994 August; 32(4): 214-7.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7947564

- **The inhibitory effect of curcumin, genistein, quercetin and cisplatin on the growth of oral cancer cells in vitro.**
  Author(s): Elattar TM, Virji AS.

Source: Anticancer Res. 2000 May-June; 20(3A): 1733-8.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10928101

- **The involvement of reactive oxygen species in oral cancers of betel quid/tobacco chewers.**
  Author(s): Stich HF, Anders F.
  Source: Mutation Research. 1989 September; 214(1): 47-61. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2671701

- **Tobacco use and oral cancer: a global perspective.**
  Author(s): Johnson N.
  Source: J Dent Educ. 2001 April; 65(4): 328-39. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11336118

Additional Web Resources

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

- Alternative Medicine Foundation, Inc.: **http://www.herbmed.org/**
- AOL: **http://search.aol.com/cat.adp?id=169&layer=&from=subcats**
- Chinese Medicine: **http://www.newcenturynutrition.com/**
- drkoop.com®: **http://www.drkoop.com/InteractiveMedicine/IndexC.html**
- Family Village: **http://www.familyvillage.wisc.edu/med_altn.htm**
- Google: **http://directory.google.com/Top/Health/Alternative/**
- Healthnotes: **http://www.healthnotes.com/**
- MedWebPlus: **http://medwebplus.com/subject/Alternative_and_Complementary_Medicine**
- Open Directory Project: **http://dmoz.org/Health/Alternative/**
- HealthGate: **http://www.tnp.com/**
- WebMD®Health: **http://my.webmd.com/drugs_and_herbs**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**
- Yahoo.com: **http://dir.yahoo.com/Health/Alternative_Medicine/**

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

- **General Overview**

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

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

- **Herbs and Supplements**

  Blue-Green Algae
  Source: Healthnotes, Inc.; www.healthnotes.com

  Blue-Green Algae
  Source: Integrative Medicine Communications; www.drkoop.com

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

  Spirulina
  Alternative names: Blue-green Algae
  Source: Integrative Medicine Communications; www.drkoop.com

General References

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

CHAPTER 4. DISSERTATIONS ON ORAL CANCER

Overview

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

Dissertations on Oral Cancer

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

- **Modulation of the Risk to Oral Cancer** by Hornby, Antony Paul; PhD from The University of British Columbia (Canada), 1989
  http://wwwlib.umi.com/dissertations/fullcit/NL55152

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. CLINICAL TRIALS AND ORAL CANCER

Overview

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

Recent Trials on Oral Cancer

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

- **Combination Chemotherapy in Treating Patients With Metastatic or Recurrent Head and Neck Cancer**

  Condition(s): Nose Cancers; Oral Cancer; Throat Cancer

  Study Status: This study is currently recruiting patients.

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

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

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00006248

- **Diagnostic Trial in Patients Who Are Undergoing Surgery for Early Stage Mouth Cancer**

  Condition(s): stage I squamous cell carcinoma of the lip and oral cavity; stage II squamous cell carcinoma of the lip and oral cavity

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

Study Status: This study is currently recruiting patients.

Sponsor(s): American College of Surgeons; National Cancer Institute (NCI)

Purpose - Excerpt: RATIONALE: Diagnostic procedures to detect cancer cells in sentinel lymph nodes may help plan effective cancer treatment. PURPOSE: Diagnostic trial to study the effectiveness of lymph node mapping and sentinel lymph node lymphadenectomy in patients who are undergoing surgery to remove early-stage cancer of the mouth.

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00042926

- **Celecoxib in Treating Patients With Precancerous Lesions of the Mouth**

  Condition(s): lip and oral cavity cancer; prevention of oral cancer

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); Memorial Sloan-Kettering Cancer Center

  Purpose - Excerpt: RATIONALE: Chemoprevention therapy is the use of certain drugs to try to prevent the development of cancer. The use of celecoxib may be an effective way to prevent the further development of precancerous lesions in the mouth. PURPOSE: Randomized phase II trial to compare the effectiveness of different regimens of celecoxib in treating patients who have precancerous lesions in the mouth.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00014404

- **Chemotherapy Plus Radiation Therapy in Treating Patients With Head and Neck Cancer**

  Condition(s): Gastrointestinal Cancer; Neck Cancer; Oral Cancer; Throat Cancer

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): University of Chicago Cancer Research Center; National Cancer Institute (NCI)

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

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002951

- **Dentures and Dental Implants in Treating Patients Undergoing Surgery for Mouth Cancer**

  Condition(s): oral complications of cancer and cancer therapy; stage III lip and oral cavity cancer; stage II lip and oral cavity cancer; Quality of Life; stage I lip and oral cavity cancer

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): Jonsson Comprehensive Cancer Center

  Purpose - Excerpt: RATIONALE: The use of dentures and dental implants may help maintain chewing and speaking ability following surgery to remove tumors in the mouth. PURPOSE: Phase II trial to study the effectiveness of dentures and dental implants in maintaining the ability to chew and speak in patients undergoing surgery for **mouth cancer.**

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00006341

- **Fenretinide in Treating Patients With Recurrent or Metastatic Head and Neck Cancer**

  Condition(s): Oral Cancer; Neck Cancer; Throat Cancer

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): M.D. Anderson Cancer Center; National Cancer Institute (NCI)

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

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00006471

- **Liposomal Lurtotecan in Treating Patients With Metastatic or Locally Recurrent Head and Neck Cancer**

  Condition(s): Neck Cancer; Oral Cancer; Throat Cancer

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): European Organization for Research and Treatment of Cancer

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. PURPOSE: Phase II trial to study the effectiveness of liposomal lurtotecan in treating patients who have metastatic or locally recurrent head and neck cancer.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00022594

- **Paclitaxel and Radiation Therapy Plus Chemoprotection With Amifostine in Treating Patients With Stage III or Stage IV Head and Neck Cancer**

  Condition(s): Oral Cancer; Throat Cancer

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): Massachusetts General Hospital

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Radiation therapy uses high-energy x-rays to damage tumor cells. Chemoprotective drugs, such as amifostine, may protect normal cells from the side effects of chemotherapy. PURPOSE: Phase I/II trial to study the effectiveness of paclitaxel and radiation therapy plus chemoprotection with amifostine in treating patients with stage III or stage IV head and neck cancer.

  Phase(s): Phase I; Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00003193

- **Physician-Initiated Stop-Smoking Program for Patients Receiving Treatment for Early-Stage Cancer**

  Condition(s): Leukemia; Lymphoma; Head and Neck Cancer; Lung Cancer; Eye Cancer; Gastrointestinal Cancer; Oral Cancer; Reproductive Cancer

  Study Status: This study is no longer recruiting patients.

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

  Purpose - Excerpt: RATIONALE: Physician-initiated smoking cessation strategies may be effective in getting early-stage cancer patients to quit smoking. PURPOSE: Randomized clinical trial to compare the effectiveness of a physician-initiated stop-smoking program with the usual care for patients receiving treatment for early-stage cancer.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002520

- **Radiation Therapy With or Without Cetuximab in Treating Patients With Stage III or Stage IV Cancer of the Oropharynx, Hypopharynx, or Larynx**

  Condition(s): Oral Cancer; Throat Cancer

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): UAB Comprehensive Cancer Center; National Cancer Institute (NCI)

  Purpose - Excerpt: RATIONALE: Radiation therapy uses high-energy x-rays to damage tumor cells. Monoclonal antibodies such as cetuximab can locate tumor cells and either kill them or deliver tumor-killing substances to them without harming normal cells. It is not yet known if radiation therapy is more effective with or without cetuximab for cancer of the oropharynx, hypopharynx, or larynx. PURPOSE: Randomized phase III trial to compare the effectiveness of radiation therapy with or without cetuximab in treating patients who have stage III or stage IV cancer of the oropharynx, hypopharynx, or larynx.

Phase(s): Phase III

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00004227

- **Radiation Therapy With or Without Epoetin alfa in Treating Patients With Head and Neck Cancer**

  Condition(s): Oral Cancer; Throat Cancer

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): EORTC Radiotherapy Cooperative Group; EORTC Head and Neck Cancer Cooperative Group; Trans-Tasman Radiation Oncological Group; Arbeitsgemeinschaft Radiologische Onkologie; Groupe d'Oncologie et Radiotherapie Tete et Cou; Radius Hungaricus Oncology Group; Grup per l'Estudi dels Limfomes de Catalunya i Balears

  Purpose - Excerpt: RATIONALE: Radiation therapy uses high-energy x-rays to damage tumor cells. Epoetin alfa may help prevent or treat cancer-related anemia. It is not yet known whether radiation therapy is more effective with or without epoetin alfa in treating head and neck cancer. PURPOSE: Randomized phase III trial to compare the effectiveness of radiation therapy with or without epoetin alfa in treating patients who have head and neck cancer.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00017277

- **Computer-Assisted Scheduling of Nicotine Inhaler Use in Participants Who Plan to Stop Smoking**

  Condition(s): Small Cell Lung Cancer; prevention of lung cancer; prevention of esophageal cancer; Non-small cell lung cancer; prevention of head and neck cancer; prevention of oral cancer

  Study Status: This study is completed.

  Sponsor(s): Personal Improvement Computer Systems

  Purpose - Excerpt: RATIONALE: Computer-assisted scheduling of nicotine inhaler use may be an effective method to help people stop smoking. PURPOSE: Randomized phase II trial to compare the effectiveness of computer-assisted scheduling of nicotine inhaler use with that of self-scheduled nicotine inhaler use in participants who plan to stop smoking.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00021138

- **Photodynamic Therapy System for Patients with Refractory/Unresponsive Solid Tumors**

  Condition(s): Liver Metastasis; Pelvic Cancer; Head and Neck Cancer; Sarcoma; Rectal Cancer; Breast Cancer; Colorectal Cancer; Mouth Cancer

Study Status: This study is completed.

Sponsor(s): Light Sciences Corporation

Purpose - Excerpt: This multi-center photodynamic therapy study plans to treat patients with large tumors in any superficial location, sarcoma, tumors of oral/oro-pharyngeal cavity, tumors with extensive pelvic involvement, or liver metastasis. The treatment is limited to patients that have failed to respond to currently approved methods of treatment. The study involves a single, intravenous administration of an investigational drug, LS11 (previously studied in approximately 80 cancer patients) and the placement of a novel, flexible light delivery catheter inside the tumor by a minor surgical procedure. The activation of LS11 by the light delivery catheter over a period of 1-24 hrs may result in destruction of tumor tissue.

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00028405

Keeping Current on Clinical Trials

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

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

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

- For clinical studies at the Warren Grant Magnuson Clinical Center located in Bethesda, Maryland, visit their Web site: **http://clinicalstudies.info.nih.gov/**
- For clinical studies conducted at the Bayview Campus in Baltimore, Maryland, visit their Web site: **http://www.jhbmc.jhu.edu/studies/index.html**
- For cancer trials, visit the National Cancer Institute: **http://cancertrials.nci.nih.gov/**
- For eye-related trials, visit and search the Web page of the National Eye Institute: **http://www.nei.nih.gov/neitrials/index.htm**
- For heart, lung and blood trials, visit the Web page of the National Heart, Lung and Blood Institute: **http://www.nhlbi.nih.gov/studies/index.htm**
- For trials on aging, visit and search the Web site of the National Institute on Aging: **http://www.grc.nia.nih.gov/studies/index.htm**

- For rare diseases, visit and search the Web site sponsored by the Office of Rare Diseases: **http://ord.aspensys.com/asp/resources/rsch_trials.asp**
- For alcoholism, visit the National Institute on Alcohol Abuse and Alcoholism: **http://www.niaaa.nih.gov/intramural/Web_dicbr_hp/particip.htm**
- For trials on infectious, immune, and allergic diseases, visit the site of the National Institute of Allergy and Infectious Diseases: **http://www.niaid.nih.gov/clintrials/**
- For trials on arthritis, musculoskeletal and skin diseases, visit newly revised site of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health: **http://www.niams.nih.gov/hi/studies/index.htm**
- For hearing-related trials, visit the National Institute on Deafness and Other Communication Disorders: **http://www.nidcd.nih.gov/health/clinical/index.htm**
- For trials on diseases of the digestive system and kidneys, and diabetes, visit the National Institute of Diabetes and Digestive and Kidney Diseases: **http://www.niddk.nih.gov/patient/patient.htm**
- For drug abuse trials, visit and search the Web site sponsored by the National Institute on Drug Abuse: **http://www.nida.nih.gov/CTN/Index.htm**
- For trials on mental disorders, visit and search the Web site of the National Institute of Mental Health: **http://www.nimh.nih.gov/studies/index.cfm**
- For trials on neurological disorders and stroke, visit and search the Web site sponsored by the National Institute of Neurological Disorders and Stroke of the NIH: **http://www.ninds.nih.gov/funding/funding_opportunities.htm#Clinical_Trials**

CHAPTER 6. PATENTS ON ORAL CANCER

Overview

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

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

Patents on Oral Cancer

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

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

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

- **Areca food additives and its foods**

  Inventor(s): Shiao; Shin Jen (1001 Tahsueh Road, Institute of Applied Chemistry, Chiao Tung University, Hsinchu 300, TW)

  Assignee(s): None Reported

  Patent Number: 5,389,371

  Date filed: January 21, 1993

  Abstract: This invention relates to areca food additives, especially, to additives for areca quids and foods containing areca component, and their preparation methods. High alkaline lime always exists in conventional areca food additive. Many problems consequently result such as **oral cancer** and the polluting of the environment by the spitting of a bright red liquid. A series of eatable neutral calcium salts of organic acid and compounds containing at least one of the following functional groups selected from the group consisting of --NH2,.dbd.NH,.tbd.N, --NH--, --CONH--, --HCO--, --CO--, --COOR--, --S--, and their salts were invented to replace lime. The taste of astringent and harms caused by the polyphenolic compounds of areca quid could be completely improved. The disease of quid chewer would be decreased and the problem of environmental pollution would be improved.

  Excerpt(s): Areca quid chewing is an almost universal indulgence in many regions of southeastern Asia, and in small and large islands adjacent to the coast, and in the Southwest Pacific area. The preparation of the areca quid is fairly uniform in this part of the world, with variations existing only in the compositions of areca food additives. Lime is the most important component of areca food additive. The other constituent may have been selected from the group consisting of gambit, tobacco, coffee, cocoa, Chinese herbs, and modifier such as sweetener, perfume, preserver, stabilizer, color pigment and fillers. The areca food additive is usually in the form of paste. The preparation of traditional areca quid has been done in several ways.

  Web site: http://www.delphion.com/details?pn=US05389371__

- **Novel CSF and method for obtaining the same**

  Inventor(s): Nomura; Hitoshi (Tokyo, JP), Ono; Masayoshi (Saitama, JP)

  Assignee(s): Chugai Seiyaku Kabushiki Kaisha (tokyo, Jp)

  Patent Number: 4,833,127

  Date filed: July 12, 1985

  Abstract: A novel colony stimulating factor (CSF) that has the ability to promote the differentiation and proliferation of human bone marrow cells to neutrophiles, and a method for obtaining the same are disclosed. This CSF is produced from a novel cell line which has been established from tumor cells in patients with **oral cancer.**This CSF has the potential for use only as a curative for leukopenia but also as a reagent for clinical testing and research studies.N

  Excerpt(s): The present invention relates to a colony stimulating factor (hereunder referred to as CSF) that has the ability to promote the differentiation and proliferation of

bone marrow cells. More particularly, the invention relates to a novel CSF that has the ability to promote the differentiation and proliferation of human bone marrow cells to neutrophiles (such particular CSF may hereunder sometimes be referred to as human G-CSF) and a method for obtaining the same. The CSF in accordance with the present invention has the potential for use not only as a curative for leukopenia but also as a reagent for clinical testing and research studies. The present inventors have suceeded in establishing a novel cell line from tumor cells in patients with **oral cancer.** The cell line had a great ability to produce CSF and exhibited highly proliferative capabilities. Named CHU-1, this cell line has been deposited with Collection Nationale de Cultures de Microorganismes, (C.N.C.M.) Pasteur Institute, France on July 11, 1984 under Deposit Number I-315.

Web site: http://www.delphion.com/details?pn=US04833127__

Patent Applications on Oral Cancer

As of December 2000, U.S. patent applications are open to public viewing.[10] Applications are patent requests which have yet to be granted. (The process to achieve a patent can take several years.) The following patent applications have been filed since December 2000 relating to oral cancer:

- **Stable human oral cancer cell carcinoma cell line**

  Inventor(s): Kaur, Jatinder; (New Delhi, IN), Ralhan, Ranju; (New Delhi, IN)

  Correspondence: Venable; Post Office Box 34385; Washington; DC; 20043-9998; US

  Patent Application Number: 20020110912

  Date filed: December 7, 2000

  Abstract: The present invention is directed to a stable, continuous, human oral squamous cell carcinoma cell line from the floor of the mouth of a habitual tabacco consumer using a variety of growth supplements and complement mediated lysis to obtain a fibroblast free culture. This cell line has the ability to produce tumor in athymic nude mice. The cell line of the present invention constitutes a system that is suitable for detecting and screening for new and effective anti-cancer therapies. This cell line provides in vitro and in vivo (xenographts in athymic mice) oral tumor model which is useful for understanding molecular basis of **oral cancer** development, identifying targets for designing novel therapeutic strategies, testing new gene therapy approaches for **oral cancer** and testing novel synthetic retinoids for chemoprevention of **oral cancer.**

  Excerpt(s): This invention relates to a stable human **oral cancer** cell carcinoma cell line suitable for understanding the differences in the tumorigenic pathways implicated in the development and progression of oral squamous cell carcinoma obtained from the floor of the mouth of a chronic tabacco consumer. Oral cancer ranks as the sixth most common globally and is a major cause of cancer-related morbidity and mortality. The aetiology of betel and tobacco related **oral cancer** is considerably different to that resulting from smoking of tobacco. Exposure of the oral mucosa of habitual betel quid chewers to a plethora of carcinogenic constituents of tobacco and areca nut causes multiple genotoxic insults at the site bolus application, often resulting in the development of clinically distinct premalignant lesions, leukoplakia or erthroplakia,

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

which undergo malignant transformation. Established human **oral cancer** cell lines are widely used to study the mechanism implicated in oral tumorigenesis. The human **oral cancer** cell lines available in Cell Repositories and Culture Collections around the world have been established from the Western or Japanese population and resulting from smoking of tabacco. In this respect, reference is made to Table 1. Presently, there are no **oral cancer** cell lines resulting from chewing of tabacco. Majority of the studies on oral carcinogenesis have been carried out using tissue specimens (biopsy or surgically resected oral premalignant and malignant lesions) or cell lines resulting from smoking of tobacco. Majority of the studies on oral carcinogenesis has been carried out using tissue specimens (biopsy or surgically resected oral premalignant and malignant lesions) or cell lines resulting from smoking of tobacco. The recent awareness of inherited nature of some cancers, ethnic groups, existence of cancer families and importance of surveillance of high risk individuals using cancer susceptibility genes as markers emphasizes the need to establish **oral cancer** cell lines resulting from chewing of tabacco to provide a much needed model for oral tumorigenesis. The existing **oral cancer** cell lines are from tobacco smokers and thus are not suitable for studies pertaining to cancer susceptibility originating from chewing of tobacco. It may be argued that these studies could be carried in human **oral cancer** tissue specimens. However, in-depth studies carried out by the applicants have shown that the availability of the tissue specimen poses a major constraint on the work. Often the biopsy/FNAC specimens yield insufficient number of tumor cells for detailed molecular analysis. Furthermore, the yield of RNA from biopsy/surgically resected tissue specimens may be low reducing the feasibility of conducting studies aimed at identification of genes that are differentially expressed in different stages of oral tumorigenesis by Differential Display Reverse Transcription Polymerase Chain Research (DDRT-PCR). Hence, the non-availability of an experimental model system for tobacco induced **oral cancer** is a major obstacle in understanding the mechanism underlying oral tumorigenesis. Establishment of human **oral cancer** cell lines from betel and tobacco consumers is of utmost importance to provide an in vitro experimental model system for oral tumorigenesis.

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 oral cancer, you can access the U.S. Patent Office archive via the Internet at the following Web address: **http://www.uspto.gov/patft/index.html**. You will see two broad options: (1) Issued Patent, and (2) Published Applications. To see a list of issued patents, perform the following steps: Under "Issued Patents," click "Quick Search." Then, type "oral cancer" (or synonyms) into the "Term 1" box. After clicking on the search button, scroll down to see the various patents which have been granted to date on oral cancer.

You can also use this procedure to view pending patent applications concerning oral cancer. Simply go back to **http://www.uspto.gov/patft/index.html**. Select "Quick Search" under "Published Applications." Then proceed with the steps listed above.

CHAPTER 7. BOOKS ON ORAL CANCER

Overview

This chapter provides bibliographic book references relating to oral cancer. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on oral cancer include the Combined Health Information Database and the National Library of Medicine. Your local medical library also may have these titles available for loan.

Book Summaries: Federal Agencies

The Combined Health Information Database collects various book abstracts from a variety of healthcare institutions and federal agencies. To access these summaries, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. You will need to use the "Detailed Search" option. To find book summaries, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer. For the format option, select "Monograph/Book." Now type "oral cancer" (or synonyms) into the "For these words:" box. You should check back periodically with this database which is updated every three months. The following is a typical result when searching for books on oral cancer:

- **Oral Cancer: The Dentist's Role in Diagnosis, Management, Rehabilitation, and Prevention**

  Source: Chicago, IL: Quintessence Publishing Co, Inc. 1999. 244 p.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $79.00 plus shipping and handling. ISBN: 0867153571.

  Summary: Dentists are involved in the diagnosis, treatment, rehabilitation, reconstruction, and prevention of **oral cancer.** This book is written specifically for dental health care providers, including dental students, general dentists, dental specialists, and hygienists. The authors focus on the major contributions that the dental profession can make in the field of **oral cancer** health care delivery. The book offers 19 chapters, covering the epidemiology of **oral cancer;** the pathogenesis and progression of **oral**

cancer; the **oral cancer** examination; diagnostic procedures; premalignant lesions; types of **oral cancer;** the surgical management of **oral cancer;** contemporary principles of surgical reconstruction of the oral cavity; principles and complications of radiation therapy; principles and complications of chemotherapy; the oral care of the patient receiving chemotherapy and that of the patient receiving radiation therapy; surgical treatment of the patient receiving radiation therapy; prosthodontic reconstruction of the hard and soft palate; the role of implant supported prostheses; speech production and swallowing; psychosocial considerations; the dentist's role in tobacco cessation; and chemoprevention. Each chapter concludes with a list of references and a subject index concludes the book. The book is illustrated with numerous full color photographs.

- **Working with Oral Cancer**

  Source: Vero Beach, FL: Speech Bin. 1995. 100 p.

  Contact: Available from Speech Bin. 1965 Twenty-Fifth Avenue, Vero Beach, FL 32960. (800) 4-SPEECH. PRICE: $49.95 plus shipping and handling. ISBN: 0863881297. Also available from Imaginart. 307 Arizona Street, Bisbee, AZ 85603. (800) 828-1376; Fax (602) 432-5134. PRICE: $49.95 plus shipping and handling.

  Summary: This manual provides practical information on the assessment and treatment of both speech and swallowing difficulties associated with **oral cancer.** Chapter 1 gives an overview of the anatomy and physiology of the oral cavity, including normal swallowing and speech and a summary of current surgical interventions used for **oral cancer.** Chapter 2 discusses the assessment of swallowing problems arising from surgical management of oral cavity tumors. Chapter 3 discusses the treatment and management of swallowing disorders and offers practical advice on what to do to help achieve functional swallowing. Chapter 4 gives a comprehensive view on effects of surgery on articulation, including appropriate assessment and treatment strategies. The final chapter discusses the impact of altered body image and the effects of disfiguring surgery on psychological well-being; the authors emphasize strategies to help patients adapt post-surgically. The manual includes practice worksheets and a list of resource organizations for professionals and patients. A subject index concludes the manual.

Book Summaries: Online Booksellers

Commercial Internet-based booksellers, such as Amazon.com and Barnes&Noble.com, offer summaries which have been supplied by each title's publisher. Some summaries also include customer reviews. Your local bookseller may have access to in-house and commercial databases that index all published books (e.g. Books in Print®). **IMPORTANT NOTE:** Online booksellers typically produce search results for medical and non-medical books. When searching for "oral cancer" at online booksellers' Web sites, you may discover non-medical books that use the generic term "oral cancer" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "oral cancer" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **Colour Atlas of Oral Cancers: The Diagnosis and Classification of Leukoplakias, Precancerous Conditions and Carcinomas** by Arne Burkhardt; ISBN: 0815113374; http://www.amazon.com/exec/obidos/ASIN/0815113374/icongroupinterna
- **Contemporary Issues in Oral Cancer** by D. Saranath (Editor); ISBN: 0195650239; http://www.amazon.com/exec/obidos/ASIN/0195650239/icongroupinterna

- **Detecting oral cancer a guide for health care professionals (SuDoc HE 20.3408:D 48/2)** by U.S. Dept of Health and Human Services; ISBN: B00010PNEC; http://www.amazon.com/exec/obidos/ASIN/B00010PNEC/icongroupinterna
- **Management of Oral Cancer (Oxford Medical Publications)** by Nicholas Stafford (Editor), John Waldron (Contributor); ISBN: 0192616099; http://www.amazon.com/exec/obidos/ASIN/0192616099/icongroupinterna
- **Oral Cancer** by Jatan P. Shah, et al; ISBN: 189906687X; http://www.amazon.com/exec/obidos/ASIN/189906687X/icongroupinterna
- **Oral cancer**; ISBN: 0944235050; http://www.amazon.com/exec/obidos/ASIN/0944235050/icongroupinterna
- **Oral Cancer (Book with CD-ROM)** by Sol Silverman, et al; ISBN: 155009050X; http://www.amazon.com/exec/obidos/ASIN/155009050X/icongroupinterna
- **Oral Cancer and Precancer** by J. J. Pindborg; ISBN: 0723605297; http://www.amazon.com/exec/obidos/ASIN/0723605297/icongroupinterna
- **Oral cancer-- confronting the enemy (SuDoc HE 20.3417:OR 1/2)** by U.S. Dept of Health and Human Services; ISBN: B000111FH0; http://www.amazon.com/exec/obidos/ASIN/B000111FH0/icongroupinterna
- **Oral Cancer Fact Pack**; ISBN: 0752106384; http://www.amazon.com/exec/obidos/ASIN/0752106384/icongroupinterna
- **Oral cancer in England and Wales; a national study of morbidity, mortality, curability and related factors**; ISBN: 0116901217; http://www.amazon.com/exec/obidos/ASIN/0116901217/icongroupinterna
- **Oral Cancer: A Practical Guide to Understanding Oral Cancer [ILLUSTRATED]** by D.M.D., M.D. Lewis Clayman (Author); ISBN: 097172430X; http://www.amazon.com/exec/obidos/ASIN/097172430X/icongroupinterna
- **Oral Cancer: A Synopsis of Pathology and Management** by George Dimitroulis, Brian S. Avery; ISBN: 0723610223; http://www.amazon.com/exec/obidos/ASIN/0723610223/icongroupinterna
- **Oral Cancer: Clinical and Pathological Considerations** by Bruce A. Wright, et al; ISBN: 0849367743; http://www.amazon.com/exec/obidos/ASIN/0849367743/icongroupinterna
- **Oral Cancer: Epidemiology, Etiology, and Pathology** by C. Pismith, et al; ISBN: 089116541X; http://www.amazon.com/exec/obidos/ASIN/089116541X/icongroupinterna
- **Oral Cancer: The Dentist's Role in Diagnosis, Management, Rehabilitation, and Prevention** by Robert A. Ord (Editor), Remy H. Blanchaert (Editor); ISBN: 0867153571; http://www.amazon.com/exec/obidos/ASIN/0867153571/icongroupinterna
- **Oral Cancer: The Diagnosis, Therapy, Management and Rehabilitationof the Oral Cancer Patient** by Gerald Shklar (Editor); ISBN: 0721612717; http://www.amazon.com/exec/obidos/ASIN/0721612717/icongroupinterna
- **Oral cancers : research report (SuDoc HE 20.3166:Or 1/992)** by U.S. Dept of Health and Human Services; ISBN: B00010A6X0; http://www.amazon.com/exec/obidos/ASIN/B00010A6X0/icongroupinterna

- **Risk Markers for Oral Diseases: Volume 2, Oral Cancer, Detection of Patients and Lesions at Risk** by N. W. Johnson (Editor); ISBN: 0521374219; http://www.amazon.com/exec/obidos/ASIN/0521374219/icongroupinterna
- **What you need to know about, oral cancer (SuDoc HE 20.3152:OR 1/996)** by U.S. Dept of Health and Human Services; ISBN: B00010XCW2; http://www.amazon.com/exec/obidos/ASIN/B00010XCW2/icongroupinterna
- **Working with Oral Cancer (Working With. Series)** by Julia Appleton, Jane Machin; ISBN: 0863881297; http://www.amazon.com/exec/obidos/ASIN/0863881297/icongroupinterna

Chapters on Oral Cancer

In order to find chapters that specifically relate to oral cancer, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and oral cancer using the "Detailed Search" option. Go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find book chapters, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Book Chapter." Type "oral cancer" (or synonyms) into the "For these words:" box. The following is a typical result when searching for book chapters on oral cancer:

- **Epidemiology of Oral Cancer**

  Source: in Ord, R.A. and Blanchaert, R.H., eds. Oral Cancer: The Dentist's Role in Diagnosis, Management, Rehabilitation, and Prevention. Chicago, IL: Quintessence Publishing Co, Inc. 1999. p. 3-8.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $79.00 plus shipping and handling. ISBN: 0867153571.

  Summary: Dentists are involved in the diagnosis, treatment, rehabilitation, reconstruction, and prevention of **oral cancer.** This chapter on the epidemiology of **oral cancer** is from a book written specifically for dental health care providers, including dental students, general dentists, dental specialists, and hygienists. The author of this chapter provides an understanding of the incidence, prevalence, and risk of oral and pharyngeal cancer. Sections describe the methods by which data are gathered and reported; the age at which oral and pharyngeal cancer is identified; and the impact of the development of second primary cancers, cigarette smoking, and alcohol abuse. The final section of this chapter gives epidemiologic data for a group of 200 patients in the Department of Oral and Maxillofacial Surgery at the University of Maryland. These data provide further understanding of the roles of dentistry and dental related subspecialities in the diagnosis and management of **oral cancer.** 3 tables. 12 references.

- **Oral Health-Related Quality of Life in Patients with Oral Cancer**

  Source: in Inglehart, M.R.; Bagramian, R.A., eds. Oral Health-Related Quality of Life. Chicago, IL: Quintessence Publishing Co, Inc. 2002. p.153-167.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail:

quintpub@aol.com. Website: www.quintpub.com. PRICE: $42.00 plus shipping and handling. ISBN: 0867154217.

Summary: Oral conditions can have a significant impact both on an individual's sense of personal well-being and on the function of a society as a whole. This chapter on **oral cancer** is from a book on oral health-related quality of life. Cancers of the oral cavity and oropharynx region have significant rates of morbidity and mortality associated with them. Treatment of these conditions often causes permanent esthetic, function, and quality of life (QOL) problems. The author discusses epidemiology and demographics, risk factors and etiopathogenesis (how the conditions arise and cause disease), early detection, characterization of oral cancers, signs and symptoms of **oral cancer,** diagnosis of **oral cancer,** treatment methods, effects of treatment on QOL (surgery, radiation therapy, chemotherapy), preservation of QOL in patients with **oral cancer,** general reduction of toxicity, salivary gland-sparing radiotherapy techniques, salivary hypofunction and xerostomia therapies, mucositis therapies, fluoride therapies, replacement of teeth with prostheses, prevention and treatment of osteoradionecrosis (bone tissue death after radiation), surgery-sparing cancer therapy, and prevention of new cancers. The authors conclude that collaboration is required among basic, clinical, behavioral, and epidemiological scientists, as well as patients and their team of caregivers, to advance the early detection and management of the disease and the rehabilitation of these patients. 1 figure. 3 tables. 101 references.

- **Oral Cancer Examination**

  Source: in Ord, R.A. and Blanchaert, R.H., eds. Oral Cancer: The Dentist's Role in Diagnosis, Management, Rehabilitation, and Prevention. Chicago, IL: Quintessence Publishing Co, Inc. 1999. p. 21-37.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $79.00 plus shipping and handling. ISBN: 0867153571.

  Summary: The detection of **oral cancer** at an early state, when it is most amenable to treatment, is an important goal for the dental profession. Too often squamous cell carcinomas are dismissed as innocuous, benign ulcers, traumatic lesions, or soft tissue aberrations. This chapter on the **oral cancer** examination is from a book on the dentist's role in the diagnosis, management, rehabilitation, and prevention of **oral cancer.** The author reviews the diagnosis of early stage oral carcinomas, likely outcomes of a delay in diagnosis, components of the **oral cancer** examination (patient's medical and dental history, visual assessment of the head, neck and oral cavity, and manual palpation of the regional cervical lymph nodes), the sequence of procedures in the **oral cancer** examination, and identification of findings. The author concludes that to date, dentists and other oral health care providers have not offered comprehensive **oral cancer** examinations on a routine basis. Continuing education courses are needed to provide clinicians with the information and practical applications to detect, diagnose, and manage **oral cancer.** The chapter includes a photographic depiction of the full recommendation **oral cancer** screening examination, with a textual description of each step. 21 figures. 3 tables. 56 references.

- **Oral Cancer: Management**

  Source: in Clinician's Guide to Treatment of Medically Compromised Patients. Baltimore, MD: American Academy of Oral Medicine (AAOM). 1995. p. 64-67.

Contact: Available from American Academy of Oral Medicine (AAOM). 2910 Lightfoot Drive, Baltimore, MD 21209-1452. (410) 602-8585. Website: www.aaom.com. PRICE: $21.00 plus shipping and handling.

Summary: This chapter, from a guide for dentists on managing problems of medically compromised dental patients, discusses managing patients with **oral cancer.** The authors stress that management consists of utilizing the knowledge of the biologic and epidemiological aspects of cancer, its prevention, early detection, diagnosis, treatment, rehabilitation, and understanding the psychosocial and economic aspects of the disease. Topics covered include a definition, epidemiology, clinical findings and symptoms, diagnostic tests, and dental management considerations. Oral management is described in three phases: the diagnosis and pretreatment assessment, the management during medical therapy, and the management following cancer therapy (posttreatment phase). The majority of the information is presented in chart format. (AA-M).

CHAPTER 8. MULTIMEDIA ON ORAL CANCER

Overview

In this chapter, we show you how to keep current on multimedia sources of information on oral cancer. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine.

Video Recordings

An excellent source of multimedia information on oral cancer is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "oral cancer" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find video productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Videorecording (videotape, videocassette, etc.)." Type "oral cancer" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on oral cancer:

- **Health Care Professionals' Guide to Oral Cancer**

  Source: Fairburn, GA: Oral Health Education Foundation. 1996. (videocassette).

  Contact: Available from American Dental Hygienists' Association (ADHA). 444 North Michigan Avenue, Suite 3400, Chicago, IL 60611. (800) 243-2342 (press 2) or (312) 440-8900. Fax (312) 467-1806. Website: www.adha.org. PRICE: $15.00 each. Item Number 3673 DEV.

  Summary: The diagnosis, treatment, rehabilitation, and maintenance of **oral cancer** patients are explored in this multi-disciplinary educational video for health care professionals. Throughout the video, the importance of early detection and diagnosis is emphasized. The program discusses risk factors, including age and lifestyle factors such as alcohol and tobacco use. The video reviews epidemiology, including the most common types of **oral cancer.** The program describes typical symptoms, appearance, and classification of oral cancers and precancerous conditions including leukoplakia and erythroplakia. The potential role of diet in reducing risk for **oral cancer** is discussed. The

program addresses diagnostic issues, including step-by-step guidelines for performing an **oral cancer** examination, the common presenting signs of **oral cancer,** the role of histologic confirmation of suspected lesions, and the use of imaging. Treatment considerations discussed include radiation therapy, surgery, chemotherapy, indications for surgery, the benefits and disadvantages of surgery, the importance of speech and swallowing assessments prior to surgery, and the need for dental evaluation and possible treatment before surgery. Rehabilitation and maintenance issues described includes prostheses, cosmetic surgery, speech and swallowing rehabilitation, audiologic monitoring, physical therapy, psychological testing and counseling, and ongoing oral health and dental care. The program briefly mentions the SPOHNC (Support for People with Oral and Head and Neck Cancer) organization and its newsletter. Each segment provides recommendations for referral services and the program concludes by reiterating the importance of coordination among health care providers involved in the care of patients with **oral cancer.**

- **Oral Cancer Screening: A Brief Review**

  Source: Pittsburgh, PA: Oral Cancer Center, University of Pittsburgh. 2002. (video).

  Contact: Available from University of Pittsburgh Oral Cancer Center. (412) 648-8513. E-mail: mmkst56@pitt.edu. Website: www.upci.upmc.edu/internet/occ/. PRICE: Available for free on the Web. Contact for availability of VHS copies.

  Summary: The head and neck cancer exam is a brief procedure that can be routinely performed by all health care providers. It requires no special equipment and is considered non-invasive. This procedure may discover cancer in an early stage and can help patients avoid major potentially-disfiguring surgery. In this video, health professionals can quickly review how to conduct the examination of the oral cavity and the head and neck. Narrated by Dr. Nancy Snyderman, the video includes an interview with a patient who had tongue cancer that was not identified early in its development. The program briefly reviews the risk factors for **oral cancer,** including male gender, age older than 50 years, tobacco use (including smokeless tobacco), and alcohol use. The program then demonstrates the oral cavity exam, describes what the examiner should look for, and shows examples of significant lesions. The program concludes with a section demonstrating the use of the brush biopsy technique.

- **What you should know about oral cancer**

  Source: No place: Bonner Communications. 1994. 1 videotape (8.5 minutes, VHS, 1/2 inch).

  Contact: Available from Spectrum Healthcare Group, P.O. Box 396, Fairburn, GA 30213. Telephone: (404) 969-7400.

  Summary: This videotape discusses the importance of having a healthy mouth and how having an unhealthy mouth can have serious, life-threatening consequences. Dentists spotlighted in the video illustrate the seriousness of **oral cancer,** citing fatality statistics and emphasizing the importance of early detection. Cal Ripken, of the Baltimore Orioles, delivers s short segment regarding the particular dangers of smokeless tobacco.

CHAPTER 9. PERIODICALS AND NEWS ON ORAL CANCER

Overview

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

News Services and Press Releases

One of the simplest ways of tracking press releases on oral cancer is to search the news wires. In the following sample of sources, we will briefly describe how to access each service. These services only post recent news intended for public viewing.

PR Newswire

To access the PR Newswire archive, simply go to **http://www.prnewswire.com/**. Select your country. Type "oral cancer" (or synonyms) into the search box. You will automatically receive information on relevant news releases posted within the last 30 days. The search results are shown by order of relevance.

Reuters Health

The Reuters' Medical News and Health eLine databases can be very useful in exploring news archives relating to oral cancer. While some of the listed articles are free to view, others are available for purchase for a nominal fee. To access this archive, go to **http://www.reutershealth.com/en/index.html** and search by "oral cancer" (or synonyms). The following was recently listed in this archive for oral cancer:

- **Bayer, Onyx report phase I data on oral cancer drug**
  Source: Reuters Industry Breifing
  Date: May 21, 2002
- **Gene therapy slows oral cancer in mice**
  Source: Reuters Health eLine
  Date: December 31, 2001

- **Bipartisan bill calls for Medicare to cover oral cancer drugs**
  Source: Reuters Medical News
  Date: May 17, 2001
- **Bill calls for Medicare to cover oral cancer drugs**
  Source: Reuters Health eLine
  Date: May 17, 2001
- **Multiphasic screening worthwhile for early diagnosis of oral cancer**
  Source: Reuters Medical News
  Date: February 28, 2001
- **Oral sex shown to be linked to mouth cancer**
  Source: Reuters Health eLine
  Date: February 25, 2004
- **Iressa may help combat oral cancer**
  Source: Reuters Health eLine
  Date: January 02, 2004
- **Gefitinib shows multifaceted action against oral cancer**
  Source: Reuters Industry Breifing
  Date: January 02, 2004
- **Human papillomavirus tied to oral cancer**
  Source: Reuters Health eLine
  Date: December 10, 2003
- **Findings tie gum disease to mouth cancer**
  Source: Reuters Health eLine
  Date: March 20, 2003
- **Periodontal disease linked with oral cancer**
  Source: Reuters Medical News
  Date: March 17, 2003
- **Arthritis drugs studied to prevent oral cancer**
  Source: Reuters Health eLine
  Date: November 21, 2002
- **Oral cancer vaccine blocks tumor spread in mice**
  Source: Reuters Health eLine
  Date: November 04, 2002
- **IL-2 improves postoperative survival in oral cancer patients**
  Source: Reuters Medical News
  Date: August 01, 2002
- **Healthy diet linked to lower risk of oral cancer**
  Source: Reuters Health eLine
  Date: July 04, 2002
- **Nuclear receptor ligand inhibits oral cancer cell growth**
  Source: Reuters Medical News
  Date: August 02, 2000
- **HSP70 inhibition blocks oral cancer cell proliferation**
  Source: Reuters Medical News
  Date: January 05, 2000

- **Buffalo team retracts hypothesis of link between hydrogen peroxide, oral cancer**
  Source: Reuters Medical News
  Date: March 23, 1999
- **FDA panel votes against approval of Zila's OraTest for mouth cancer**
  Source: Reuters Medical News
  Date: January 14, 1999
- **HPV type 16 linked to some oral cancers, but smoking remains major factor**
  Source: Reuters Medical News
  Date: November 04, 1998
- **Zila's Oral Cancer Test Approved In Several European Countries**
  Source: Reuters Medical News
  Date: April 14, 1998
- **Cigars' Uncool Risk: Oral Cancer**
  Source: Reuters Health eLine
  Date: April 22, 1997
- **Oral Lichen Planus Linked To Risk Of Oral Cancer**
  Source: Reuters Medical News
  Date: January 27, 1997
- **Consensus Conferees Launch Oral Cancer Awareness Campaign**
  Source: Reuters Medical News
  Date: August 12, 1996
- **Zila's Oral Cancer Diagnostic Highly Sensitive**
  Source: Reuters Medical News
  Date: April 23, 1996
- **Court Affirms Zila's Rights To Oral Cancer Diagnostic**
  Source: Reuters Medical News
  Date: April 03, 1996
- **Zila And Procter Gamble Sign Agreement On New Oral Cancer Test**
  Source: Reuters Medical News
  Date: February 02, 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 "oral cancer" (or synonyms) into the search box, and click on "Search News." As this service is technology oriented, you may wish to use it when searching for press releases covering diagnostic procedures or tests.

Search Engines

Medical news is also available in the news sections of commercial Internet search engines. See the health news page at Yahoo (**http://dir.yahoo.com/Health/News_and_Media/**), or you can use this Web site's general news search page at **http://news.yahoo.com/**. Type in "oral cancer" (or synonyms). If you know the name of a company that is relevant to oral cancer, you can go to any stock trading Web site (such as **http://www.etrade.com/**) and search for the company name there. News items across various news sources are reported on indicated hyperlinks. Google offers a similar service at **http://news.google.com/**.

BBC

Covering news from a more European perspective, the British Broadcasting Corporation (BBC) allows the public free access to their news archive located at **http://www.bbc.co.uk/**. Search by "oral cancer" (or synonyms).

Newsletter Articles

Use the Combined Health Information Database, and limit your search criteria to "newsletter articles." Again, you will need to use the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter Article." Type "oral cancer" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months. The following is a typical result when searching for newsletter articles on oral cancer:

- **Oral Cancer Overview**

  Source: News from SPOHNC. News from Support for People with Oral and Head and Neck Cancer, Inc. 12(7): 1-3. April 2003.

  Contact: Available from Support for People with Oral and Head and Neck Cancer, Inc. (SPOHNC). P.O. Box 53, Locust Valley, NY 11560-0053. (800) 377-0928 or (516) 759-5333. E-mail: info@spohnc.org. Website: www.spohnc.org.

  Summary: Cancers of the head and neck region, aside from skin cancer, are predominantly **oral cancer,** specifically squamous cell carcinoma (SCC). This article provides an overview of **oral cancer,** defining the oral cavity as including the lips,

buccal (cheek side) mucosa, anterior two-thirds of the tongue, floor of the mouth, hard palate, and gum tissues (gingiva) in both the upper and lower jaws. The author discusses incidence, etiology (cause), clinical presentation or symptoms, and treatment. The author notes that the mainstay of **oral cancer** treatment remains complete surgical excision with adequate margins of resection in order to achieve local control of disease. The author discusses staging or classification, including whether or not there is evidence of enlarged lymph nodes in the neck, usually on the same side where the **oral cancer** is located. Management of reconstruction and rehabilitation of any surgically created deficits is crucial as many individuals with **oral cancer** face significant functional as well as psychological problems associated with the diagnosis and treatment of their cancer. The author also discusses the acute and long term complications of radiation therapy in oral and head and neck cancer management.

- **Oral Cancer Revisited: Rates and Risk Factors**

  Source: Oral Care Report. 9(2): 1-3, 5. 1999.

  Contact: Available from Oral Care Report. Dr. Chester W. Douglass, Department of Oral Health Policy, Harvard School of Dental Medicine, 188 Longwood Avenue, Boston, MA 02115. Website: www.colgate.com.

  Summary: This article, from a continuing education newsletter produced by Colgate, offers statistics and other information about **oral cancer** rates and risk factors. **Oral cancer** ranks as the fourth most frequent cancer among men, and eighth for women, with its incidence varying broadly from one geographical region to another. The incidence of **oral cancer** is associated with increasing age, although racial differences have also been reported. The article discusses specific risk factors, including age, smoking and alcohol, loss of teeth, genetics, and human papillomavirus and concludes with a discussion of the role of the dental care provider in reducing risk factors. If they are aware of the risk factors for **oral cancer,** dental care providers are in a position to identify those patients who are most at risk, provide a thorough examination, and biopsy or refer any suspicious lesions. Most important, the course of action for preventing **oral cancer** depends on patient education. 2 tables. 17 references.

- **New Oral Cancer Scanner May Help Save Lives, Study Says**

  Source: Midwestern Dentist. 76(1): 20. January 2000.

  Contact: Available from Greater Kansas City Dental Society. 5907 Raytown Trafficway, Kansas City, MO 64133. (816) 737-5353.

  Summary: This brief article familiarizes dentists with a new technique for the early detection of precancerous and cancerous mouth lesions. This computer assisted analysis of oral tissues is highly effective and could have a dramatic impact on reducing **oral cancer** deaths. The article notes that a study was undertaken to compare results of the computer assisted image analysis with those of scalpel biopsy of suspicious oral lesions, as well as using the computer assisted analysis on oral lesions that appeared benign clinically. In 945 patients, computer assisted analysis independently detected every case of histologically confirmed oral dysplasia and carcinoma. Also in the study, 4.5 percent of clinically benign appearing lesions that would not have received additional testing or attention other than a clinical follow up, were identified through the computer assisted analysis as dysplasia or carcinoma. The results of this study demonstrate that this type of testing can be reliably used on oral lesions with tissue abnormalities.

Academic Periodicals covering Oral Cancer

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to oral cancer. In addition to these sources, you can search for articles covering oral cancer that have been published by any of the periodicals listed in previous chapters. To find the latest studies published, go to **http://www.ncbi.nlm.nih.gov/pubmed**, type the name of the periodical into the search box, and click "Go."

If you want complete details about the historical contents of a journal, you can also visit the following Web site: **http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi**. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At **http://locatorplus.gov/**, you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search."

APPENDICES

APPENDIX A. PHYSICIAN RESOURCES

Overview

In this chapter, we focus on databases and Internet-based guidelines and information resources created or written for a professional audience.

NIH Guidelines

Commonly referred to as "clinical" or "professional" guidelines, the National Institutes of Health publish physician guidelines for the most common diseases. Publications are available at the following by relevant Institute[11]:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://www.cancer.gov/cancerinfo/list.aspx?viewid=5f35036e-5497-4d86-8c2c-714a9f7c8d25**
- National Eye Institute (NEI); guidelines available at **http://www.nei.nih.gov/order/index.htm**
- National Heart, Lung, and Blood Institute (NHLBI); guidelines available at **http://www.nhlbi.nih.gov/guidelines/index.htm**
- National Human Genome Research Institute (NHGRI); research available at **http://www.genome.gov/page.cfm?pageID=10000375**
- National Institute on Aging (NIA); guidelines available at **http://www.nia.nih.gov/health/**

[11] These publications are typically written by one or more of the various NIH Institutes.

- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at **http://www.niaaa.nih.gov/publications/publications.htm**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); fact sheets and guidelines available at **http://www.niams.nih.gov/hi/index.htm**
- National Institute of Child Health and Human Development (NICHD); guidelines available at **http://www.nichd.nih.gov/publications/pubskey.cfm**
- National Institute on Deafness and Other Communication Disorders (NIDCD); fact sheets and guidelines at **http://www.nidcd.nih.gov/health/**
- National Institute of Dental and Craniofacial Research (NIDCR); guidelines available at **http://www.nidr.nih.gov/health/**
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); guidelines available at **http://www.niddk.nih.gov/health/health.htm**
- National Institute on Drug Abuse (NIDA); guidelines available at **http://www.nida.nih.gov/DrugAbuse.html**
- National Institute of Environmental Health Sciences (NIEHS); environmental health information available at **http://www.niehs.nih.gov/external/facts.htm**
- National Institute of Mental Health (NIMH); guidelines available at **http://www.nimh.nih.gov/practitioners/index.cfm**
- National Institute of Neurological Disorders and Stroke (NINDS); neurological disorder information pages available at **http://www.ninds.nih.gov/health_and_medical/disorder_index.htm**
- National Institute of Nursing Research (NINR); publications on selected illnesses at **http://www.nih.gov/ninr/news-info/publications.html**
- National Institute of Biomedical Imaging and Bioengineering; general information at **http://grants.nih.gov/grants/becon/becon_info.htm**
- Center for Information Technology (CIT); referrals to other agencies based on keyword searches available at **http://kb.nih.gov/www_query_main.asp**
- National Center for Complementary and Alternative Medicine (NCCAM); health information available at **http://nccam.nih.gov/health/**
- National Center for Research Resources (NCRR); various information directories available at **http://www.ncrr.nih.gov/publications.asp**
- Office of Rare Diseases; various fact sheets available at **http://rarediseases.info.nih.gov/html/resources/rep_pubs.html**
- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/publications.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[12] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[13]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[12] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[13] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

The NLM Gateway[14]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing one-stop searching for many of NLM's information resources or databases.[15] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "oral cancer" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

Results Summary

Category	Items Found
Journal Articles	35717
Books / Periodicals / Audio Visual	280
Consumer Health	1033
Meeting Abstracts	4
Other Collections	63
Total	37097

HSTAT[16]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[17] These documents include clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[18] Simply search by "oral cancer" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

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

[15] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

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

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

[18] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services' *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

Coffee Break: Tutorials for Biologists[19]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[20] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[21] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

The Genome Project and Oral Cancer

In the following section, we will discuss databases and references which relate to the Genome Project and oral cancer.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[22] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

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

[20] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[21] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

[22] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "oral cancer" (or synonyms) into the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. In particular, the option "Database Links" will search across technical databases that offer an abundance of information. The following is an example of the results you can obtain from the OMIM for oral cancer:

- **Oral Cancer Overexpressed Gene 1**
  Web site: http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=607224

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by system of the body. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to revisit it from time to time. The following systems and associated disorders are addressed:

- **Cancer:** Uncontrolled cell division.
  Examples: Breast and ovarian cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Cancer.html**

- **Immune System:** Fights invaders.
  Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe combined immunodeficiency.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Immune.html**

- **Metabolism:** Food and energy.
  Examples: Adreno-leukodystrophy, atherosclerosis, Best disease, Gaucher disease, glucose galactose malabsorption, gyrate atrophy, juvenile-onset diabetes, obesity, paroxysmal nocturnal hemoglobinuria, phenylketonuria, Refsum disease, Tangier disease, Tay-Sachs disease.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Metabolism.html**

- **Muscle and Bone:** Movement and growth.
  Examples: Duchenne muscular dystrophy, Ellis-van Creveld syndrome, Marfan syndrome, myotonic dystrophy, spinal muscular atrophy.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Muscle.html**

- **Nervous System:** Mind and body.
  Examples: Alzheimer disease, amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease, Prader-Willi syndrome, Rett syndrome, spinocerebellar atrophy, Williams syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Brain.html**

- **Signals:** Cellular messages.
  Examples: Ataxia telangiectasia, Cockayne syndrome, glaucoma, male-patterned baldness, SRY: sex determination, tuberous sclerosis, Waardenburg syndrome, Werner syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Signals.html**
- **Transporters:** Pumps and channels.
  Examples: Cystic fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Transporters.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**
- **Nucleotide Sequence Database (Genbank):**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide**
- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**
- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**
- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Taxonomy:** Organisms in GenBank,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome**, and then

select the database that you would like to search. The databases available are listed in the drop box next to "Search." Enter "oral cancer" (or synonyms) into the search box and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[23]

This online resource has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually limited or completely omitted in existing reference sources due to space limitations of the printed form.

At **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html**, you can search across syndromes using an alphabetical index**.** Search by keywords at **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

The Genome Database[24]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "oral cancer" (or synonyms) into the search box, and review the results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms).

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[23] Adapted from the National Library of Medicine: **http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html**.

[24] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html - mission**.

APPENDIX B. PATIENT RESOURCES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines written with the patient in mind. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. Since new guidelines on oral cancer can appear at any moment and be published by a number of sources, the best approach to finding guidelines is to systematically scan the Internet-based services that post them.

Patient Guideline Sources

The remainder of this chapter directs you to sources which either publish or can help you find additional guidelines on topics related to oral cancer. Due to space limitations, these sources are listed in a concise manner. Do not hesitate to consult the following sources by either using the Internet hyperlink provided, or, in cases where the contact information is provided, contacting the publisher or author directly.

The National Institutes of Health

The NIH gateway to patients is located at **http://health.nih.gov/**. From this site, you can search across various sources and institutes, a number of which are summarized below.

Topic Pages: MEDLINEplus

The National Library of Medicine has created a vast and patient-oriented healthcare information portal called MEDLINEplus. Within this Internet-based system are "health topic pages" which list links to available materials relevant to oral cancer. To access this system, log on to **http://www.nlm.nih.gov/medlineplus/healthtopics.html**. From there you can either search using the alphabetical index or browse by broad topic areas. Recently, MEDLINEplus listed the following when searched for "oral cancer":

Breast Cancer
http://www.nlm.nih.gov/medlineplus/breastcancer.html

Cancer
http://www.nlm.nih.gov/medlineplus/cancer.html

Dental Health
http://www.nlm.nih.gov/medlineplus/dentalhealth.html

Head and Neck Cancer
http://www.nlm.nih.gov/medlineplus/headandneckcancer.html

Mouth Disorders
http://www.nlm.nih.gov/medlineplus/mouthdisorders.html

Oral Cancer
http://www.nlm.nih.gov/medlineplus/oralcancer.html

Ovarian Cancer
http://www.nlm.nih.gov/medlineplus/ovariancancer.html

Salivary Gland Disorders
http://www.nlm.nih.gov/medlineplus/salivaryglanddisorders.html

Within the health topic page dedicated to oral cancer, the following was listed:

- General/Overviews

  Oral Cancer Facts
  Source: Oral Cancer Foundation
  http://www.oralcancerfoundation.org/facts/index.htm

  What Is Oral Cavity and Oropharyngeal Cancer?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_1x_what_is_oral_cavity_and_oropharyngeal_cancer_60.asp?sitearea=cri

- Diagnosis/Symptoms

  Can Oral Cavity and Oropharyngeal Cancer Be Found Early?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_3x_can_oral_cavity_and_oropharyngeal_cancer_be_found_early_60.asp?sitearea=cri

  How Is Oral Cavity and Oropharyngeal Cancer Diagnosed?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_3x_how_is_oral_cavity_and_oropharyngeal_cancer_diagnosed_60.asp?sitearea=cri

  How Is Oral Cavity and Oropharyngeal Cancer Staged?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_3x_how_is_oral_cavity_and_oropharyngeal_cancer_staged_60.asp?sitearea=cri

  Mouth Problems
  Source: American Academy of Family Physicians
  http://familydoctor.org/509.xml

- Treatment

  Lip and Oral Cavity Cancer (PDQ): Treatment
  Source: National Cancer Institute
  http://www.cancer.gov/cancerinfo/pdq/treatment/lip-and-oral-cavity/patient/

  Treatment Options by Stage (Oral Cavity and Oropharyngeal Cancer)
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_4x_treatment_options_by_stage_60.asp?sitearea=cri

  What Should You Ask Your Doctor about Oral Cavity and Oropharyngeal Cancer?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_5x_what_should_you_ask_your_physician_about_oral_cavity_and_oropharyngeal_cancer_60.asp?sitearea=cri

- Specific Conditions/Aspects

  Cigarette Smoking and Cancer: Questions and Answers
  Source: National Cancer Institute
  http://cis.nci.nih.gov/fact/3_14.htm

  Head and Neck Radiation Treatment and Your Mouth
  Source: National Oral Health Information Clearinghouse
  http://www.nohic.nidcr.nih.gov/campaign/rad_bro.htm

  Questions and Answers about Cigar Smoking and Cancer
  Source: National Cancer Institute
  http://cis.nci.nih.gov/fact/3_65.htm

  Smokeless Tobacco and Cancer: Questions and Answers
  Source: National Cancer Institute
  http://cis.nci.nih.gov/fact/3_63.htm

- From the National Institutes of Health

  Oral Cancer -- Confronting the Enemy
  Source: National Institute of Dental and Craniofacial Research
  http://www.nidcr.nih.gov/Spectrum/NIDCR3/3menu.htm

  Oral Health U.S., 2002
  Source: NIDCR/CDC Dental, Oral and Craniofacial Data Resource Center
  http://drc.nidcr.nih.gov/report/index.htm

  What You Need to Know about Oral Cancer
  Source: National Cancer Institute
  http://www.cancer.gov/cancerinfo/wyntk/oral

- Latest News

  Oral Sex Shown to Be Linked to Mouth Cancer
  Source: 02/25/2004, Reuters Health
  http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_16262.html

- Organizations

  American Academy of Otolaryngology--Head and Neck Surgery
  http://www.entnet.org/

  American Association of Oral and Maxillofacial Surgeons
  http://www.aaoms.org/

  American Cancer Society
  http://www.cancer.org/

  National Cancer Institute
  http://www.cancer.gov/

  National Institute of Dental and Craniofacial Research
  http://www.nidcr.nih.gov/

  National Oral Health Information Clearinghouse
  Source: National Institute of Dental and Craniofacial Research
  http://www.nohic.nidcr.nih.gov/

  Oral Cancer Foundation
  http://www.oralcancerfoundation.org/

- Prevention/Screening

  Brush Twice a Day and See Your Dentist for Oral Cancer Screening
  Source: American Dental Association
  http://www.ada.org/public/media/releases/0210_release01.asp

  Oral Cancer (PDQ): Screening
  Source: National Cancer Institute
  http://www.cancer.gov/CancerInformation/oralscreening/patient/

  Oral Cancer: Are You at Risk?
  http://www.nohic.nidcr.nih.gov/pdfs/OralCancer.pdf

  What Are the Risk Factors for Oral Cavity and Oropharyngeal Cancer?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_2x_what_are_the_risk_factors_for_oral_cavity_and_oropharyngeal_cancer_60.asp?sitearea=ped

- Research

  What's New in Oral Cavity and Oropharyngeal Cancer Research and Treatment?
  Source: American Cancer Society
  http://www.cancer.org/docroot/cri/content/cri_2_4_6x_whats_new_in_oral_cavity_and_oropharyngeal_cancer_research_and_treatment_60.asp?sitearea=cri

- Statistics

  National Oral Health Surveillance System
  Source: Centers for Disease Control and Prevention
  http://www.cdc.gov/nohss/

Oral Cancer: Deadly to Ignore
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/OralHealth/factsheets/oc-facts.htm

Oral Health U.S., 2002
Source: NIDCR/CDC Dental, Oral and Craniofacial Data Resource Center
http://drc.nidcr.nih.gov/report/index.htm

What Are the Key Statistics about Oral Cavity and Oropharyngeal Cancer?
Source: American Cancer Society
http://www.cancer.org/docroot/cri/content/cri_2_4_1x_what_are_the_key_statistics_for_oral_cavity_and_oropharyngeal_cancer_60.asp?sitearea=cri

You may also choose to use the search utility provided by MEDLINEplus at the following Web address: **http://www.nlm.nih.gov/medlineplus/**. Simply type a keyword into the search box and click "Search." This utility is similar to the NIH search utility, with the exception that it only includes materials that are linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on oral cancer. CHID offers summaries that describe the guidelines available, including contact information and pricing. CHID's general Web site is **http://chid.nih.gov/**. To search this database, go to **http://chid.nih.gov/detail/detail.html**. In particular, you can use the advanced search options to look up pamphlets, reports, brochures, and information kits. The following was recently posted in this archive:

- **Oral Cancer: How to Protect Yourself**

  Source: JADA. Journal of the American Dental Association. 131(9): 1383. September 2000.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611.

  Summary: As with many forms of cancer, early detection of oral cancerous lesions can improve the chances of successful treatment. This handout reminds dental patients of the signs of **oral cancer** and the importance of self checking of the oral tissues. The handout recommends that readers take a few minutes to examine their lips, gums, cheek lining, and tongue, as well as the floor and roof of the mouth. Readers are advised to note any of the following: a color change in the oral tissues; a lump, thickening, rough spot, crust, or small eroded area; a sore that bleeds easily or does not heal; pain, tenderness, or numbness anywhere in the mouth or on the lips; difficulty in chewing, swallowing, speaking, or moving the jaw or tongue; changes in the voice; or a change in the way the teeth fit together. In addition, readers are advised to reduce their risk of developing **oral cancer** by avoiding behaviors including use of tobacco and prolonged exposure to the sun. Regular visits to the dentist are also important. The handout concludes with the address of the American Dental Association's website (www.ada.org). 2 figures.

- **Oral Cancer**

  Source: Bethesda, MD: U.S. Department of Health and Human Services. National Institute of Dental and Craniofacial Research (NIDCR), National Institutes of Health (NIH). 2003. [2 p.].

  Contact: National Oral Health Information Clearinghouse (NOHIC). 1 NOHIC Way, Bethesda, MD 20892-3500. (301) 402-7364. Fax (301) 907-8830. E-mail: nohic@nidcr.nih.gov. Website: www.nohic.nidcr.nih.gov. PRICE: Single copy free. Order Number NR-80.

  Summary: The term **oral cancer** includes cancers of the mouth and the pharynx, part of the throat. This brochure reviews the risk factors for **oral cancer,** the possible signs and symptoms of the disease, and early detection strategies. The brochure stresses that most **oral cancer** is preventable. Seventy-five percent of oral cancers are related to tobacco use, alcohol use, or use of both substances together. The brochure lists the symptoms of **oral cancer.** An **oral cancer** examination can detect early signs of cancer. **Oral cancer** exams are painless and quick and an appropriate part of regular dental care. The brochure provides the contact information for the National Institute of Dental and Craniofacial Research (www.nidcr.nih.gov).

- **What You Need to Know About Oral Cancer**

  Source: Bethesda, MD: National Cancer Institute (NCI). 2002. 28 p.

  Contact: Available from National Cancer Institute (NCI). Publications Ordering Service, P.O. Box 24128, Baltimore, MD 21227. Voice (800) 422-6237. TTY (800) 332-8615. Fax (301) 330-7968. PRICE: Single copy free. NIH Publication Number 97-1574. Also available from National Oral Health Information Clearinghouse (NOHIC). 1 NOHIC Way, Bethesda, MD 20892-3500. (301) 402-7364. Fax (301) 907-8830. E-mail: nohic@nidcr.nih.gov. Website: www.nohic.nidcr.nih.gov. PRICE: Single copy free; bulk orders up to 10 copies available. Order Number OP-24.

  Summary: This booklet was prepared to help patients, their families, and their friends better understand **oral cancer.** The booklet provides information on the symptoms, diagnosis, and treatment of **oral cancer** and on living with the disease. The booklet's topics include the basic anatomy of the oral cavity; definitions of cancer, and specifically **oral cancer;** early detection; symptoms of oral cancers; diagnostic and staging tests for **oral cancer;** treatment issues, including planning treatment, methods of treatment, and side effects; rehabilitation and follow-up care; adjusting to the disease; support for cancer patients; and cancer research in the areas of cause and prevention, detection and diagnosis, and treatment. The brochure concludes with a glossary, an annotated list of resources, and a list of NCI booklets.

- **Lip and Mouth Cancer Self-Examination: The Look That Can Save a Life**

  Source: Rosemont, IL: American Association of Oral and Maxillofacial Surgeons. 1990. [2 p.]. Surgeons (AAOMS). Publications, P.O. Box 4229, Lisle, IL 60532. (800) 366-6725; Fax (630) 241-9805; http://www.aaoms.org. PRICE: Single copy free; bulk rates available.

  Contact: Available from American Association of Oral and Maxillofacial Surgeons. 9700 Bryn Mawr Avenue, Rosemont, IL 60018. (800) 467-5268 or (708) 678-6200. PRICE: Single copy free; $20.00 per 100.

  Summary: This brief patient education brochure discusses the importance of self-examination in the detection of **oral cancer.** Topics covered include why an oral self-

examination is important, things to look for when performing an **oral cancer** self-examination, the steps to completing an **oral cancer** examination, how early detection and treatment lead to a better chance of cure, and factors that may cause cancer.

- **Self-Examination Guide for Early Oral Cancer Detection**

  Source: Oklahoma City, OK: Oklahoma State Department of Health. 199x. 2 p.

  Contact: Available from Oklahoma State Department of Health. Film and Publications Division, 1000 Northeast Tenth Street, P.O. Box 53551, Oklahoma City, OK 73152. PRICE: Single copy free; bulk quantities free.

  Summary: This brochure explains how to perform a self-examination for early **oral cancer** detection. These self-examinations are recommended monthly, especially for tobacco users, and can lead to early detection and simpler, more successful treatment. Topics covered include preparing for the self-examination, what to look for, doing a facial exam, examining the lips, checking the cheeks and gums, examining the tongue, inspecting the roof of the mouth, checking the floor of the mouth, and what to do if a warning sign appears. Black-and-white photographs depict a model performing each step of the self-examination.

- **Having an oral cancer exam**

  Source: Baltimore, MD: Office of Oral Health, Maryland Department of Health and Mental Hygiene. 2002. 4 pp.

  Contact: Available from Maryland Department of Health and Mental Hygiene, Office of Oral Health, 201 West Preston Street, Baltimore, MD 21201. Telephone: (410) 767-5688 / e-mail: oralhealth@dhmh.state.md.us / Web site: http://www.mdpublichealth.org/oralhealth. Available at no charge.

  Summary: This brochure for consumers defines and describes **oral cancer,** explains the exam procedure, and discusses the causes and early signs or **oral cancer.**

- **On the Tobacco Front.Oral Cancer Facts**

  Source: AAOM News. 3(1): [1 p. insert]. Spring 2002.

  Contact: Available from American Academy of Oral Medicine (AAOM). Editor, AAOM News, 193 Somerset Road, Norwood, NJ 07648-1929. E-mail: amichaelk@juno.com.

  Summary: This fact sheet offers a series of **oral cancer** facts, designed for dentists and for dentists to share with their patients. Topics include the incidence and prevalence of **oral cancer,** age factors, risk factors, prognosis, mortality, morbidity, symptoms, the different types of **oral cancer,** lifestyle factors, and screening for **oral cancer** as part of the dental examination. The fact sheet concludes that the oral medicine professional community has a significant clinical impact on the diagnosis, prevention, treatment, and rehabilitation of **oral cancer.** The dentist has the primary responsibility to screen for **oral cancer.** As advocates of health promotion, dentists can educate patients on **oral cancer** risk factors and can advocate tobacco cessation, moderate alcohol consumption, sunlight avoidance protection, and a healthy diet and lifestyle.

- **Oral cancer: Deadly to ignore**

  Source: Sacramento, CA: Maternal and Child Health Branch, California Department of Health Services. 2000. 2 pp.

Contact: Available from Andrea Azevedo, California Department of Health Services, Maternal and Child Health Branch, 714 P Street, Room 750, Sacramento, CA 95814. Telephone: (916) 654-9927 / fax: (916) 657- 3069. Available at no charge.

Summary: This fact sheet on **oral cancer** presents data collected during the California Behavioral Risk Factor Surveillance System (BRFSS). It also explains the methodology of the BRFSS.

- **Oral health: Self exam for oral cancer**

  Source: [Richmond, VA]: Division of Dental Health, Virginia Department of Health. n. d. 4 pp.

  Contact: Available from Virginia Department of Health, Division of Dental Health, 1500 East Main Street, Room 136, Richmond, VA 23219. Telephone: (804) 786-3556 / fax: (804) 371-4004 / Web site: http://www.vahealth.org/teeth/index.htm. Available at no charge.

  Summary: This illustrated brochure provides step-by-step instructions for self-exam for **oral cancer.** Warning signs and risk factors are also provided. The brochure is also available in Spanish.

- **Detecting Oral Cancer: A Slide Program for Health Care Professionals**

  Source: Bethesda, MD: National Oral Health Information Clearinghouse (NOHIC), National Institute of Dental and Craniofacial Research (NIDCR), National Institutes of Health (NIH). 1997. (instructional kit).

  Contact: Available from National Oral Health Information Clearinghouse (NOHIC). 1 NOHIC Way, Bethesda, MD 20892-3500. (301) 402-7364. Fax (301) 907-8830. E-mail: nohic@nidcr.nih.gov. Website: www.nohic.nidcr.nih.gov. PRICE: $24.00 for orders in the United States; $57.00 for orders in Canada or Latin America; $97.00 for orders in Europe. Order Number OP-38.

  Summary: This instructional kit is designed as an education tool for health care professionals. The kit includes a set of 28 color slides that provide step by step instruction on how to perform an oral examination and that illustrate oral lesions that are suspicious for **oral cancer.** An accompanying text introduces each slide. The kit also offers samples of a variety of instructional materials. A poster includes the same illustrations and information contained in the slide program and can be used as a clinical reference. A patient education brochure provides an overview of the detection, treatment, and follow-up care for **oral cancer,** along with information on causes and prevention. A literature search (bibliography) on **oral cancer** from the Oral Health Database is also included. This search lists and abstracts patient education materials as well as journal articles and other materials for further reading. The packet also includes an order form with which readers can request additional copies of the poster and patient education materials. All materials in the packet, including the slides, may be reproduced. The kit is packaged in a folder; the slides are in three-hole punched slide pockets.

- **Facts About Oral Cancer**

  Source: Rockville, MD: Consumer Affairs Division, American Speech-Language-Hearing Association. 199x. 2 p.

Contact: Available from American Speech-Language-Hearing Association. Consumer Affairs Division, 10801 Rockville Pike, Rockville, MD 20852. (800) 638-8255. PRICE: Single copy free; $7.00 for 100 copies; bulk orders available.

Summary: This issue of the Let's Talk series focuses on **oral cancer. Oral cancer** is defined as a malignant growth that affects any part of the oral cavity, including the lips, upper or lower jaw, tongue, gums, cheeks, and throat. Topics covered include the causes, incidence, warning signs, early detection, and medical treatment of **oral cancer;** the effects of **oral cancer** on speech and swallowing; and the role of the speech language pathologist in the evaluation and treatment of persons with **oral cancer.**

- **Oral Cancer Exam**

  Source: Bethesda, MD: U.S. Department of Health and Human Services. National Institute of Dental and Craniofacial Research (NIDCR), National Institutes of Health (NIH). 2003. [2 p.].

  Contact: National Oral Health Information Clearinghouse (NOHIC). 1 NOHIC Way, Bethesda, MD 20892-3500. (301) 402-7364. Fax (301) 907-8830. E-mail: nohic@nidcr.nih.gov. Website: www.nohic.nidcr.nih.gov. PRICE: Single copy free. Order Number NR-81.

  Summary: This pocket brochure reviews the eight steps of the recommended **oral cancer** exam. The brochure notes that an **oral cancer** exam is painless and quick, and can be accomplished most effectively as part of a regular dental checkup. The eight steps include: preparing for the exam; the inspection of the face, neck, lips and mouth; the palpation of the area under the jaw and the side of the neck; the inspection and palpation of the insides of the lips and cheeks; the inspection of the tongue for swelling or abnormal color or texture; the inspection of the sides and underneath of the tongue; the inspection of the palate and back of the throat; and the palpation of the floor of the mouth. Clever, colorful graphics are used in the brochure. The contact information for the National Institute of Dental and Craniofacial Research is provided (www.nidcr.nih.gov).

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http://www.guideline.gov/** by using the keyword "oral cancer" (or synonyms). The following was recently posted:

- **(1) Best practice evidence-based guideline for the appropriate prescribing of hormone replacement therapy. (2) Guideline update: hormone replacement therapy**

  Source: Effective Practice Institute, University of Auckland - Academic Institution; 2001 May (revised information released on 2002 September 30); 185 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3107&nbr=2333&string=oral+AND+cancer

- **(1) Measles, mumps, and rubella: vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps. Recommendations of the Advisory Committee on Immunization Practices (ACIP)**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1998 May 22; 45 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2378&nbr=1604&string=oral+AND+cancer

- **2001 consensus guidelines for the management of women with cervical cytological abnormalities**

  Source: American Society for Colposcopy and Cervical Pathology - Medical Specialty Society; 2002 April 24; 10 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3286&nbr=2512&string=oral+AND+cancer

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

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

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

- **2002 update of recommendations for the use of chemotherapy and radiotherapy protectants: clinical practice guidelines of the American Society of Clinical Oncology**

  Source: American Society of Clinical Oncology - Medical Specialty Society; 1999 October (revised 2002 Jun); 9 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3348&nbr=2574&string=oral+AND+cancer

- **AACE medical guidelines for clinical practice for management of menopause**

  Source: American Association of Clinical Endocrinologists - Medical Specialty Society; 1999 Nov-December; 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2138&nbr=1364&string=oral+AND+cancer

- **AACE medical guidelines for clinical practice for the diagnosis and treatment of hyperandrogenic disorders**

  Source: American Association of Clinical Endocrinologists - Medical Specialty Society; 2001 Mar-April; 15 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2847&nbr=2073&string=oral+AND+cancer

- **AACE/AAES medical/surgical guidelines for clinical practice: management of thyroid carcinoma**

  Source: American Association of Clinical Endocrinologists - Medical Specialty Society; 1997 (updated 2001 May-Jun); 19 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2848&nbr=2074&string=oral+AND+cancer

- **ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on**

  Source: American College of Cardiology Foundation - Medical Specialty Society; 2000 (revised online 2002 Mar); 95 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3190&nbr=2416&string=oral+AND+cancer

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

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

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

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

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

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

- **Acute pain management**

  Source: University of Iowa Gerontological Nursing Interventions Research Center, Research Dissemination Core - Academic Institution; 1997 (revised 1999 April 6); 38 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=1888&nbr=1114&string=oral+AND+cancer

- **Acute pharyngitis**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1998 August (revised 2003 May); 27 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3873&nbr=3082&string=mouth+AND+cancer

- **Adjuvant systemic therapy for node-negative breast cancer**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 1998 November 12 (new information released online 2002 Feb); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3280&nbr=2506&string=oral+AND+cancer

- **Adjuvant therapy for stage II colon cancer following complete resection**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 1997 August 25 (updated online 2000 Apr); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3009&nbr=2235&string=oral+AND+cancer

- **Adjuvant therapy for stage III colon cancer following complete resection**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 1997 August 25 (updated online 2000 Apr); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3016&nbr=2242&string=oral+AND+cancer

- **Adult low back pain**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1994 June (revised 2002 Sep); 61 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3498&nbr=2724&string=oral+AND+cancer

- **Altered nutritional status**

  Source: American Medical Directors Association - Professional Association; 2001; 32 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3304&nbr=2530&string=mouth+AND+cancer

- **American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children--2003 update**

  Source: American Association of Clinical Endocrinologists - Medical Specialty Society; 1998 (revised 2003); 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3726&nbr=2952&string=oral+AND+cancer

- **American Cancer Society guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity**

  Source: American Cancer Society - Disease Specific Society; 2002 Mar-April; 28 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3531&nbr=2757&string=oral+AND+cancer

- **American Gastroenterological Association medical position statement on management of oropharyngeal dysphagia**

  Source: American Gastroenterological Association - Medical Specialty Society; 1998 July 24 (reviewed 2001); 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3067&nbr=2293&string=oral+AND+cancer

- **American Gastroenterological Association medical position statement on obesity**

  Source: American Gastroenterological Association - Medical Specialty Society; 2002 September; 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3490&nbr=2716&string=mouth+AND+cancer

- **American Gastroenterological Association medical position statement: celiac sprue**

  Source: American Gastroenterological Association - Medical Specialty Society; 2000 November 12 (reviewed 2001); 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3058&nbr=2284&string=oral+AND+cancer

- **American Gastroenterological Association medical position statement: evaluation and management of occult and obscure gastrointestinal bleeding**

  Source: American Gastroenterological Association - Medical Specialty Society; 1999 July 18 (reviewed 2001); 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3062&nbr=2288&string=oral+AND+cancer

- **American Gastroenterological Association medical position statement: guidelines for the evaluation and management of chronic diarrhea**

  Source: American Gastroenterological Association - Medical Specialty Society; 1998 November 8 (reviewed 2001); 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3065&nbr=2291&string=oral+AND+cancer

- **American Gastroenterological Association medical position statement: nausea and vomiting**

  Source: American Gastroenterological Association - Medical Specialty Society; 2000 May 21 (reviewed 2001); 2 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3060&nbr=2286&string=oral+AND+cancer

- **American Gastroenterological Association medical position statement: parenteral nutrition**

  Source: American Gastroenterological Association - Medical Specialty Society; 2001 May 18; 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3056&nbr=2282&string=oral+AND+cancer

- **American Society of Clinical Oncology 2003 update on the role of bisphosphonates and bone health issues in women with breast cancer**

  Source: American Society of Clinical Oncology - Medical Specialty Society; 2000 March (revised 2003 November 1); 16 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=4541&nbr=3355&string=oral+AND+cancer

- **Antithrombotic therapy for venous thromboembolic disease. In: Sixth ACCP Consensus Conference on Antithrombotic Therapy**

  Source: American College of Chest Physicians - Medical Specialty Society; 2001 January; 18 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2725&nbr=1951&string=oral+AND+cancer

- **Antithrombotic therapy in valvular heart disease. In: Sixth ACCP Consensus Conference on Antithrombotic Therapy**

  Source: American College of Chest Physicians - Medical Specialty Society; 2001 January; 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2727&nbr=1953&string=mouth+AND+cancer

- **Antithrombotic therapy. A national clinical guideline**

  Source: Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]; 1999 March; 70 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2907&nbr=2133&string=oral+AND+cancer

- **ASHP guidelines on preventing medication errors with antineoplastic agents**

  Source: American Society of Health-System Pharmacists - Professional Association; 2002 September; 21 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=4312&nbr=3267&string=oral+AND+cancer

- **ASHP therapeutic guidelines on antimicrobial prophylaxis in surgery**

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

  http://www.guideline.gov/summary/summary.aspx?doc_id=2182&nbr=1408&string=oral+AND+cancer

- **Assessment and management of acute pain**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 2000 October (revised 2002 Oct); 74 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3500&nbr=2726&string=oral+AND+cancer

- **Assessment and management of pain**

  Source: Registered Nurses Association of Ontario - Professional Association; 2002 November; 142 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3720&nbr=2946&string=oral+AND+cancer

- **Cancer pain**

  Source: Singapore Ministry of Health - National Government Agency [Non-U.S.]; 2003 March; 88 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3748&nbr=2974&string=oral+AND+cancer

- **Cervical cancer screening**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1994 September (revised 2002 Jun); 24 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3405&nbr=2631&string=oral+AND+cancer

- **Chemoprevention of breast cancer: recommendations and rationale**

  Source: United States Preventive Services Task Force - Independent Expert Panel; 2002 July; 24 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3229&nbr=2455&string=oral+AND+cancer

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

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

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

- **Chronic pain management in the long-term care setting**

  Source: American Medical Directors Association - Professional Association; 1999; 34 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2158&nbr=1384&string=oral+AND+cancer

- **Clinical practice guideline for post-deployment health evaluation and management**

  Source: Department of Defense - Federal Government Agency [U.S.]; 2000 September (revised 2001 Dec); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3223&nbr=2449&string=oral+AND+cancer

- **Clinical practice guideline for the management of postoperative pain**

  Source: Department of Defense - Federal Government Agency [U.S.]; 2001 July (revised 2002 May); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3284&nbr=2510&string=oral+AND+cancer

- **Clinical practice guideline for the management of rheumatoid arthritis**

  Source: Advanced Research Techniques in the Health Services - Private For Profit Research Organization; 2001; 170 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3683&nbr=2909&string=oral+AND+cancer

- **Clinical practice guidelines for nutrition in chronic renal failure**

  Source: National Kidney Foundation - Disease Specific Society; 2000 June; 121 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2545&nbr=1771&string=oral+AND+cancer

- **Colorectal cancer screening**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1995 May (revised 2002 Jun); 45 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3406&nbr=2632&string=mouth+AND+cancer

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

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

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

- **Community-acquired pneumonia in adults**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1999 August (revised 2002 May); 41 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3351&nbr=2577&string=oral+AND+cancer

- **Constipation in infants and children: evaluation and treatment**

  Source: North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition - Professional Association; 1999 November; 15 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3595&nbr=2821&string=oral+AND+cancer

- **Control of pain in patients with cancer. A national clinical guideline**

  Source: Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]; 2000 June; 61 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2910&nbr=2136&string=oral+AND+cancer

- **Deep venous thrombosis**

  Source: Finnish Medical Society Duodecim - Professional Association; 2001 April 30 (revised 2002 Apr 20); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3384&nbr=2610&string=oral+AND+cancer

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

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

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

- **Dyspepsia**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1998 October (revised 2003 Jan); 48 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3664&nbr=2890&string=oral+AND+cancer

- **Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy. Parts I and II**

  Source: American Urological Association, Inc. - Medical Specialty Society; 2001 April; 12 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2920&nbr=2146&string=oral+AND+cancer

- **Evidence-based guidelines for weaning and discontinuation of ventilatory support**

  Source: American Association for Respiratory Care - Professional Association; 2001 December; 21 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3214&nbr=2440&string=oral+AND+cancer

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

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

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

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

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

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

- **Guidelines for the management of heavy menstrual bleeding**

  Source: New Zealand National Health Committee - National Government Agency [Non-U.S.]; 1998

  http://www.guideline.gov/summary/summary.aspx?doc_id=2184&nbr=1410&string=oral+AND+cancer

- **Guidelines for the management of uterine fibroids**

  Source: New Zealand Guidelines Group - Private Nonprofit Organization; 1999 August; 120 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2279&nbr=1505&string=oral+AND+cancer

- **Guidelines on diagnosis and management of acute pulmonary embolism**

  Source: European Society of Cardiology - Medical Specialty Society; 2000 August; 36 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2592&nbr=1818&string=oral+AND+cancer

- **Human papillomavirus infection. Sexually transmitted diseases treatment guidelines 2002**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1993 (revised 2002 May 10); 5 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3240&nbr=2466&string=oral+AND+cancer

- **Intravenous immunoglobulin preparations**

  Source: University HealthSystem Consortium - Private Nonprofit Organization; 1999 March; 216 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=1976&nbr=1202&string=oral+AND+cancer

- **Laboratory guidelines for screening, diagnosis, and monitoring of hepatic injury**

  Source: American Association for the Study of Liver Diseases - Private Nonprofit Research Organization; 2000; 42 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3520&nbr=2746&string=oral+AND+cancer

- **Low back pain or sciatica in the primary care setting**

  Source: Department of Defense - Federal Government Agency [U.S.]; 1999 May; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=2578&nbr=1804&string=oral+AND+cancer

- **Major depression, panic disorder and generalized anxiety disorder in adults in primary care**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1996 January (revised 2002 May); 55 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3350&nbr=2576&string=oral+AND+cancer

- **Management of breastfeeding for healthy full-term infants**

  Source: Singapore Ministry of Health - National Government Agency [Non-U.S.]; 2002 December; 89 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3624&nbr=2850&string=oral+AND+cancer

- **Management of chronic kidney disease and pre-ESRD in the primary care setting**

  Source: Department of Defense - Federal Government Agency [U.S.]; 2000 November; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3099&nbr=2325&string=oral+AND+cancer

- **Management of Crohn's disease in adults**

  Source: American College of Gastroenterology - Medical Specialty Society; 2001 March; 9 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2802&nbr=2028&string=oral+AND+cancer

- **Management of ulcerative colitis**

  Source: Society for Surgery of the Alimentary Tract, Inc - Medical Specialty Society; 2000 (revised 2001); 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2967&nbr=2193&string=oral+AND+cancer

- **Management of unerupted and impacted third molar teeth. A national clinical guideline**

  Source: Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]; 2000 March; 24 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2305&nbr=1531&string=oral+AND+cancer

- **Massachusetts guidelines for adult diabetes care**

  Source: Massachusetts Department of Public Health, Bureau of Family and Community Health, Diabetes Control Program - State/Local Government Agency [U.S.]; 1999 June (revised 2001 Jun); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3429&nbr=2655&string=oral+AND+cancer

- **Mealtime difficulties for older persons: assessment and management**

  Source: The John A. Hartford Foundation Institute for Geriatric Nursing - Academic Institution; 2003; 23 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3506&nbr=2732&string=oral+AND+cancer

- **Nutrition practice guidelines for gestational diabetes mellitus**

  Source: American Dietetic Association - Professional Association; 2001 September; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3294&nbr=2520&string=oral+AND+cancer

- **Osteoporosis: prevention and treatment**

  Source: University of Michigan Health System - Academic Institution; 2002 March; 12 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3541&nbr=2767&string=oral+AND+cancer

- **Palliative treatment of cancer**

  Source: Finnish Medical Society Duodecim - Professional Association; 2001 December 27 (revised 2003 May 30); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=4374&nbr=3296&string=oral+AND+cancer

- **Parameter on periodontitis associated with systemic conditions**

  Source: American Academy of Periodontology - Professional Association; 1996 October (revised 2000 May); 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2333&nbr=1559&string=oral+AND+cancer

- **Poliomyelitis prevention in the United States**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1997 January 24 (revised 2000 May 19); 30 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2299&nbr=1525&string=oral+AND+cancer

- **Postoperative adjuvant radiotherapy and/or chemotherapy for resected stage II or III rectal cancer**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 1998 September 5 (updated online 2001 Dec); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3282&nbr=2508&string=oral+AND+cancer

- **Practice guideline for the treatment of patients with major depressive disorder**

  Source: American Psychiatric Association - Medical Specialty Society; 1993 (revised 2000); 45 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2605&nbr=1831&string=mouth+AND+cancer

- **Practice parameter: management of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology**

  Source: American Academy of Neurology - Medical Specialty Society; 2001 May; 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2818&nbr=2044&string=oral+AND+cancer

- **Practice parameters for the prevention of venous thromboembolism**

  Source: American Society of Colon and Rectal Surgeons - Medical Specialty Society; 2000 August; 11 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2593&nbr=1819&string=oral+AND+cancer

- **Practice parameters for the treatment of sigmoid diverticulitis**

  Source: American Society of Colon and Rectal Surgeons - Medical Specialty Society; 2000; 9 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2596&nbr=1822&string=oral+AND+cancer

- **Prevention of thromboembolism in spinal cord injury**

  Source: Consortium for Spinal Cord Medicine - Private Nonprofit Organization; 1997 February (updated 1999 Sep); 29 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2965&nbr=2191&string=oral+AND+cancer

- **Prevention of venous thromboembolism. In: Sixth ACCP Consensus Conference on Antithrombotic Therapy**

  Source: American College of Chest Physicians - Medical Specialty Society; 2001 January; 43 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2724&nbr=1950&string=oral+AND+cancer

- **Preventive counseling and education**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1995 May (revised 2002 Jul); 67 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3660&nbr=2886&string=oral+AND+cancer

- **Preventive health care, 1999 update: prevention of oral cancer mortality**

  Source: Canadian Task Force on Preventive Health Care - National Government Agency [Non-U.S.]; 1999; 1 page

  http://www.guideline.gov/summary/summary.aspx?doc_id=2706&nbr=1932&string=oral+AND+cancer

- **Preventive services for adults**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1995 June (revised 2002 Sep); 50 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3501&nbr=2727&string=oral+AND+cancer

- **Preventive services for children and adolescents**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1995 June (revised 2002 Sep); 32 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3502&nbr=2728&string=oral+AND+cancer

- **Procedure guideline for extended scintigraphy for differentiated thyroid cancer**

  Source: Society of Nuclear Medicine, Inc - Medical Specialty Society; 1999 February; 15 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=1363&nbr=621&string=oral+AND+cancer

- **Prophylaxis of venous thromboembolism. A national clinical guideline**

  Source: Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]; 2002 October; 47 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3485&nbr=2711&string=oral+AND+cancer

- **Prostate cancer**

  Source: National Committee on Cancer Care (Singapore) - National Government Agency [Non-U.S.]; 2000 May; 49 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2836&nbr=2062&string=oral+AND+cancer

- **Psoriasis**

  Source: Finnish Medical Society Duodecim - Professional Association; 2002 May 7; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3388&nbr=2614&string=mouth+AND+cancer

- **Recommendation for the management of stress and urge urinary incontinence in women**

  Source: University of Texas at Austin School of Nursing, Family Nurse Practitioner Program - Academic Institution; 2002 May; 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3227&nbr=2453&string=oral+AND+cancer

- **Recommendations on selected interventions to prevent dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2002 July; 5 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3287&nbr=2513&string=oral+AND+cancer

- **Rhinitis**

  Source: Institute for Clinical Systems Improvement - Private Nonprofit Organization; 1998 August (revised 2003 May); 34 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3875&nbr=3084&string=mouth+AND+cancer

- **Role of progestogen in hormone therapy for postmenopausal women: position statement of The North American Menopause Society**

  Source: The North American Menopause Society - Private Nonprofit Organization; 2003 Mar-April; 20 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3736&nbr=2962&string=oral+AND+cancer

- **Smallpox vaccination and adverse reactions. Guidance for clinicians**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2003 January 24; 29 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3597&nbr=2823&string=mouth+AND+cancer

- **Society of Nuclear Medicine procedure guideline for therapy of thyroid disease with iodine-131 (sodium iodide)**

  Source: Society of Nuclear Medicine, Inc - Medical Specialty Society; 2002 February 10; 11 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3191&nbr=2417&string=oral+AND+cancer

- **Specialty referral guidelines for cardiovascular evaluation and management**

  Source: American Healthways, Inc - Public For Profit Organization; 2002; 26 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3168&nbr=2394&string=oral+AND+cancer

- **Substance abuse treatment for persons with HIV/AIDS**

  Source: Substance Abuse and Mental Health Services Administration (U.S.) - Federal Government Agency [U.S.]; 2000; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=2544&nbr=1770&string=mouth+AND+cancer

- **Summary of policy recommendations for periodic health examinations**

  Source: American Academy of Family Physicians - Medical Specialty Society; 1996 November (revised 2003 Aug); 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=4183&nbr=3208&string=oral+AND+cancer

- **Symptomatic treatment of radiation-induced xerostomia in head and neck cancer patients**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 1998 October 15 (updated online 2002 Oct); 15 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3534&nbr=2760&string=oral+AND+cancer

- **Systemic lupus erythematosus (SLE)**

  Source: Finnish Medical Society Duodecim - Professional Association; 2001 April 30; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3390&nbr=2616&string=oral+AND+cancer

- **The role of octreotide in the management of patients with cancer**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 2003 May 7; 27 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=4260&nbr=3260&string=oral+AND+cancer

- **Thrombocytopenia**

  Source: Finnish Medical Society Duodecim - Professional Association; 2001 April 30; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3393&nbr=2619&string=oral+AND+cancer

- **Unstable chest pain**

  Source: University of Texas Medical Branch Correctional Managed Care - Academic Institution; 2001 February (revised 2002 Nov); 4 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3551&nbr=2777&string=oral+AND+cancer

- **Urinary incontinence**

  Source: American Medical Directors Association - Professional Association; 1996 (reviewed January 2001, 2002 and 2003); 16 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=1812&nbr=1038&string=oral+AND+cancer

- **Use of antibiotics in paediatric care**

  Source: Singapore Ministry of Health - National Government Agency [Non-U.S.]; 2002 March; 109 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3436&nbr=2662&string=mouth+AND+cancer

- **Use of bisphosphonates in women with breast cancer**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 1998 November 9 (revised December 2002); 23 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3705&nbr=2931&string=oral+AND+cancer

- **Use of irinotecan (CamptosarÂ®, CPT-11) combined with 5-fluorouracil and leucovorin (5FU/LV) as first-line therapy for metastatic colorectal cancer**

  Source: Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]; 2001 October 23 (updated online 2003 Feb); 20 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3763&nbr=2989&string=oral+AND+cancer

- **VHA/DOD clinical practice guideline for the management of chronic obstructive pulmonary disease.**

  Source: Department of Defense - Federal Government Agency [U.S.]; 1999 August; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=2584&nbr=1810&string=mouth+AND+cancer

- **VHA/DOD clinical practice guideline for the management of major depressive disorder in adults**

  Source: Department of Defense - Federal Government Agency [U.S.]; 1997 (updated 2000); Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=2585&nbr=1811&string=oral+AND+cancer

- **VHA/DoD clinical practice guideline for the management of substance use disorders**

  Source: Department of Defense - Federal Government Agency [U.S.]; 2001 September; Various pagings

  http://www.guideline.gov/summary/summary.aspx?doc_id=3169&nbr=2395&string=oral+AND+cancer

Healthfinder™

Healthfinder™ is sponsored by the U.S. Department of Health and Human Services and offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **Oral Cancer (PDQ®): Screening**

  Summary: This up-to-date information from the National Cancer Institute's PDQ® database is intended for use by patients.

  Source: National Cancer Institute, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=2443

- **What You Need To Know About™ Oral Cancer**

  Summary: This booklet describes symptoms, diagnosis, and treatment. It also has information about rehabilitation and about sources of support to help patients cope with oral cancer.

  Source: Cancer Information Service, National Cancer Institute

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=7126

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 oral cancer. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and patients. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

Additional Web Sources

A number of Web sites are available to the public that often link to government sites. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**

- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**
- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to oral cancer. By consulting all of associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with oral cancer.

The National Health Information Center (NHIC)

The National Health Information Center (NHIC) offers a free referral service to help people find organizations that provide information about oral cancer. For more information, see the NHIC's Web site at **http://www.health.gov/NHIC/** or contact an information specialist by calling 1-800-336-4797.

Directory of Health Organizations

The Directory of Health Organizations, provided by the National Library of Medicine Specialized Information Services, is a comprehensive source of information on associations. The Directory of Health Organizations database can be accessed via the Internet at **http://www.sis.nlm.nih.gov/Dir/DirMain.html**. It is composed of two parts: DIRLINE and Health Hotlines.

The DIRLINE database comprises some 10,000 records of organizations, research centers, and government institutes and associations that primarily focus on health and biomedicine. To access DIRLINE directly, go to the following Web site: **http://dirline.nlm.nih.gov/**. Simply type in "oral cancer" (or a synonym), and you will receive information on all relevant organizations listed in the database.

Health Hotlines directs you to toll-free numbers to over 300 organizations. You can access this database directly at **http://www.sis.nlm.nih.gov/hotlines/**. On this page, you are given the option to search by keyword or by browsing the subject list. When you have received your search results, click on the name of the organization for its description and contact information.

The Combined Health Information Database

Another comprehensive source of information on healthcare associations is the Combined Health Information Database. Using the "Detailed Search" option, you will need to limit

your search to "Organizations" and "oral cancer". Type the following hyperlink into your Web browser: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Then, select your preferred language and the format option "Organization Resource Sheet." Type "oral cancer" (or synonyms) into the "For these words:" box. You should check back periodically with this database since it is updated every three months.

The National Organization for Rare Disorders, Inc.

The National Organization for Rare Disorders, Inc. has prepared a Web site that provides, at no charge, lists of associations organized by health topic. You can access this database at the following Web site: **http://www.rarediseases.org/search/orgsearch.html**. Type "oral cancer" (or a synonym) into the search box, and click "Submit Query."

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Your local public library and medical libraries have interlibrary loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[25]

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

[25] 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)[26]:

- **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/**

[26] 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 oral cancer:

- **Basic Guidelines for Oral Cancer**

  Oral cancer
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001035.htm

- **Signs & Symptoms for Oral Cancer**

  Abnormal taste
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003050.htm

  Mouth sores
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003059.htm

  Skin lesion
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003220.htm

  Speech difficulties
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003204.htm

Stress
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003211.htm

Swallowing difficulties
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003115.htm

Swallowing difficulty
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003115.htm

Tongue problems
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003047.htm

- **Diagnostics and Tests for Oral Cancer**

Biopsy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003416.htm

Gum biopsy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003852.htm

Tongue biopsy
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003849.htm

Ulcer
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003225.htm

- **Background Topics for Oral Cancer**

Alcohol use
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001944.htm

Cancer - support group
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002166.htm

Chronic
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002312.htm

Cigarettes
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001992.htm

Cigars
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002775.htm

Metastasis
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002260.htm

Oral hygiene
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001957.htm

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

Smoking
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002032.htm

Support group
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002150.htm

Surgical excision
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002305.htm

Tobacco use
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002032.htm

Online Dictionary Directories

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

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

ORAL CANCER DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Abdominal Pain: Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

Aberrant: Wandering or deviating from the usual or normal course. [EU]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

Acetaldehyde: A colorless, flammable liquid used in the manufacture of acetic acid, perfumes, and flavors. It is also an intermediate in the metabolism of alcohol. It has a general narcotic action and also causes irritation of mucous membranes. Large doses may cause death from respiratory paralysis. [NIH]

Actin: Essential component of the cell skeleton. [NIH]

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

Adaptation: 1. The adjustment of an organism to its environment, or the process by which it enhances such fitness. 2. The normal ability of the eye to adjust itself to variations in the intensity of light; the adjustment to such variations. 3. The decline in the frequency of firing of a neuron, particularly of a receptor, under conditions of constant stimulation. 4. In dentistry, (a) the proper fitting of a denture, (b) the degree of proximity and interlocking of restorative material to a tooth preparation, (c) the exact adjustment of bands to teeth. 5. In microbiology, the adjustment of bacterial physiology to a new environment. [EU]

Adenine: A purine base and a fundamental unit of adenine nucleotides. [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]

Adenovirus: A group of viruses that cause respiratory tract and eye infections. Adenoviruses used in gene therapy are altered to carry a specific tumor-fighting gene. [NIH]

Adherens Junctions: Anchoring points where the cytoskeleton of neighboring cells are connected to each other. They are composed of specialized areas of the plasma membrane where bundles of microfilaments attach to the membrane through the transmembrane linkers, cadherins, which in turn attach through their extracellular domains to cadherins in the neighboring cell membranes. In sheets of cells, they form into adhesion belts (zonula adherens) that go all the way around a cell. [NIH]

Adhesions: Pathological processes consisting of the union of the opposing surfaces of a wound. [NIH]

Adhesives: Substances that cause the adherence of two surfaces. They include glues (properly collagen-derived adhesives), mucilages, sticky pastes, gums, resins, or latex. [NIH]

Adjustment: The dynamic process wherein the thoughts, feelings, behavior, and

biophysiological mechanisms of the individual continually change to adjust to the environment. [NIH]

Adjuvant: A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

Adrenal Medulla: The inner part of the adrenal gland; it synthesizes, stores and releases catecholamines. [NIH]

Adrenergic: Activated by, characteristic of, or secreting epinephrine or substances with similar activity; the term is applied to those nerve fibres that liberate norepinephrine at a synapse when a nerve impulse passes, i.e., the sympathetic fibres. [EU]

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

Aetiology: Study of the causes of disease. [EU]

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

Agar: A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

Age Factors: Age as a constituent element or influence contributing to the production of a result. It may be applicable to the cause or the effect of a circumstance. It is used with human or animal concepts but should be differentiated from aging, a physiological process, and time factors which refers only to the passage of time. [NIH]

Age-Adjusted: Summary measures of rates of morbidity or mortality in a population using statistical procedures to remove the effect of age differences in populations that are being compared. Age is probably the most important and the most common variable in determining the risk of morbidity and mortality. [NIH]

Aggressiveness: The quality of being aggressive (= characterized by aggression; militant; enterprising; spreading with vigour; chemically active; variable and adaptable). [EU]

Agonist: In anatomy, a prime mover. In pharmacology, a drug that has affinity for and stimulates physiologic activity at cell receptors normally stimulated by naturally occurring substances. [EU]

Alcohol Dehydrogenase: An enzyme that catalyzes reversibly the final step of alcoholic fermentation by reducing an aldehyde to an alcohol. In the case of ethanol, acetaldehyde is reduced to ethanol in the presence of NADH and hydrogen. The enzyme is a zinc protein which acts on primary and secondary alcohols or hemiacetals. EC 1.1.1.1. [NIH]

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

Alimentary: Pertaining to food or nutritive material, or to the organs of digestion. [EU]

Alkaline: Having the reactions of an alkali. [EU]

Alkaloid: A member of a large group of chemicals that are made by plants and have nitrogen in them. Some alkaloids have been shown to work against cancer. [NIH]

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Allogeneic: Taken from different individuals of the same species. [NIH]

Alpha Particles: Positively charged particles composed of two protons and two neutrons, i.e., helium nuclei, emitted during disintegration of very heavy isotopes; a beam of alpha particles or an alpha ray has very strong ionizing power, but weak penetrability. [NIH]

Alpha-helix: One of the secondary element of protein. [NIH]

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

Alveoli: Tiny air sacs at the end of the bronchioles in the lungs. [NIH]

Amifostine: A phosphorothioate proposed as a radiation-protective agent. It causes splenic vasodilation and may block autonomic ganglia. [NIH]

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

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

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

Aminolevulinic Acid: A compound produced from succinyl-CoA and glycine as an intermediate in heme synthesis. [NIH]

Amino-terminal: The end of a protein or polypeptide chain that contains a free amino group (-NH2). [NIH]

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

Anal: Having to do with the anus, which is the posterior opening of the large bowel. [NIH]

Analgesic: An agent that alleviates pain without causing loss of consciousness. [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]

Anaphase: The third phase of cell division, in which the chromatids separate and migrate to opposite poles of the spindle. [NIH]

Anaphylatoxins: The family of peptides C3a, C4a, C5a, and C5a des-arginine produced in

the serum during complement activation. They produce smooth muscle contraction, mast cell histamine release, affect platelet aggregation, and act as mediators of the local inflammatory process. The order of anaphylatoxin activity from strongest to weakest is C5a, C3a, C4a, and C5a des-arginine. The latter is the so-called "classical" anaphylatoxin but shows no spasmogenic activity though it contains some chemotactic ability. [NIH]

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

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

Angina: Chest pain that originates in the heart. [NIH]

Angiogenesis: Blood vessel formation. Tumor angiogenesis is the growth of blood vessels from surrounding tissue to a solid tumor. This is caused by the release of chemicals by the tumor. [NIH]

Animal 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]

Anogenital: Pertaining to the anus and external genitals. [EU]

Anoikis: Apoptosis triggered by loss of contact with the extracellular matrix. [NIH]

Antiangiogenic: Having to do with reducing the growth of new blood vessels. [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]

Antidepressant: A drug used to treat depression. [NIH]

Antidote: A remedy for counteracting a poison. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antigen-Antibody Complex: The complex formed by the binding of antigen and antibody molecules. The deposition of large antigen-antibody complexes leading to tissue damage causes immune complex diseases. [NIH]

Antigen-presenting cell: APC. A cell that shows antigen on its surface to other cells of the immune system. This is an important part of an immune response. [NIH]

Anti-infective: An agent that so acts. [EU]

Anti-Infective Agents: Substances that prevent infectious agents or organisms from spreading or kill infectious agents in order to prevent the spread of infection. [NIH]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

Anti-Inflammatory Agents: Substances that reduce or suppress inflammation. [NIH]

Antimetabolite: A chemical that is very similar to one required in a normal biochemical reaction in cells. Antimetabolites can stop or slow down the reaction. [NIH]

Antimicrobial: Killing microorganisms, or suppressing their multiplication or growth. [EU]

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

Antineoplastic Agents: Substances that inhibit or prevent the proliferation of neoplasms. [NIH]

Antioxidants: Naturally occurring or synthetic substances that inhibit or retard the oxidation of a substance to which it is added. They counteract the harmful and damaging effects of oxidation in animal tissues. [NIH]

Antiproliferative: Counteracting a process of proliferation. [EU]

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

Anxiety: Persistent feeling of dread, apprehension, and impending disaster. [NIH]

Anxiety Disorders: Disorders in which anxiety (persistent feelings of apprehension, tension, or uneasiness) is the predominant disturbance. [NIH]

Apoptosis: One of the two mechanisms by which cell death occurs (the other being the pathological process of necrosis). Apoptosis is the mechanism responsible for the physiological deletion of cells and appears to be intrinsically programmed. It is characterized by distinctive morphologic changes in the nucleus and cytoplasm, chromatin cleavage at regularly spaced sites, and the endonucleolytic cleavage of genomic DNA (DNA fragmentation) at internucleosomal sites. This mode of cell death serves as a balance to mitosis in regulating the size of animal tissues and in mediating pathologic processes associated with tumor growth. [NIH]

Applicability: A list of the commodities to which the candidate method can be applied as presented or with minor modifications. [NIH]

Aqueous: Having to do with water. [NIH]

Arachidonic Acid: An unsaturated, essential fatty acid. It is found in animal and human fat as well as in the liver, brain, and glandular organs, and is a constituent of animal phosphatides. It is formed by the synthesis from dietary linoleic acid and is a precursor in the biosynthesis of prostaglandins, thromboxanes, and leukotrienes. [NIH]

Areca: A small genus of East Indian palms (Palmae) whose leaves and nuts yield arecoline. Its leaves and nuts have been used as masticatories, stimulants, and astringents in traditional medicine. [NIH]

Arecoline: An alkaloid obtained from the betel nut (Areca catechu), fruit of a palm tree. It is an agonist at both muscarinic and nicotinic acetycholine receptors. It is used in the form of various salts as a ganglionic stimulant, a parasympathomimetic, and a vermifuge, especially in veterinary practice. It has been used as a euphoriant in the Pacific Islands. [NIH]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Aromatic: Having a spicy odour. [EU]

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

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

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Articulation: The relationship of two bodies by means of a moveable joint. [NIH]

Aspartic: The naturally occurring substance is L-aspartic acid. One of the acidic-amino-acids is obtained by the hydrolysis of proteins. [NIH]

Aspiration: The act of inhaling. [NIH]

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

Astringent: Causing contraction, usually locally after topical application. [EU]

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

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

ATP: ATP an abbreviation for adenosine triphosphate, a compound which serves as a carrier of energy for cells. [NIH]

Atrophy: Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Attenuated: Strain with weakened or reduced virulence. [NIH]

Atypical: Irregular; not conformable to the type; in microbiology, applied specifically to strains of unusual type. [EU]

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

Autonomic: Self-controlling; functionally independent. [EU]

Back Pain: Acute or chronic pain located in the posterior regions of the trunk, including the thoracic, lumbar, sacral, or adjacent regions. [NIH]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccal, rodlike or bacillary, and spiral or spirochetal. [NIH]

Bacterial Physiology: Physiological processes and activities of bacteria. [NIH]

Bactericidal: Substance lethal to bacteria; substance capable of killing bacteria. [NIH]

Bacteriophage: A virus whose host is a bacterial cell; A virus that exclusively infects bacteria. It generally has a protein coat surrounding the genome (DNA or RNA). One of the coliphages most extensively studied is the lambda phage, which is also one of the most important. [NIH]

Basal cells: Small, round cells found in the lower part (or base) of the epidermis, the outer layer of the skin. [NIH]

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

Basal Ganglia Diseases: Diseases of the basal ganglia including the putamen; globus pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical

manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [NIH]

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

Base Sequence: The sequence of purines and pyrimidines in nucleic acids and polynucleotides. It is also called nucleotide or nucleoside sequence. [NIH]

Basement Membrane: Ubiquitous supportive tissue adjacent to epithelium and around smooth and striated muscle cells. This tissue contains intrinsic macromolecular components such as collagen, laminin, and sulfated proteoglycans. As seen by light microscopy one of its subdivisions is the basal (basement) lamina. [NIH]

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

Bile: An emulsifying agent produced in the liver and secreted into the duodenum. Its composition includes bile acids and salts, cholesterol, and electrolytes. It aids digestion of fats in the duodenum. [NIH]

Binding Sites: The reactive parts of a macromolecule that directly participate in its specific combination with another molecule. [NIH]

Bioavailability: The degree to which a drug or other substance becomes available to the target tissue after administration. [EU]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Biofilms: Films of bacteria or other microbial organisms, usually embedded in extracellular polymers such as implanted medical devices, which adhere to surfaces submerged in, or subjected to, aquatic environments (From Singleton & Sainsbury, Dictionary of Microbiology and Molecular Biology, 2d ed). Biofilms consist of multilayers of microbial cells glued together to form microbial communities which are highly resistant to both phagocytes and antibiotics. [NIH]

Biological response modifier: BRM. A substance that stimulates the body's response to infection and disease. [NIH]

Biological therapy: Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

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]

Bladder: The organ that stores urine. [NIH]

Bleomycin: A complex of related glycopeptide antibiotics from Streptomyces verticillus consisting of bleomycin A2 and B2. It inhibits DNA metabolism and is used as an antineoplastic, especially for solid tumors. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

Blood Glucose: Glucose in blood. [NIH]

Blood pressure: The pressure of blood against the walls of a blood vessel or heart chamber. Unless there is reference to another location, such as the pulmonary artery or one of the heart chambers, it refers to the pressure in the systemic arteries, as measured, for example, in the forearm. [NIH]

Blood vessel: A tube in the body through which blood circulates. Blood vessels include a network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Blot: To transfer DNA, RNA, or proteins to an immobilizing matrix such as nitrocellulose. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Body Image: Individuals' personal concept of their bodies as objects in and bound by space, independently and apart from all other objects. [NIH]

Bolus: A single dose of drug usually injected into a blood vessel over a short period of time. Also called bolus infusion. [NIH]

Bolus infusion: A single dose of drug usually injected into a blood vessel over a short period of time. Also called bolus. [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 Cells: Cells contained in the bone marrow including fat cells, stromal cells, megakaryocytes, and the immediate precursors of most blood cells. [NIH]

Boron: A trace element with the atomic symbol B, atomic number 5, and atomic weight 10.81. Boron-10, an isotope of boron, is used as a neutron absorber in boron neutron capture therapy. [NIH]

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

Bowel Movement: Body wastes passed through the rectum and anus. [NIH]

Brachytherapy: A collective term for interstitial, intracavity, and surface radiotherapy. It uses small sealed or partly-sealed sources that may be placed on or near the body surface or within a natural body cavity or implanted directly into the tissues. [NIH]

Branch: Most commonly used for branches of nerves, but applied also to other structures. [NIH]

Breakdown: A physical, metal, or nervous collapse. [NIH]

Breast Self-Examination: The inspection of one's breasts, usually for signs of disease, especially neoplastic disease. [NIH]

Bronchitis: Inflammation (swelling and reddening) of the bronchi. [NIH]

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

Buccal mucosa: The inner lining of the cheeks and lips. [NIH]

Bupropion: A unicyclic, aminoketone antidepressant. The mechanism of its therapeutic actions is not well understood, but it does appear to block dopamine uptake. The hydrochloride is available as an aid to smoking cessation treatment. [NIH]

Cadherins: A group of functionally related glycoproteins responsible for the calcium-dependent cell-to-cell adhesion mechanism. They are divided into subclasses E-, P-, and N-cadherins, which are distinct in immunological specificity and tissue distribution. They promote cell adhesion via a homophilic mechanism. These compounds play a role in the construction of tissues and of the whole animal body. [NIH]

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

Camptothecin: An alkaloid isolated from the stem wood of the Chinese tree, Camptotheca acuminata. This compound selectively inhibits the nuclear enzyme DNA topoisomerase. Several semisynthetic analogs of camptothecin have demonstrated antitumor activity. [NIH]

Cancer vaccine: A vaccine designed to prevent or treat cancer. [NIH]

Capillary: Any one of the minute vessels that connect the arterioles and venules, forming a network in nearly all parts of the body. Their walls act as semipermeable membranes for the interchange of various substances, including fluids, between the blood and tissue fluid; called also vas capillare. [EU]

Capillary Fragility: The lack of resistance, or susceptibility, of capillaries to damage or disruption under conditions of increased stress. [NIH]

Carbon Dioxide: A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carcinogen: Any substance that causes cancer. [NIH]

Carcinogenesis: The process by which normal cells are transformed into cancer cells. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

Carcinoma in Situ: A malignant tumor that has not yet invaded the basement membrane of the epithelial cell of origin and has not spread to other tissues. [NIH]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

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]

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

Catalytic Domain: The region of an enzyme that interacts with its substrate to cause the enzymatic reaction. [NIH]

Catechin: Extracted from Uncaria gambier, Acacia catechu and other plants; it stabilizes collagen and is therefore used in tanning and dyeing; it prevents capillary fragility and abnormal permeability, but was formerly used as an antidiarrheal. [NIH]

Catecholamine: A group of chemical substances manufactured by the adrenal medulla and secreted during physiological stress. [NIH]

Cathepsin E: An aspartic endopeptidase of the hydrolase class that is similar to cathepsin D but has a slightly broader specificity. EC 3.4.23.34. [NIH]

Cathepsins: A group of lysosomal proteinases or endopeptidases found in aqueous extracts of a variety of animal tissue. They function optimally within an acidic pH range. [NIH]

Cauda Equina: The lower part of the spinal cord consisting of the lumbar, sacral, and coccygeal nerve roots. [NIH]

Causal: Pertaining to a cause; directed against a cause. [EU]

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

Celecoxib: A drug that reduces pain. Celecoxib belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is being studied for cancer prevention. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Adhesion: Adherence of cells to surfaces or to other cells. [NIH]

Cell Cycle: The complex series of phenomena, occurring between the end of one cell division and the end of the next, by which cellular material is divided between daughter cells. [NIH]

Cell Death: The termination of the cell's ability to carry out vital functions such as metabolism, growth, reproduction, responsiveness, and adaptability. [NIH]

Cell Differentiation: Progressive restriction of the developmental potential and increasing specialization of function which takes place during the development of the embryo and leads to the formation of specialized cells, tissues, and organs. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell membrane: Cell membrane = plasma membrane. The structure enveloping a cell, enclosing the cytoplasm, and forming a selective permeability barrier; it consists of lipids, proteins, and some carbohydrates, the lipids thought to form a bilayer in which integral proteins are embedded to varying degrees. [EU]

Cell motility: The ability of a cell to move. [NIH]

Cell Movement: The movement of cells from one location to another. [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]

Cellular Structures: Components of a cell. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

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

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

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

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

Cetuximab: A type of monoclonal antibody being studied as an anticancer drug. Monoclonal antibodies are laboratory-produced substances that can locate and bind to cancer cells. [NIH]

Checkup: A general physical examination. [NIH]

Check-up: A general physical examination. [NIH]

Chemoprevention: The use of drugs, vitamins, or other agents to try to reduce the risk of, or delay the development or recurrence of, cancer. [NIH]

Chemopreventive: Natural or synthetic compound used to intervene in the early precancerous stages of carcinogenesis. [NIH]

Chemotactic Factors: Chemical substances that attract or repel cells or organisms. The concept denotes especially those factors released as a result of tissue injury, invasion, or immunologic activity, that attract leukocytes, macrophages, or other cells to the site of infection or insult. [NIH]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Chest Pain: Pressure, burning, or numbness in the chest. [NIH]

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

Cholinergic: Resembling acetylcholine in pharmacological action; stimulated by or releasing acetylcholine or a related compound. [EU]

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 Disease: Disease or ailment of long duration. [NIH]

Chronic Obstructive Pulmonary Disease: Collective term for chronic bronchitis and emphysema. [NIH]

Chronic renal: Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

CIS: Cancer Information Service. The CIS is the National Cancer Institute's link to the public, interpreting and explaining research findings in a clear and understandable manner, and providing personalized responses to specific questions about cancer. Access the CIS by

calling 1-800-4-CANCER, or by using the Web site at http://cis.nci.nih.gov. [NIH]

Cisplatin: An inorganic and water-soluble platinum complex. After undergoing hydrolysis, it reacts with DNA to produce both intra and interstrand crosslinks. These crosslinks appear to impair replication and transcription of DNA. The cytotoxicity of cisplatin correlates with cellular arrest in the G2 phase of the cell cycle. [NIH]

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]

Cleave: A double-stranded cut in DNA with a restriction endonuclease. [NIH]

Clinical Protocols: Precise and detailed plans for the study of a medical or biomedical problem and/or plans for a regimen of therapy. [NIH]

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

Clone: The term "clone" has acquired a new meaning. It is applied specifically to the bits of inserted foreign DNA in the hybrid molecules of the population. Each inserted segment originally resided in the DNA of a complex genome amid millions of other DNA segment. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Clot Retraction: Retraction of a clot resulting from contraction of platelet pseudopods attached to fibrin strands that is dependent on the contractile protein thrombosthenin. Used as a measure of platelet function. [NIH]

Codon: A set of three nucleotides in a protein coding sequence that specifies individual amino acids or a termination signal (codon, terminator). Most codons are universal, but some organisms do not produce the transfer RNAs (RNA, transfer) complementary to all codons. These codons are referred to as unassigned codons (codons, nonsense). [NIH]

Cofactor: A substance, microorganism or environmental factor that activates or enhances the action of another entity such as a disease-causing agent. [NIH]

Cohort Studies: Studies in which subsets of a defined population are identified. These groups may or may not be exposed to factors hypothesized to influence the probability of the occurrence of a particular disease or other outcome. Cohorts are defined populations which, as a whole, are followed in an attempt to determine distinguishing subgroup characteristics. [NIH]

Colitis: Inflammation of the colon. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in mammalian organisms. It is the main constituent of skin, connective tissue, and the organic substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

Collapse: 1. A state of extreme prostration and depression, with failure of circulation. 2. Abnormal falling in of the walls of any part of organ. [EU]

Colorectal: Having to do with the colon or the rectum. [NIH]

Colorectal Cancer: Cancer that occurs in the colon (large intestine) or the rectum (the end of the large intestine). A number of digestive diseases may increase a person's risk of colorectal

cancer, including polyposis and Zollinger-Ellison Syndrome. [NIH]

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

Comorbidity: The presence of co-existing or additional diseases with reference to an initial diagnosis or with reference to the index condition that is the subject of study. Comorbidity may affect the ability of affected individuals to function and also their survival; it may be used as a prognostic indicator for length of hospital stay, cost factors, and outcome or survival. [NIH]

Complement: A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin system) and complement regulatory proteins are known by semisystematic or trivial names. Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

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

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

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]

Confounding: Extraneous variables resulting in outcome effects that obscure or exaggerate the "true" effect of an intervention. [NIH]

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

Connective Tissue Cells: A group of cells that includes fibroblasts, cartilage cells, adipocytes, smooth muscle cells, and bone cells. [NIH]

Consciousness: Sense of awareness of self and of the environment. [NIH]

Constriction: The act of constricting. [NIH]

Consultation: A deliberation between two or more physicians concerning the diagnosis and the proper method of treatment in a case. [NIH]

Consumption: Pulmonary tuberculosis. [NIH]

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]

Contralateral: Having to do with the opposite side of the body. [NIH]

Control group: In a clinical trial, the group that does not receive the new treatment being studied. This group is compared to the group that receives the new treatment, to see if the new treatment works. [NIH]

Conventional therapy: A currently accepted and widely used treatment for a certain type of disease, based on the results of past research. Also called conventional treatment. [NIH]

Conventional treatment: A currently accepted and widely used treatment for a certain type of disease, based on the results of past research. Also called conventional therapy. [NIH]

Coordination: Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [NIH]

Cornea: The transparent part of the eye that covers the iris and the pupil and allows light to enter the inside. [NIH]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

Coronary Thrombosis: Presence of a thrombus in a coronary artery, often causing a myocardial infarction. [NIH]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Crowns: A prosthetic restoration that reproduces the entire surface anatomy of the visible natural crown of a tooth. It may be partial (covering three or more surfaces of a tooth) or complete (covering all surfaces). It is made of gold or other metal, porcelain, or resin. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Curcumin: A dye obtained from tumeric, the powdered root of Curcuma longa Linn. It is used in the preparation of curcuma paper and the detection of boron. Curcumin appears to possess a spectrum of pharmacological properties, due primarily to its inhibitory effects on metabolic enzymes. [NIH]

Cutaneous: Having to do with the skin. [NIH]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cyclin: Molecule that regulates the cell cycle. [NIH]

Cytochrome: Any electron transfer hemoprotein having a mode of action in which the transfer of a single electron is effected by a reversible valence change of the central iron atom of the heme prosthetic group between the +2 and +3 oxidation states; classified as cytochromes a in which the heme contains a formyl side chain, cytochromes b, which contain protoheme or a closely similar heme that is not covalently bound to the protein, cytochromes c in which protoheme or other heme is covalently bound to the protein, and cytochromes d in which the iron-tetrapyrrole has fewer conjugated double bonds than the hemes have. Well-known cytochromes have been numbered consecutively within groups and are designated by subscripts (beginning with no subscript), e.g. cytochromes c, c1, C2, . New cytochromes are named according to the wavelength in nanometres of the absorption maximum of the a-band of the iron (II) form in pyridine, e.g., c-555. [EU]

Cytogenetics: A branch of genetics which deals with the cytological and molecular behavior of genes and chromosomes during cell division. [NIH]

Cytokine: Small but highly potent protein that modulates the activity of many cell types, including T and B cells. [NIH]

Cytomegalovirus: A genus of the family Herpesviridae, subfamily Betaherpesvirinae, infecting the salivary glands, liver, spleen, lungs, eyes, and other organs, in which they produce characteristically enlarged cells with intranuclear inclusions. Infection with Cytomegalovirus is also seen as an opportunistic infection in AIDS. [NIH]

Cytomegalovirus Infections: Infection with Cytomegalovirus, characterized by enlarged cells bearing intranuclear inclusions. Infection may be in almost any organ, but the salivary glands are the most common site in children, as are the lungs in adults. [NIH]

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]

Cytoskeleton: The network of filaments, tubules, and interconnecting filamentous bridges which give shape, structure, and organization to the cytoplasm. [NIH]

Cytotoxic: Cell-killing. [NIH]

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

Data Collection: Systematic gathering of data for a particular purpose from various sources, including questionnaires, interviews, observation, existing records, and electronic devices. The process is usually preliminary to statistical analysis of the data. [NIH]

Databases, Bibliographic: Extensive collections, reputedly complete, of references and citations to books, articles, publications, etc., generally on a single subject or specialized subject area. Databases can operate through automated files, libraries, or computer disks. The concept should be differentiated from factual databases which is used for collections of data and facts apart from bibliographic references to them. [NIH]

Decarboxylation: The removal of a carboxyl group, usually in the form of carbon dioxide, from a chemical compound. [NIH]

Defense Mechanisms: Unconscious process used by an individual or a group of individuals in order to cope with impulses, feelings or ideas which are not acceptable at their conscious level; various types include reaction formation, projection and self reversal. [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]

Demethylation: Process that releases substantial amounts of carbon dioxide in the liver. [NIH]

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

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

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

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Dental Abutments: Natural teeth or teeth roots used as anchorage for a fixed or removable denture or other prosthesis (such as an implant) serving the same purpose. [NIH]

Dental Care: The total of dental diagnostic, preventive, and restorative services provided to meet the needs of a patient (from Illustrated Dictionary of Dentistry, 1982). [NIH]

Dental Caries: Localized destruction of the tooth surface initiated by decalcification of the enamel followed by enzymatic lysis of organic structures and leading to cavity formation. If left unchecked, the cavity may penetrate the enamel and dentin and reach the pulp. The three most prominent theories used to explain the etiology of the disase are that acids produced by bacteria lead to decalcification; that micro-organisms destroy the enamel protein; or that keratolytic micro-organisms produce chelates that lead to decalcification. [NIH]

Dental Clinics: Facilities where dental care is provided to patients. [NIH]

Dental Hygienists: Persons trained in an accredited school or dental college and licensed by the state in which they reside to provide dental prophylaxis under the direction of a licensed dentist. [NIH]

Dental implant: A small metal pin placed inside the jawbone to mimic the root of a tooth. Dental implants can be used to help anchor a false tooth or teeth, or a crown or bridge. [NIH]

Dentists: Individuals licensed to practice dentistry. [NIH]

Dentition: The teeth in the dental arch; ordinarily used to designate the natural teeth in position in their alveoli. [EU]

Dentures: An appliance used as an artificial or prosthetic replacement for missing teeth and adjacent tissues. It does not include crowns, dental abutments, nor artificial teeth. [NIH]

Depersonalization: Alteration in the perception of the self so that the usual sense of one's own reality is lost, manifested in a sense of unreality or self-estrangement, in changes of

body image, or in a feeling that one does not control his own actions and speech; seen in depersonalization disorder, schizophrenic disorders, and schizotypal personality disorder. Some do not draw a distinction between depersonalization and derealization, using depersonalization to include both. [EU]

Depolarization: The process or act of neutralizing polarity. In neurophysiology, the reversal of the resting potential in excitable cell membranes when stimulated, i.e., the tendency of the cell membrane potential to become positive with respect to the potential outside the cell. [EU]

Depressive Disorder: An affective disorder manifested by either a dysphoric mood or loss of interest or pleasure in usual activities. The mood disturbance is prominent and relatively persistent. [NIH]

Deprivation: Loss or absence of parts, organs, powers, or things that are needed. [EU]

Derealization: Is characterized by the loss of the sense of reality concerning one's surroundings. [NIH]

Dermal: Pertaining to or coming from the skin. [NIH]

DES: Diethylstilbestrol. A synthetic hormone that was prescribed from the early 1940s until 1971 to help women with complications of pregnancy. DES has been linked to an increased risk of clear cell carcinoma of the vagina in daughters of women who used DES. DES may also increase the risk of breast cancer in women who used DES. [NIH]

Desmin: An intermediate filament protein found predominantly in smooth, skeletal, and cardiac muscle cells. Localized at the Z line. MW 50,000 to 55,000 is species dependent. [NIH]

Desmosomes: Attachment bodies between cells such as in the corneal epithelium, which possibly allow tonofibrils to pass from cell to cell and which can degenerate to allow cells to migrate to cover a denuded area. [NIH]

Detoxification: Treatment designed to free an addict from his drug habit. [EU]

Deuterium: Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

Developed Countries: Countries that have reached a level of economic achievement through an increase of production, per capita income and consumption, and utilization of natural and human resources. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

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

Diagnostic Services: Organized services for the purpose of providing diagnosis to promote and maintain health. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diarrhoea: Abnormal frequency and liquidity of faecal discharges. [EU]

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 system: The organs that take in food and turn it into products that the body can use to stay healthy. Waste products the body cannot use leave the body through bowel movements. The digestive system includes the salivary glands, mouth, esophagus, stomach, liver, pancreas, gallbladder, small and large intestines, and rectum. [NIH]

Digestive tract: The organs through which food passes when food is eaten. These organs are

the mouth, esophagus, stomach, small and large intestines, and rectum. [NIH]

Dihydrotestosterone: Anabolic agent. [NIH]

Dilatation: The act of dilating. [NIH]

Dilution: A diluted or attenuated medicine; in homeopathy, the diffusion of a given quantity of a medicinal agent in ten or one hundred times the same quantity of water. [NIH]

Diploid: Having two sets of chromosomes. [NIH]

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

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

Disinfectant: An agent that disinfects; applied particularly to agents used on inanimate objects. [EU]

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]

Dissociative Disorders: Sudden temporary alterations in the normally integrative functions of consciousness. [NIH]

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]

Diverticula: Plural form of diverticulum. [NIH]

Diverticulitis: Inflammation of a diverticulum or diverticula. [NIH]

Diverticulum: A pathological condition manifested as a pouch or sac opening from a tubular or sacular organ. [NIH]

Dizziness: An imprecise term which may refer to a sense of spatial disorientation, motion of the environment, or lightheadedness. [NIH]

DNA Topoisomerase: An enzyme catalyzing ATP-independent breakage of single-stranded DNA, followed by passage and rejoining of another single-stranded DNA. This enzyme class brings about the conversion of one topological isomer of DNA into another, e.g., the relaxation of superhelical turns in DNA, the interconversion of simple and knotted rings of single-stranded DNA, and the intertwisting of single-stranded rings of complementary sequences. (From Enzyme Nomenclature, 1992) EC 5.99.1.2. [NIH]

Dopamine: An endogenous catecholamine and prominent neurotransmitter in several systems of the brain. In the synthesis of catecholamines from tyrosine, it is the immediate precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain, and important in regulating movement. A family of dopaminergic receptor subtypes mediate its action. Dopamine is used pharmacologically for its direct (beta adrenergic agonist) and indirect (adrenergic releasing) sympathomimetic effects including its actions as an inotropic agent and as a renal vasodilator. [NIH]

Dorsal: 1. Pertaining to the back or to any dorsum. 2. Denoting a position more toward the back surface than some other object of reference; same as posterior in human anatomy; superior in the anatomy of quadrupeds. [EU]

Dorsum: A plate of bone which forms the posterior boundary of the sella turcica. [NIH]

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]

Dysphagia: Difficulty in swallowing. [EU]

Dysphoric: A feeling of unpleasantness and discomfort. [NIH]

Dysplasia: Cells that look abnormal under a microscope but are not cancer. [NIH]

Dyspnea: Difficult or labored breathing. [NIH]

Dystrophy: Any disorder arising from defective or faulty nutrition, especially the muscular dystrophies. [EU]

Ectopic: Pertaining to or characterized by ectopia. [EU]

Edema: Excessive amount of watery fluid accumulated in the intercellular spaces, most commonly present in subcutaneous tissue. [NIH]

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

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

Elastin: The protein that gives flexibility to tissues. [NIH]

Electrolyte: A substance that dissociates into ions when fused or in solution, and thus becomes capable of conducting electricity; an ionic solute. [EU]

Electrons: Stable elementary particles having the smallest known negative charge, present in all elements; also called negatrons. Positively charged electrons are called positrons. The numbers, energies and arrangement of electrons around atomic nuclei determine the chemical identities of elements. Beams of electrons are called cathode rays or beta rays, the latter being a high-energy biproduct of nuclear decay. [NIH]

Emboli: 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]

Embolization: The blocking of an artery by a clot or foreign material. Embolization can be done as treatment to block the flow of blood to a tumor. [NIH]

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

Emphysema: A pathological accumulation of air in tissues or organs. [NIH]

Enamel: A very hard whitish substance which covers the dentine of the anatomical crown of a tooth. [NIH]

Encapsulated: Confined to a specific, localized area and surrounded by a thin layer of tissue. [NIH]

Endopeptidases: A subclass of peptide hydrolases. They are classified primarily by their catalytic mechanism. Specificity is used only for identification of individual enzymes. They comprise the serine endopeptidases, EC 3.4.21; cysteine endopeptidases, EC 3.4.22; aspartic endopeptidases, EC 3.4.23, metalloendopeptidases, EC 3.4.24; and a group of enzymes yet to be assigned to any of the above sub-classes, EC 3.4.99. EC 3.4.-. [NIH]

Endothelial cell: The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart. [NIH]

Endothelium: A layer of epithelium that lines the heart, blood vessels (endothelium, vascular), lymph vessels (endothelium, lymphatic), and the serous cavities of the body. [NIH]

Endothelium, Lymphatic: Unbroken cellular lining (intima) of the lymph vessels (e.g., the high endothelial lymphatic venules). It is more permeable than vascular endothelium, lacking selective absorption and functioning mainly to remove plasma proteins that have filtered through the capillaries into the tissue spaces. [NIH]

Endothelium, Vascular: Single pavement layer of cells which line the luminal surface of the entire vascular system and regulate the transport of macromolecules and blood components from interstitium to lumen; this function has been most intensively studied in the blood capillaries. [NIH]

Endotoxin: Toxin from cell walls of bacteria. [NIH]

End-stage renal: Total chronic kidney failure. When the kidneys fail, the body retains fluid and harmful wastes build up. A person with ESRD needs treatment to replace the work of the failed kidneys. [NIH]

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

Enteropeptidase: A specialized proteolytic enzyme secreted by intestinal cells. It converts trypsinogen into its active form trypsin by removing the N-terminal peptide. EC 3.4.21.9. [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]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epidermal: Pertaining to or resembling epidermis. Called also epidermic or epidermoid. [EU]

Epidermal Growth Factor: A 6 kD polypeptide growth factor initially discovered in mouse submaxillary glands. Human epidermal growth factor was originally isolated from urine based on its ability to inhibit gastric secretion and called urogastrone. epidermal growth factor exerts a wide variety of biological effects including the promotion of proliferation and differentiation of mesenchymal and epithelial cells. [NIH]

Epidermis: Nonvascular layer of the skin. It is made up, from within outward, of five layers: 1) basal layer (stratum basale epidermidis); 2) spinous layer (stratum spinosum

epidermidis); 3) granular layer (stratum granulosum epidermidis); 4) clear layer (stratum lucidum epidermidis); and 5) horny layer (stratum corneum epidermidis). [NIH]

Epidermoid carcinoma: A type of cancer in which the cells are flat and look like fish scales. Also called squamous cell carcinoma. [NIH]

Epidural: The space between the wall of the spinal canal and the covering of the spinal cord. An epidural injection is given into this space. [NIH]

Epigastric: Having to do with the upper middle area of the abdomen. [NIH]

Epinephrine: The active sympathomimetic hormone from the adrenal medulla in most species. It stimulates both the alpha- and beta- adrenergic systems, causes systemic vasoconstriction and gastrointestinal relaxation, stimulates the heart, and dilates bronchi and cerebral vessels. It is used in asthma and cardiac failure and to delay absorption of local anesthetics. [NIH]

Epithelial: Refers to the cells that line the internal and external surfaces of the body. [NIH]

Epithelial Cells: Cells that line the inner and outer surfaces of the body. [NIH]

Epithelium: One or more layers of epithelial cells, supported by the basal lamina, which covers the inner or outer surfaces of the body. [NIH]

Epitope: A molecule or portion of a molecule capable of binding to the combining site of an antibody. For every given antigenic determinant, the body can construct a variety of antibody-combining sites, some of which fit almost perfectly, and others which barely fit. [NIH]

Epoetin alfa: A colony-stimulating factor that is made in the laboratory. It increases the production of red blood cells. [NIH]

ERV: The expiratory reserve volume is the largest volume of gas that can be expired from the end-expiratory level. [NIH]

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

Erythroplakia: A reddened patch with a velvety surface found in the mouth. [NIH]

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

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

Essential Tremor: A rhythmic, involuntary, purposeless, oscillating movement resulting from the alternate contraction and relaxation of opposing groups of muscles. [NIH]

Estrogen: One of the two female sex hormones. [NIH]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Ethnic Groups: A group of people with a common cultural heritage that sets them apart from others in a variety of social relationships. [NIH]

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

Excipients: Usually inert substances added to a prescription in order to provide suitable consistency to the dosage form; a binder, matrix, base or diluent in pills, tablets, creams, salves, etc. [NIH]

Excitation: An act of irritation or stimulation or of responding to a stimulus; the addition of energy, as the excitation of a molecule by absorption of photons. [EU]

Exocrine: Secreting outwardly, via a duct. [EU]

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]

Expectorant: 1. Promoting the ejection, by spitting, of mucus or other fluids from the lungs and trachea. 2. An agent that promotes the ejection of mucus or exudate from the lungs, bronchi, and trachea; sometimes extended to all remedies that quiet cough (antitussives). [EU]

Expiratory: The volume of air which leaves the breathing organs in each expiration. [NIH]

Expiratory Reserve Volume: The extra volume of air that can be expired with maximum effort beyond the level reached at the end of a normal, quiet expiration. Common abbreviation is ERV. [NIH]

External-beam radiation: Radiation therapy that uses a machine to aim high-energy rays at the cancer. Also called external radiation. [NIH]

Extracellular: Outside a cell or cells. [EU]

Extracellular Matrix: A meshwork-like substance found within the extracellular space and in association with the basement membrane of the cell surface. It promotes cellular proliferation and provides a supporting structure to which cells or cell lysates in culture dishes adhere. [NIH]

Extracellular Matrix Proteins: Macromolecular organic compounds that contain carbon, hydrogen, oxygen, nitrogen, and usually, sulfur. These macromolecules (proteins) form an intricate meshwork in which cells are embedded to construct tissues. Variations in the relative types of macromolecules and their organization determine the type of extracellular matrix, each adapted to the functional requirements of the tissue. The two main classes of macromolecules that form the extracellular matrix are: glycosaminoglycans, usually linked to proteins (proteoglycans), and fibrous proteins (e.g., collagen, elastin, fibronectins and laminin). [NIH]

Extracellular Space: Interstitial space between cells, occupied by fluid as well as amorphous and fibrous substances. [NIH]

Extraction: The process or act of pulling or drawing out. [EU]

Extrapyramidal: Outside of the pyramidal tracts. [EU]

Eye Infections: Infection, moderate to severe, caused by bacteria, fungi, or viruses, which occurs either on the external surface of the eye or intraocularly with probable inflammation, visual impairment, or blindness. [NIH]

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

Facial Nerve: The 7th cranial nerve. The facial nerve has two parts, the larger motor root which may be called the facial nerve proper, and the smaller intermediate or sensory root. Together they provide efferent innervation to the muscles of facial expression and to the lacrimal and salivary glands, and convey afferent information for taste from the anterior two-thirds of the tongue and for touch from the external ear. [NIH]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Family Practice: A medical specialty concerned with the provision of continuing,

comprehensive primary health care for the entire family. [NIH]

Fat: Total lipids including phospholipids. [NIH]

Fatty acids: A major component of fats that are used by the body for energy and tissue development. [NIH]

Febrile: Pertaining to or characterized by fever. [EU]

Fenretinide: A synthetic retinoid that is used orally as a chemopreventive against prostate cancer and in women at risk of developing contralateral breast cancer. It is also effective as an antineoplastic agent. [NIH]

Fermentation: An enzyme-induced chemical change in organic compounds that takes place in the absence of oxygen. The change usually results in the production of ethanol or lactic acid, and the production of energy. [NIH]

Fever of Unknown Origin: Fever in which the etiology cannot be ascertained. [NIH]

Fibrin: A protein derived from fibrinogen in the presence of thrombin, which forms part of the blood clot. [NIH]

Fibrinogen: Plasma glycoprotein clotted by thrombin, composed of a dimer of three non-identical pairs of polypeptide chains (alpha, beta, gamma) held together by disulfide bonds. Fibrinogen clotting is a sol-gel change involving complex molecular arrangements: whereas fibrinogen is cleaved by thrombin to form polypeptides A and B, the proteolytic action of other enzymes yields different fibrinogen degradation products. [NIH]

Fibroblast Growth Factor: Peptide isolated from the pituitary gland and from the brain. It is a potent mitogen which stimulates growth of a variety of mesodermal cells including chondrocytes, granulosa, and endothelial cells. The peptide may be active in wound healing and animal limb regeneration. [NIH]

Fibroblasts: Connective tissue cells which secrete an extracellular matrix rich in collagen and other macromolecules. [NIH]

Fibronectin: An adhesive glycoprotein. One form circulates in plasma, acting as an opsonin; another is a cell-surface protein which mediates cellular adhesive interactions. [NIH]

Fibrosarcoma: A type of soft tissue sarcoma that begins in fibrous tissue, which holds bones, muscles, and other organs in place. [NIH]

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

Fibula: The bone of the lower leg lateral to and smaller than the tibia. In proportion to its length, it is the most slender of the long bones. [NIH]

Fistula: Abnormal communication most commonly seen between two internal organs, or between an internal organ and the surface of the body. [NIH]

Flavoring Agents: Substances added to foods and medicine to improve the quality of taste. [NIH]

Flexor: Muscles which flex a joint. [NIH]

Fluorescence: The property of emitting radiation while being irradiated. The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Fluorouracil: A pyrimidine analog that acts as an antineoplastic antimetabolite and also has immunosuppressant. It interferes with DNA synthesis by blocking the thymidylate synthetase conversion of deoxyuridylic acid to thymidylic acid. [NIH]

Focus Groups: A method of data collection and a qualitative research tool in which a small group of individuals are brought together and allowed to interact in a discussion of their opinions about topics, issues, or questions. [NIH]

Fold: A plication or doubling of various parts of the body. [NIH]

Folic Acid: N-(4-(((2-Amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl)amino)benzoyl)-L-glutamic acid. A member of the vitamin B family that stimulates the hematopoietic system. It is present in the liver and kidney and is found in mushrooms, spinach, yeast, green leaves, and grasses. Folic acid is used in the treatment and prevention of folate deficiencies and megaloblastic anemia. [NIH]

Food Additives: Substances which are of little or no nutritive value, but are used in the processing or storage of foods or animal feed, especially in the developed countries; includes antioxidants, food preservatives, food coloring agents, flavoring agents, anti-infective agents (both plain and local), vehicles, excipients and other similarly used substances. Many of the same substances are pharmaceutic aids when added to pharmaceuticals rather than to foods. [NIH]

Food Coloring Agents: Natural or synthetic dyes used as coloring agents in processed foods. [NIH]

Food Preservatives: Substances capable of inhibiting, retarding or arresting the process of fermentation, acidification or other deterioration of foods. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Fractionation: Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days. [NIH]

Frameshift: A type of mutation which causes out-of-phase transcription of the base sequence; such mutations arise from the addition or delection of nucleotide(s) in numbers other than 3 or multiples of 3. [NIH]

Fungi: A kingdom of eukaryotic, heterotrophic organisms that live as saprobes or parasites, including mushrooms, yeasts, smuts, molds, etc. They reproduce either sexually or asexually, and have life cycles that range from simple to complex. Filamentous fungi refer to those that grow as multicelluar colonies (mushrooms and molds). [NIH]

Galanin: A neurotransmitter. [NIH]

Gallate: Antioxidant present in tea. [NIH]

Gallbladder: The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

Gamma Rays: Very powerful and penetrating, high-energy electromagnetic radiation of shorter wavelength than that of x-rays. They are emitted by a decaying nucleus, usually between 0.01 and 10 MeV. They are also called nuclear x-rays. [NIH]

Ganciclovir: Acyclovir analog that is a potent inhibitor of the Herpesvirus family including cytomegalovirus. Ganciclovir is used to treat complications from AIDS-associated cytomegalovirus infections. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

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

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

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

Gastrointestinal tract: The stomach and intestines. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

Gene Amplification: A selective increase in the number of copies of a gene coding for a specific protein without a proportional increase in other genes. It occurs naturally via the excision of a copy of the repeating sequence from the chromosome and its extrachromosomal replication in a plasmid, or via the production of an RNA transcript of the entire repeating sequence of ribosomal RNA followed by the reverse transcription of the molecule to produce an additional copy of the original DNA sequence. Laboratory techniques have been introduced for inducing disproportional replication by unequal crossing over, uptake of DNA from lysed cells, or generation of extrachromosomal sequences from rolling circle replication. [NIH]

Gene Deletion: A genetic rearrangement through loss of segments of DNA or RNA, bringing sequences which are normally separated into close proximity. This deletion may be detected using cytogenetic techniques and can also be inferred from the phenotype, indicating a deletion at one specific locus. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Genes, p53: Tumor suppressor genes located on the short arm of human chromosome 17 and coding for the phosphoprotein p53. [NIH]

Genetic Engineering: Directed modification of the gene complement of a living organism by such techniques as altering the DNA, substituting genetic material by means of a virus, transplanting whole nuclei, transplanting cell hybrids, etc. [NIH]

Genetic Markers: A phenotypically recognizable genetic trait which can be used to identify a genetic locus, a linkage group, or a recombination event. [NIH]

Genetic Screening: Searching a population or individuals for persons possessing certain genotypes or karyotypes that: (1) are already associated with disease or predispose to disease; (2) may lead to disease in their descendants; or (3) produce other variations not known to be associated with disease. Genetic screening may be directed toward identifying phenotypic expression of genetic traits. It includes prenatal genetic screening. [NIH]

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

Genistein: An isoflavonoid derived from soy products. It inhibits protein-tyrosine kinase and topoisomerase-ii (dna topoisomerase (atp-hydrolysing)) activity and is used as an antineoplastic and antitumor agent. Experimentally, it has been shown to induce G2 phase arrest in human and murine cell lines. [NIH]

Genital: Pertaining to the genitalia. [EU]

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]

Germ Cells: The reproductive cells in multicellular organisms. [NIH]

Gestational: Psychosis attributable to or occurring during pregnancy. [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]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glucose Intolerance: A pathological state in which the fasting plasma glucose level is less than 140 mg per deciliter and the 30-, 60-, or 90-minute plasma glucose concentration following a glucose tolerance test exceeds 200 mg per deciliter. This condition is seen frequently in diabetes mellitus but also occurs with other diseases. [NIH]

Glutathione Peroxidase: An enzyme catalyzing the oxidation of 2 moles of glutathione in the presence of hydrogen peroxide to yield oxidized glutathione and water. EC 1.11.1.9. [NIH]

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]

Grading: A system for classifying cancer cells in terms of how abnormal they appear when examined under a microscope. The objective of a grading system is to provide information about the probable growth rate of the tumor and its tendency to spread. The systems used to grade tumors vary with each type of cancer. Grading plays a role in treatment decisions. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

Graft Rejection: An immune response with both cellular and humoral components, directed against an allogeneic transplant, whose tissue antigens are not compatible with those of the recipient. [NIH]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [NIH]

Growth factors: Substances made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy. [NIH]

Habitual: Of the nature of a habit; according to habit; established by or repeated by force of habit, customary. [EU]

Haploid: An organism with one basic chromosome set, symbolized by n; the normal condition of gametes in diploids. [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]

Health Promotion: Encouraging consumer behaviors most likely to optimize health potentials (physical and psychosocial) through health information, preventive programs, and access to medical care. [NIH]

Health Status: The level of health of the individual, group, or population as subjectively assessed by the individual or by more objective measures. [NIH]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

Hematuria: Presence of blood in the urine. [NIH]

Heme: The color-furnishing portion of hemoglobin. It is found free in tissues and as the prosthetic group in many hemeproteins. [NIH]

Hemidesmosomes: An anchoring junction of the cell to a non-cellular substrate, similar in morphology to halves of desmosomes. They are composed of specialized areas of the plasma membrane where intermediate filaments bind on the cytoplasmic face to the transmembrane linkers, integrins, via intracellular attachment proteins, while the extracellular domain of the integrins binds to extracellular matrix proteins. [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]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Hemostasis: The process which spontaneously arrests the flow of blood from vessels carrying blood under pressure. It is accomplished by contraction of the vessels, adhesion and aggregation of formed blood elements, and the process of blood or plasma coagulation. [NIH]

Hepatic: Refers to the liver. [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]

Hereditary: Of, relating to, or denoting factors that can be transmitted genetically from one generation to another. [NIH]

Heredity: 1. The genetic transmission of a particular quality or trait from parent to offspring. 2. The genetic constitution of an individual. [EU]

Herpes: Any inflammatory skin disease caused by a herpesvirus and characterized by the formation of clusters of small vesicles. When used alone, the term may refer to herpes simplex or to herpes zoster. [EU]

Herpes Zoster: Acute vesicular inflammation. [NIH]

Heterodimers: Zippered pair of nonidentical proteins. [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]

Histology: The study of tissues and cells under a microscope. [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]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Hormone Replacement Therapy: Therapeutic use of hormones to alleviate the effects of hormone deficiency. [NIH]

Hormone therapy: Treatment of cancer by removing, blocking, or adding hormones. Also called endocrine therapy. [NIH]

Host: Any animal that receives a transplanted graft. [NIH]

Human papillomavirus: HPV. A virus that causes abnormal tissue growth (warts) and is often associated with some types of cancer. [NIH]

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]

Hybridomas: Cells artificially created by fusion of activated lymphocytes with neoplastic cells. The resulting hybrid cells are cloned and produce pure or "monoclonal" antibodies or T-cell products, identical to those produced by the immunologically competent parent, and continually grow and divide as the neoplastic parent. [NIH]

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]

Hydrogen Peroxide: A strong oxidizing agent used in aqueous solution as a ripening agent, bleach, and topical anti-infective. It is relatively unstable and solutions deteriorate over time unless stabilized by the addition of acetanilide or similar organic materials. [NIH]

Hydrolysis: The process of cleaving a chemical compound by the addition of a molecule of water. [NIH]

Hydroxylysine: A hydroxylated derivative of the amino acid lysine that is present in certain collagens. [NIH]

Hydroxyproline: A hydroxylated form of the imino acid proline. A deficiency in ascorbic acid can result in impaired hydroxyproline formation. [NIH]

Hyperkeratosis: 1. Hypertrophy of the corneous layer of the skin. 2a. Any of various conditions marked by hyperkeratosis. 2b. A disease of cattle marked by thickening and wringling of the hide and formation of papillary outgrowths on the buccal mucous membranes, often accompanied by watery discharge from eyes and nose, diarrhoea, loss of condition, and abortion of pregnant animals, and now believed to result from ingestion of the chlorinated naphthalene of various lubricating oils. [EU]

Hyperplasia: An increase in the number of cells in a tissue or organ, not due to tumor formation. It differs from hypertrophy, which is an increase in bulk without an increase in the number of cells. [NIH]

Hypersensitivity: Altered reactivity to an antigen, which can result in pathologic reactions upon subsequent exposure to that particular antigen. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels

are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

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]

Hypopharynx: The portion of the pharynx between the inferior portion of the oropharynx and the larynx. [NIH]

Hypoxanthine: A purine and a reaction intermediate in the metabolism of adenosine and in the formation of nucleic acids by the salvage pathway. [NIH]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Immortal: Stage when the mother cell and its descendants will multiply indefinitely. [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]

Immunocompromised: Having a weakened immune system caused by certain diseases or treatments. [NIH]

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

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

Immunoglobulin: A protein that acts as an antibody. [NIH]

Immunohistochemistry: Histochemical localization of immunoreactive substances using labeled antibodies as reagents. [NIH]

Immunologic: The ability of the antibody-forming system to recall a previous experience with an antigen and to respond to a second exposure with the prompt production of large amounts of antibody. [NIH]

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

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

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Immunosuppressive therapy: Therapy used to decrease the body's immune response, such as drugs given to prevent transplant rejection. [NIH]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

Implant radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called [NIH]

In situ: In the natural or normal place; confined to the site of origin without invasion of neighbouring tissues. [EU]

In Situ Hybridization: A technique that localizes specific nucleic acid sequences within intact chromosomes, eukaryotic cells, or bacterial cells through the use of specific nucleic acid-labeled probes. [NIH]

In vitro: In the laboratory (outside the body). The opposite of in vivo (in the body). [NIH]

In vivo: In the body. The opposite of in vitro (outside the body or in the laboratory). [NIH]

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

Incisional: The removal of a sample of tissue for examination under a microscope. [NIH]

Incisional biopsy: A surgical procedure in which a portion of a lump or suspicious area is removed for diagnosis. The tissue is then examined under a microscope. [NIH]

Incontinence: Inability to control the flow of urine from the bladder (urinary incontinence) or the escape of stool from the rectum (fecal incontinence). [NIH]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

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]

Infection Control: Programs of disease surveillance, generally within health care facilities, designed to investigate, prevent, and control the spread of infections and their causative microorganisms. [NIH]

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]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Ingestion: Taking into the body by mouth [NIH]

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

Inlay: In dentistry, a filling first made to correspond with the form of a dental cavity and then cemented into the cavity. [NIH]

Inorganic: Pertaining to substances not of organic origin. [EU]

Inotropic: Affecting the force or energy of muscular contractions. [EU]

Insecticides: Pesticides designed to control insects that are harmful to man. The insects may be directly harmful, as those acting as disease vectors, or indirectly harmful, as destroyers of crops, food products, or textile fabrics. [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]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Insulin-dependent diabetes mellitus: A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune, genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Insulin-like: Muscular growth factor. [NIH]

Integrins: A family of transmembrane glycoproteins consisting of noncovalent heterodimers. They interact with a wide variety of ligands including extracellular matrix glycoproteins, complement, and other cells, while their intracellular domains interact with the cytoskeleton. The integrins consist of at least three identified families: the cytoadhesin receptors, the leukocyte adhesion receptors, and the very-late-antigen receptors. Each family contains a common beta-subunit combined with one or more distinct alpha-subunits. These receptors participate in cell-matrix and cell-cell adhesion in many physiologically important processes, including embryological development, hemostasis, thrombosis, wound healing, immune and nonimmune defense mechanisms, and oncogenic transformation. [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]

Interleukin-6: Factor that stimulates the growth and differentiation of human B-cells and is also a growth factor for hybridomas and plasmacytomas. It is produced by many different cells including T-cells, monocytes, and fibroblasts. [NIH]

Intermediate Filament Proteins: Filaments 7-11 nm in diameter found in the cytoplasm of all cells. Many specific proteins belong to this group, e.g., desmin, vimentin, prekeratin, decamin, skeletin, neurofilin, neurofilament protein, and glial fibrillary acid protein. [NIH]

Intermediate Filaments: Cytoplasmic filaments intermediate in diameter (about 10 nanometers) between the microfilaments and the microtubules. They may be composed of any of a number of different proteins and form a ring around the cell nucleus. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Internal Medicine: A medical specialty concerned with the diagnosis and treatment of diseases of the internal organ systems of adults. [NIH]

Internal radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called brachytherapy, implant radiation, or interstitial radiation therapy. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

Intervention Studies: Epidemiologic investigations designed to test a hypothesized cause-effect relation by modifying the supposed causal factor(s) in the study population. [NIH]

Intervertebral: Situated between two contiguous vertebrae. [EU]

Intervertebral Disk Displacement: An intervertebral disk in which the nucleus pulposus has protruded through surrounding fibrocartilage. This occurs most frequently in the lower lumbar region. [NIH]

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

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

Intracellular: Inside a cell. [NIH]

Intraepithelial: Within the layer of cells that form the surface or lining of an organ. [NIH]

Intramuscular: IM. Within or into muscle. [NIH]

Intravenous: IV. Into a vein. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Invasive: 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Involuntary: Reaction occurring without intention or volition. [NIH]

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]

Ionization: 1. Any process by which a neutral atom gains or loses electrons, thus acquiring a net charge, as the dissociation of a substance in solution into ions or ion production by the passage of radioactive particles. 2. Iontophoresis. [EU]

Ionizing: Radiation comprising charged particles, e. g. electrons, protons, alpha-particles, etc., having sufficient kinetic energy to produce ionization by collision. [NIH]

Ions: An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

Irinotecan: An anticancer drug that belongs to a family of anticancer drugs called topoisomerase inhibitors. It is a camptothecin analogue. Also called CPT 11. [NIH]

Irradiation: The use of high-energy radiation from x-rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Irradiation is also called radiation therapy, radiotherapy, and x-ray therapy. [NIH]

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

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kb: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA fragments are up to 50 kilobases long. [NIH]

Keratin: A class of fibrous proteins or scleroproteins important both as structural proteins and as keys to the study of protein conformation. The family represents the principal constituent of epidermis, hair, nails, horny tissues, and the organic matrix of tooth enamel. Two major conformational groups have been characterized, alpha-keratin, whose peptide backbone forms an alpha-helix, and beta-keratin, whose backbone forms a zigzag or pleated sheet structure. [NIH]

Keratinocytes: Epidermal cells which synthesize keratin and undergo characteristic changes as they move upward from the basal layers of the epidermis to the cornified (horny) layer of the skin. Successive stages of differentiation of the keratinocytes forming the epidermal layers are basal cell, spinous or prickle cell, and the granular cell. [NIH]

Keratolytic: An agent that promotes keratolysis. [EU]

Kidney Disease: Any one of several chronic conditions that are caused by damage to the cells of the kidney. People who have had diabetes for a long time may have kidney damage. Also called nephropathy. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Knowledge, Attitudes, Practice: Knowledge, attitudes, and associated behaviors which pertain to health-related events such as procedures, diseases, or family planning. [NIH]

Labile: 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

Labyrinth: The internal ear; the essential part of the organ of hearing. It consists of an osseous and a membranous portion. [NIH]

Laminin: Large, noncollagenous glycoprotein with antigenic properties. It is localized in the basement membrane lamina lucida and functions to bind epithelial cells to the basement membrane. Evidence suggests that the protein plays a role in tumor invasion. [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]

Laryngeal: Having to do with the larynx. [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]

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

Lethal: Deadly, fatal. [EU]

Leucovorin: The active metabolite of folic acid. Leucovorin is used principally as its calcium salt as an antidote to folic acid antagonists which block the conversion of folic acid to folinic acid. [NIH]

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

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Leukopenia: A condition in which the number of leukocytes (white blood cells) in the blood is reduced. [NIH]

Leukoplakia: A white patch that may develop on mucous membranes such as the cheek, gums, or tongue and may become cancerous. [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Lichen Planus: An inflammatory, pruritic disease of the skin and mucous membranes, which can be either generalized or localized. It is characterized by distinctive purplish, flat-topped papules having a predilection for the trunk and flexor surfaces. The lesions may be discrete or coalesce to form plaques. Histologically, there is a "saw-tooth" pattern of epidermal hyperplasia and vacuolar alteration of the basal layer of the epidermis along with an intense upper dermal inflammatory infiltrate composed predominantly of T-cells. Etiology is unknown. [NIH]

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

Ligands: A RNA simulation method developed by the MIT. [NIH]

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]

Lip: Either of the two fleshy, full-blooded margins of the mouth. [NIH]

Lipid: Fat. [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]

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]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Long-Term Care: Care over an extended period, usually for a chronic condition or disability, requiring periodic, intermittent, or continuous care. [NIH]

Loss of Heterozygosity: The loss of one allele at a specific locus, caused by a deletion mutation; or loss of a chromosome from a chromosome pair. It is detected when heterozygous markers for a locus appear monomorphic because one of the alleles was deleted. When this occurs at a tumor suppressor gene locus where one of the alleles is already abnormal, it can result in neoplastic transformation. [NIH]

Low Back Pain: Acute or chronic pain in the lumbar or sacral regions, which may be associated with musculo-ligamentous sprains and strains; intervertebral disk displacement; and other conditions. [NIH]

Lumbar: Pertaining to the loins, the part of the back between the thorax and the pelvis. [EU]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lurtotecan: An anticancer drug that belongs to the family of drugs called topoisomerase inhibitors. [NIH]

Lymph: The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

Lymph node: A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

Lymph node mapping: The use of dyes and radioactive substances to identify lymph nodes that contain tumor cells. [NIH]

Lymphadenectomy: A surgical procedure in which the lymph nodes are removed and examined to see whether they contain cancer. Also called lymph node dissection. [NIH]

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]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

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

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

Lysine: An essential amino acid. It is often added to animal feed. [NIH]

Macrophage: A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. [NIH]

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]

Malnutrition: A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mandible: The largest and strongest bone of the face constituting the lower jaw. It supports the lower teeth. [NIH]

Matrix metalloproteinase: A member of a group of enzymes that can break down proteins, such as collagen, that are normally found in the spaces between cells in tissues (i.e.,

extracellular matrix proteins). Because these enzymes need zinc or calcium atoms to work properly, they are called metalloproteinases. Matrix metalloproteinases are involved in wound healing, angiogenesis, and tumor cell metastasis. [NIH]

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

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

Medical Oncology: A subspecialty of internal medicine concerned with the study of neoplasms. [NIH]

Medical Records: Recording of pertinent information concerning patient's illness or illnesses. [NIH]

Medication Errors: Errors in prescribing, dispensing, or administering medication with the result that the patient fails to receive the correct drug or the indicated proper drug dosage. [NIH]

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

Megakaryocytes: Very large bone marrow cells which release mature blood platelets. [NIH]

Melanin: The substance that gives the skin its color. [NIH]

Melanocytes: Epidermal dendritic pigment cells which control long-term morphological color changes by alteration in their number or in the amount of pigment they produce and store in the pigment containing organelles called melanosomes. Melanophores are larger cells which do not exist in mammals. [NIH]

Melanoma: A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

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]

Menopause: Permanent cessation of menstruation. [NIH]

Menstruation: The normal physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus. [NIH]

Mental Disorders: Psychiatric illness or diseases manifested by breakdowns in the adaptational process expressed primarily as abnormalities of thought, feeling, and behavior producing either distress or impairment of function. [NIH]

Mental Health: The state wherein the person is well adjusted. [NIH]

Mental Processes: Conceptual functions or thinking in all its forms. [NIH]

Mentors: Senior professionals who provide guidance, direction and support to those persons desirous of improvement in academic positions, administrative positions or other career development situations. [NIH]

Mercury: A silver metallic element that exists as a liquid at room temperature. It has the atomic symbol Hg (from hydrargyrum, liquid silver), atomic number 80, and atomic weight 200.59. Mercury is used in many industrial applications and its salts have been employed therapeutically as purgatives, antisyphilitics, disinfectants, and astringents. It can be absorbed through the skin and mucous membranes which leads to mercury poisoning.

Because of its toxicity, the clinical use of mercury and mercurials is diminishing. [NIH]

Mesenchymal: Refers to cells that develop into connective tissue, blood vessels, and lymphatic tissue. [NIH]

Meta-Analysis: A quantitative method of combining the results of independent studies (usually drawn from the published literature) and synthesizing summaries and conclusions which may be used to evaluate therapeutic effectiveness, plan new studies, etc., with application chiefly in the areas of research and medicine. [NIH]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

Metastasis: The spread of cancer from one part of the body to another. Tumors formed from cells that have spread are called "secondary tumors" and contain cells that are like those in the original (primary) tumor. The plural is metastases. [NIH]

Metastatic: Having to do with metastasis, which is the spread of cancer from one part of the body to another. [NIH]

MI: Myocardial infarction. Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Microcirculation: The vascular network lying between the arterioles and venules; includes capillaries, metarterioles and arteriovenous anastomoses. Also, the flow of blood through this network. [NIH]

Microfilaments: The smallest of the cytoskeletal filaments. They are composed chiefly of actin. [NIH]

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

Micro-organism: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

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

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

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]

Mobility: Capability of movement, of being moved, or of flowing freely. [EU]

Modeling: A treatment procedure whereby the therapist presents the target behavior which the learner is to imitate and make part of his repertoire. [NIH]

Modification: A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Molecular Probes: A group of atoms or molecules attached to other molecules or cellular structures and used in studying the properties of these molecules and structures. Radioactive DNA or RNA sequences are used in molecular genetics to detect the presence of a complementary sequence by molecular hybridization. [NIH]

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]

Monocytes: Large, phagocytic mononuclear leukocytes produced in the vertebrate bone marrow and released into the blood; contain a large, oval or somewhat indented nucleus surrounded by voluminous cytoplasm and numerous organelles. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Morphine: The principal alkaloid in opium and the prototype opiate analgesic and narcotic. Morphine has widespread effects in the central nervous system and on smooth muscle. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

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

Motility: The ability to move spontaneously. [EU]

Motion Sickness: Sickness caused by motion, as sea sickness, train sickness, car sickness, and air sickness. [NIH]

Mucins: A secretion containing mucopolysaccharides and protein that is the chief constituent of mucus. [NIH]

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

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

Mucus: The viscous secretion of mucous membranes. It contains mucin, white blood cells, water, inorganic salts, and exfoliated cells. [NIH]

Multicenter study: A clinical trial that is carried out at more than one medical institution. [NIH]

Muscle Fibers: Large single cells, either cylindrical or prismatic in shape, that form the basic unit of muscle tissue. They consist of a soft contractile substance enclosed in a tubular sheath. [NIH]

Muscular Atrophy: Derangement in size and number of muscle fibers occurring with aging, reduction in blood supply, or following immobilization, prolonged weightlessness, malnutrition, and particularly in denervation. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Mustard Gas: Severe irritant and vesicant of skin, eyes, and lungs. It may cause blindness and lethal lung edema and was formerly used as a war gas. The substance has been proposed as a cytostatic and for treatment of psoriasis. It has been listed as a known carcinogen in the Fourth Annual Report on Carcinogens (NTP-85-002, 1985) (Merck, 11th ed). [NIH]

Mutagen: Any agent, such as X-rays, gamma rays, mustard gas, TCDD, that can cause abnormal mutation in living cells; having the power to cause mutations. [NIH]

Mutagenesis: Process of generating genetic mutations. It may occur spontaneously or be induced by mutagens. [NIH]

Mutagenic: Inducing genetic mutation. [EU]

Myocardial infarction: Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myosin: Chief protein in muscle and the main constituent of the thick filaments of muscle fibers. In conjunction with actin, it is responsible for the contraction and relaxation of muscles. [NIH]

Myotonic Dystrophy: A condition presenting muscle weakness and wasting which may be progressive. [NIH]

Naive: Used to describe an individual who has never taken a certain drug or class of drugs (e. g., AZT-naive, antiretroviral-naive), or to refer to an undifferentiated immune system cell. [NIH]

Narcotic: 1. Pertaining to or producing narcosis. 2. An agent that produces insensibility or stupor, applied especially to the opioids, i.e. to any natural or synthetic drug that has morphine-like actions. [EU]

Nausea: An unpleasant sensation in the stomach usually accompanied by the urge to vomit. Common causes are early pregnancy, sea and motion sickness, emotional stress, intense pain, food poisoning, and various enteroviruses. [NIH]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at http://cancer.gov. [NIH]

Neck dissection: Surgery to remove lymph nodes and other tissues in the neck. [NIH]

Necrosis: A pathological process caused by the progressive degradative action of enzymes that is generally associated with severe cellular trauma. It is characterized by mitochondrial swelling, nuclear flocculation, uncontrolled cell lysis, and ultimately cell death. [NIH]

Need: A state of tension or dissatisfaction felt by an individual that impels him to action toward a goal he believes will satisfy the impulse. [NIH]

Needs Assessment: Systematic identification of a population's needs or the assessment of individuals to determine the proper level of services needed. [NIH]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

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

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephropathy: Disease of the kidneys. [EU]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [NIH]

Networks: Pertaining to a nerve or to the nerves, a meshlike structure of interlocking fibers or strands. [NIH]

Neuronal: Pertaining to a neuron or neurons (= conducting cells of the nervous system). [EU]

Neurons: The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

Neuropathy: A problem in any part of the nervous system except the brain and spinal cord. Neuropathies can be caused by infection, toxic substances, or disease. [NIH]

Neuropeptide: A member of a class of protein-like molecules made in the brain. Neuropeptides consist of short chains of amino acids, with some functioning as neurotransmitters and some functioning as hormones. [NIH]

Neurotransmitters: Endogenous signaling molecules that alter the behavior of neurons or effector cells. Neurotransmitter is used here in its most general sense, including not only messengers that act directly to regulate ion channels, but also those that act through second messenger systems, and those that act at a distance from their site of release. Included are neuromodulators, neuroregulators, neuromediators, and neurohumors, whether or not acting at synapses. [NIH]

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

Nicotine: Nicotine is highly toxic alkaloid. It is the prototypical agonist at nicotinic cholinergic receptors where it dramatically stimulates neurons and ultimately blocks synaptic transmission. Nicotine is also important medically because of its presence in tobacco smoke. [NIH]

Nitrosamines: A class of compounds that contain a -NH2 and a -NO radical. Many members of this group have carcinogenic and mutagenic properties. [NIH]

Node-negative: Cancer that has not spread to the lymph nodes. [NIH]

Norepinephrine: Precursor of epinephrine that is secreted by the adrenal medulla and is a widespread central and autonomic neurotransmitter. Norepinephrine is the principal transmitter of most postganglionic sympathetic fibers and of the diffuse projection system in the brain arising from the locus ceruleus. It is also found in plants and is used pharmacologically as a sympathomimetic. [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]

Nurse Practitioners: Nurses who are specially trained to assume an expanded role in providing medical care under the supervision of a physician. [NIH]

Nutritional Status: State of the body in relation to the consumption and utilization of nutrients. [NIH]

Nutritive Value: An indication of the contribution of a food to the nutrient content of the diet. This value depends on the quantity of a food which is digested and absorbed and the amounts of the essential nutrients (protein, fat, carbohydrate, minerals, vitamins) which it contains. This value can be affected by soil and growing conditions, handling and storage, and processing. [NIH]

Occult: Obscure; concealed from observation, difficult to understand. [EU]

Octreotide: A potent, long-acting somatostatin octapeptide analog which has a wide range of physiological actions. It inhibits growth hormone secretion, is effective in the treatment of hormone-secreting tumors from various organs, and has beneficial effects in the management of many pathological states including diabetes mellitus, orthostatic hypertension, hyperinsulinism, hypergastrinemia, and small bowel fistula. [NIH]

Odds Ratio: The ratio of two odds. The exposure-odds ratio for case control data is the ratio of the odds in favor of exposure among cases to the odds in favor of exposure among noncases. The disease-odds ratio for a cohort or cross section is the ratio of the odds in favor of disease among the exposed to the odds in favor of disease among the unexposed. The prevalence-odds ratio refers to an odds ratio derived cross-sectionally from studies of prevalent cases. [NIH]

Odour: A volatile emanation that is perceived by the sense of smell. [EU]

Ointments: Semisolid preparations used topically for protective emollient effects or as a vehicle for local administration of medications. Ointment bases are various mixtures of fats, waxes, animal and plant oils and solid and liquid hydrocarbons. [NIH]

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]

Opacity: Degree of density (area most dense taken for reading). [NIH]

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]

Opium: The air-dried exudate from the unripe seed capsule of the opium poppy, Papaver somniferum, or its variant, P. album. It contains a number of alkaloids, but only a few - morphine, codeine, and papaverine - have clinical significance. Opium has been used as an analgesic, antitussive, antidiarrheal, and antispasmodic. [NIH]

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

Oral Health: The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

Oral Hygiene: The practice of personal hygiene of the mouth. It includes the maintenance of oral cleanliness, tissue tone, and general preservation of oral health. [NIH]

Oral surgeon: A dentist with special training in surgery of the mouth and jaw. [NIH]

Organ Culture: The growth in aseptic culture of plant organs such as roots or shoots, beginning with organ primordia or segments and maintaining the characteristics of the organ. [NIH]

Ornithine: An amino acid produced in the urea cycle by the splitting off of urea from arginine. [NIH]

Ornithine Decarboxylase: A pyridoxal-phosphate protein, believed to be the rate-limiting compound in the biosynthesis of polyamines. It catalyzes the decarboxylation of ornithine to form putrescine, which is then linked to a propylamine moiety of decarboxylated S-adenosylmethionine to form spermidine. EC 4.1.1.17. [NIH]

Orofacial: Of or relating to the mouth and face. [EU]

Oropharynx: Oral part of the pharynx. [NIH]

Orthostatic: Pertaining to or caused by standing erect. [EU]

Osteomyelitis: Inflammation of bone caused by a pyogenic organism. It may remain localized or may spread through the bone to involve the marrow, cortex, cancellous tissue, and periosteum. [EU]

Osteoradionecrosis: Necrosis of bone following radiation injury. [NIH]

Otolaryngologist: A doctor who specializes in treating diseases of the ear, nose, and throat. Also called an ENT doctor. [NIH]

Ovary: Either of the paired glands in the female that produce the female germ cells and secrete some of the female sex hormones. [NIH]

Overexpress: An excess of a particular protein on the surface of a cell. [NIH]

Oxidation: The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

P53 gene: A tumor suppressor gene that normally inhibits the growth of tumors. This gene is altered in many types of cancer. [NIH]

Paclitaxel: Antineoplastic agent isolated from the bark of the Pacific yew tree, Taxus brevifolia. Paclitaxel stabilizes microtubules in their polymerized form and thus mimics the action of the proto-oncogene proteins c-mos. [NIH]

Paediatric: Of or relating to the care and medical treatment of children; belonging to or concerned with paediatrics. [EU]

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]

Palpation: Application of fingers with light pressure to the surface of the body to determine

consistence of parts beneath in physical diagnosis; includes palpation for determining the outlines of organs. [NIH]

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

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

Pancreatic cancer: Cancer of the pancreas, a salivary gland of the abdomen. [NIH]

Panic: A state of extreme acute, intense anxiety and unreasoning fear accompanied by disorganization of personality function. [NIH]

Panic Disorder: A type of anxiety disorder characterized by unexpected panic attacks that last minutes or, rarely, hours. Panic attacks begin with intense apprehension, fear or terror and, often, a feeling of impending doom. Symptoms experienced during a panic attack include dyspnea or sensations of being smothered; dizziness, loss of balance or faintness; choking sensations; palpitations or accelerated heart rate; shakiness; sweating; nausea or other form of abdominal distress; depersonalization or derealization; paresthesias; hot flashes or chills; chest discomfort or pain; fear of dying and fear of not being in control of oneself or going crazy. Agoraphobia may also develop. Similar to other anxiety disorders, it may be inherited as an autosomal dominant trait. [NIH]

Papillary: Pertaining to or resembling papilla, or nipple. [EU]

Papilloma: A benign epithelial neoplasm which may arise from the skin, mucous membranes or glandular ducts. [NIH]

Papillomavirus: A genus of Papovaviridae causing proliferation of the epithelium, which may lead to malignancy. A wide range of animals are infected including humans, chimpanzees, cattle, rabbits, dogs, and horses. [NIH]

Paraffin: A mixture of solid hydrocarbons obtained from petroleum. It has a wide range of uses including as a stiffening agent in ointments, as a lubricant, and as a topical anti-inflammatory. It is also commonly used as an embedding material in histology. [NIH]

Paralysis: Loss of ability to move all or part of the body. [NIH]

Parasympathomimetic: 1. Producing effects resembling those of stimulation of the parasympathetic nerve supply to a part. 2. An agent that produces effects similar to those produced by stimulation of the parasympathetic nerves. Called also cholinergic. [EU]

Parenteral: Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

Parenteral Nutrition: The administering of nutrients for assimilation and utilization by a patient who cannot maintain adequate nutrition by enteral feeding alone. Nutrients are administered by a route other than the alimentary canal (e.g., intravenously, subcutaneously). [NIH]

Paresthesias: Abnormal touch sensations, such as burning or prickling, that occur without an outside stimulus. [NIH]

Parotid: The space that contains the parotid gland, the facial nerve, the external carotid artery, and the retromandibular vein. [NIH]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

Particle: A tiny mass of material. [EU]

Partnership Practice: A voluntary contract between two or more doctors who may or may

not share responsibility for the care of patients, with proportional sharing of profits and losses. [NIH]

Patch: A piece of material used to cover or protect a wound, an injured part, etc.: a patch over the eye. [NIH]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Pathologies: The study of abnormality, especially the study of diseases. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

PDQ: Physician Data Query. PDQ is an online database developed and maintained by the National Cancer Institute. Designed to make the most current, credible, and accurate cancer information available to health professionals and the public, PDQ contains peer-reviewed summaries on cancer treatment, screening, prevention, genetics, and supportive care; a registry of cancer clinical trials from around the world; and directories of physicians, professionals who provide genetics services, and organizations that provide cancer care. Most of this information is available on the CancerNet Web site, and more specific information about PDQ can be found at http://cancernet.nci.nih.gov/pdq.html. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Peplomycin: An antineoplastic agent derived from bleomycin. [NIH]

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

Periodontal disease: Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [NIH]

Periodontitis: Inflammation of the periodontal membrane; also called periodontitis simplex. [NIH]

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

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

Pharmaceutic Aids: Substances which are of little or no therapeutic value, but are necessary in the manufacture, compounding, storage, etc., of pharmaceutical preparations or drug dosage forms. They include solvents, diluting agents, and suspending agents, and emulsifying agents. Also, antioxidants; preservatives, pharmaceutical; dyes (coloring agents); flavoring agents; vehicles; excipients; ointment bases. [NIH]

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

Pharyngitis: Inflammation of the throat. [NIH]

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

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

Phenylalanine: An aromatic amino acid that is essential in the animal diet. It is a precursor

of melanin, dopamine, noradrenalin, and thyroxine. [NIH]

Phospholipases: A class of enzymes that catalyze the hydrolysis of phosphoglycerides or glycerophosphatidates. EC 3.1.-. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nevers, bones, and teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

Phosphorylated: Attached to a phosphate group. [NIH]

Phosphorylates: Attached to a phosphate group. [NIH]

Phosphorylation: The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

Photodynamic therapy: Treatment with drugs that become active when exposed to light. These drugs kill cancer cells. [NIH]

Physical Examination: Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [NIH]

Physical Therapy: The restoration of function and the prevention of disability following disease or injury with the use of light, heat, cold, water, electricity, ultrasound, and exercise. [NIH]

Physician Assistants: Persons academically trained, licensed, or credentialed to provide medical care under the supervision of a physician. The concept does not include nurses, but does include orthopedic assistants, surgeon's assistants, and assistants to other specialists. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

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

Pilot Projects: Small-scale tests of methods and procedures to be used on a larger scale if the pilot study demonstrates that these methods and procedures can work. [NIH]

Pilot study: The initial study examining a new method or treatment. [NIH]

Pituitary Gland: A small, unpaired gland situated in the sella turcica tissue. It is connected to the hypothalamus by a short stalk. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plaque: A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

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

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

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

Plasmin: A product of the lysis of plasminogen (profibrinolysin) by plasminogen activators. It is composed of two polypeptide chains, light (B) and heavy (A), with a molecular weight of 75,000. It is the major proteolytic enzyme involved in blood clot retraction or the lysis of fibrin and quickly inactivated by antiplasmins. EC 3.4.21.7. [NIH]

Plasminogen: Precursor of fibrinolysin (plasmin). It is a single-chain beta-globulin of molecular weight 80-90,000 found mostly in association with fibrinogen in plasma; plasminogen activators change it to fibrinolysin. It is used in wound debriding and has been investigated as a thrombolytic agent. [NIH]

Plasminogen Activators: A heterogeneous group of proteolytic enzymes that convert plasminogen to plasmin. They are concentrated in the lysosomes of most cells and in the vascular endothelium, particularly in the vessels of the microcirculation. EC 3.4.21.-. [NIH]

Platelet Activation: A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness, aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [NIH]

Platinum: Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

Pleated: Particular three-dimensional pattern of amyloidoses. [NIH]

Ploidy: The number of sets of chromosomes in a cell or an organism. For example, haploid means one set and diploid means two sets. [NIH]

Point Mutation: A mutation caused by the substitution of one nucleotide for another. This results in the DNA molecule having a change in a single base pair. [NIH]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Pollen: The male fertilizing element of flowering plants analogous to sperm in animals. It is released from the anthers as yellow dust, to be carried by insect or other vectors, including wind, to the ovary (stigma) of other flowers to produce the embryo enclosed by the seed. The pollens of many plants are allergenic. [NIH]

Polycystic: An inherited disorder characterized by many grape-like clusters of fluid-filled cysts that make both kidneys larger over time. These cysts take over and destroy working kidney tissue. PKD may cause chronic renal failure and end-stage renal disease. [NIH]

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]

Polymers: Compounds formed by the joining of smaller, usually repeating, units linked by covalent bonds. These compounds often form large macromolecules (e.g., polypeptides, proteins, plastics). [NIH]

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

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polyposis: The development of numerous polyps (growths that protrude from a mucous

membrane). [NIH]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Posterior: Situated in back of, or in the back part of, or affecting the back or dorsal surface of the body. In lower animals, it refers to the caudal end of the body. [EU]

Postmenopausal: Refers to the time after menopause. Menopause is the time in a woman's life when menstrual periods stop permanently; also called "change of life." [NIH]

Postoperative: After surgery. [NIH]

Postoperative Complications: Pathologic processes that affect patients after a surgical procedure. They may or may not be related to the disease for which the surgery was done, and they may or may not be direct results of the surgery. [NIH]

Postsynaptic: Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

Post-translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Potentiates: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

Potentiation: An overall effect of two drugs taken together which is greater than the sum of the effects of each drug taken alone. [NIH]

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

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

Precancerous: A term used to describe a condition that may (or is likely to) become cancer. Also called premalignant. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Premalignant: A term used to describe a condition that may (or is likely to) become cancer. Also called precancerous. [NIH]

Prenatal: Existing or occurring before birth, with reference to the fetus. [EU]

Presumptive: A treatment based on an assumed diagnosis, prior to receiving confirmatory laboratory test results. [NIH]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Prickle: Several layers of the epidermis where the individual cells are connected by cell bridges. [NIH]

Primary Prevention: Prevention of disease or mental disorders in susceptible individuals or populations through promotion of health, including mental health, and specific protection,

as in immunization, as distinguished from the prevention of complications or after-effects of existing disease. [NIH]

Primary tumor: The original tumor. [NIH]

Private Practice: Practice of a health profession by an individual, offering services on a person-to-person basis, as opposed to group or partnership practice. [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]

Procollagen: A biosynthetic precursor of collagen containing additional amino acid sequences at the amino-terminal ends of the three polypeptide chains. Protocollagen, a precursor of procollagen consists of procollagen peptide chains in which proline and lysine have not yet been hydroxylated. [NIH]

Progestogen: A term applied to any substance possessing progestational activity. [EU]

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]

Projection: A defense mechanism, operating unconsciously, whereby that which is emotionally unacceptable in the self is rejected and attributed (projected) to others. [NIH]

Proline: A non-essential amino acid that is synthesized from glutamic acid. It is an essential component of collagen and is important for proper functioning of joints and tendons. [NIH]

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

Prophylaxis: An attempt to prevent disease. [NIH]

Proportional: Being in proportion : corresponding in size, degree, or intensity, having the same or a constant ratio; of, relating to, or used in determining proportions. [EU]

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

Prostaglandin: Any of a group of components derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway that are extremely potent mediators of a diverse group of physiologic processes. The abbreviation for prostaglandin is PG; specific compounds are designated by adding one of the letters A through I to indicate the type of substituents found on the hydrocarbon skeleton and a subscript (1, 2 or 3) to indicate the number of double bonds in the hydrocarbon skeleton e.g., PGE2. The predominant naturally occurring prostaglandins all have two double bonds and are synthesized from arachidonic acid (5,8,11,14-eicosatetraenoic acid) by the pathway shown in the illustration. The 1 series and 3 series are produced by the same pathway with fatty acids having one fewer double bond (8,11,14-eicosatrienoic acid or one more double bond (5,8,11,14,17-eicosapentaenoic acid) than arachidonic acid. The subscript a or ß indicates the configuration at C-9 (a denotes a substituent below the plane of the ring, ß, above the plane). The naturally occurring PGF's have the a configuration, e.g., PGF2a. All of the prostaglandins act by binding to specific cell-surface receptors causing an increase in the level of the intracellular second messenger cyclic AMP (and in some cases cyclic GMP also). The effect produced by the cyclic AMP increase depends on the specific cell type. In some

cases there is also a positive feedback effect. Increased cyclic AMP increases prostaglandin synthesis leading to further increases in cyclic AMP. [EU]

Prostaglandins A: (13E,15S)-15-Hydroxy-9-oxoprosta-10,13-dien-1-oic acid (PGA(1)); (5Z,13E,15S)-15-hydroxy-9-oxoprosta-5,10,13-trien-1-oic acid (PGA(2)); (5Z,13E,15S,17Z)-15-hydroxy-9-oxoprosta-5,10,13,17-tetraen-1-oic acid (PGA(3)). A group of naturally occurring secondary prostaglandins derived from PGE. PGA(1) and PGA(2) as well as their 19-hydroxy derivatives are found in many organs and tissues. [NIH]

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

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

Protein Binding: The process in which substances, either endogenous or exogenous, bind to proteins, peptides, enzymes, protein precursors, or allied compounds. Specific protein-binding measures are often used as assays in diagnostic assessments. [NIH]

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

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

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

Protein-Tyrosine Kinase: An enzyme that catalyzes the phosphorylation of tyrosine residues in proteins with ATP or other nucleotides as phosphate donors. EC 2.7.1.112. [NIH]

Proteoglycans: Glycoproteins which have a very high polysaccharide content. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Protocol: The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

Protons: Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

Proto-Oncogene Proteins: Products of proto-oncogenes. Normally they do not have oncogenic or transforming properties, but are involved in the regulation or differentiation of cell growth. They often have protein kinase activity. [NIH]

Proto-Oncogene Proteins c-mos: Cellular proteins encoded by the c-mos genes. They function in the cell cycle to maintain maturation promoting factor in the active state and have protein-serine/threonine kinase activity. Oncogenic transformation can take place when c-mos proteins are expressed at the wrong time. [NIH]

Proto-Oncogenes: Normal cellular genes homologous to viral oncogenes. The products of proto-oncogenes are important regulators of biological processes and appear to be involved in the events that serve to maintain the ordered procession through the cell cycle. Proto-oncogenes have names of the form c-onc. [NIH]

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

Pruritic: Pertaining to or characterized by pruritus. [EU]

Psychology: The science dealing with the study of mental processes and behavior in man and animals. [NIH]

Puberty: The period during which the secondary sex characteristics begin to develop and the capability of sexual reproduction is attained. [EU]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

Public Policy: A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

Publishing: "The business or profession of the commercial production and issuance of literature" (Webster's 3d). It includes the publisher, publication processes, editing and editors. Production may be by conventional printing methods or by electronic publishing. [NIH]

Pulmonary: Relating to the lungs. [NIH]

Pulmonary Artery: The short wide vessel arising from the conus arteriosus of the right ventricle and conveying unaerated blood to the lungs. [NIH]

Pulmonary Embolism: Embolism in the pulmonary artery or one of its branches. [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]

Putrescine: A toxic diamine formed by putrefaction from the decarboxylation of arginine and ornithine. [NIH]

Pyogenic: Producing pus; pyopoietic (= liquid inflammation product made up of cells and a thin fluid called liquor puris). [EU]

Pyridoxal: 3-Hydroxy-5-(hydroxymethyl)-2-methyl-4- pyridinecarboxaldehyde. [NIH]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

Quercetin: Aglucon of quercetrin, rutin, and other glycosides. It is widely distributed in the plant kingdom, especially in rinds and barks, clover blossoms, and ragweed pollen. [NIH]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

Radiation 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]

Radiculopathy: Disease involving a spinal nerve root (see spinal nerve roots) which may result from compression related to intervertebral disk displacement; spinal cord injuries; spinal diseases; and other conditions. Clinical manifestations include radicular pain, weakness, and sensory loss referable to structures innervated by the involved nerve root. [NIH]

Radioactive: Giving off radiation. [NIH]

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

Radiolabeled: Any compound that has been joined with a radioactive substance. [NIH]

Radiosensitization: The use of a drug that makes tumor cells more sensitive to radiation therapy. [NIH]

Radiotherapy: The use of ionizing radiation to treat malignant neoplasms and other benign conditions. The most common forms of ionizing radiation used as therapy are x-rays, gamma rays, and electrons. A special form of radiotherapy, targeted radiotherapy, links a cytotoxic radionuclide to a molecule that targets the tumor. When this molecule is an antibody or other immunologic molecule, the technique is called radioimmunotherapy. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Ras gene: A gene that has been found to cause cancer when it is altered (mutated). Agents that block its activity may stop the growth of cancer. A ras peptide is a protein fragment produced by the ras gene. [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]

Reading Frames: The sequence of codons by which translation may occur. A segment of mRNA 5'AUCCGA3' could be translated in three reading frames, 5'AUC. or 5'UCC. or 5'CCG., depending on the location of the start codon. [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]

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

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

Rectal: By or having to do with the rectum. The rectum is the last 8 to 10 inches of the large intestine and ends at the anus. [NIH]

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]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Relapse: The return of signs and symptoms of cancer after a period of improvement. [NIH]

Relative risk: The ratio of the incidence rate of a disease among individuals exposed to a specific risk factor to the incidence rate among unexposed individuals; synonymous with risk ratio. Alternatively, the ratio of the cumulative incidence rate in the exposed to the cumulative incidence rate in the unexposed (cumulative incidence ratio). The term relative risk has also been used synonymously with odds ratio. This is because the odds ratio and relative risk approach each other if the disease is rare (5 percent of population) and the number of subjects is large. [NIH]

Reliability: Used technically, in a statistical sense, of consistency of a test with itself, i. e. the extent to which we can assume that it will yield the same result if repeated a second time. [NIH]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [NIH]

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]

Research Design: A plan for collecting and utilizing data so that desired information can be obtained with sufficient precision or so that an hypothesis can be tested properly. [NIH]

Resected: Surgical removal of part of an organ. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [NIH]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

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

Restoration: Broad term applied to any inlay, crown, bridge or complete denture which restores or replaces loss of teeth or oral tissues. [NIH]

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

Retinoblastoma Protein: Product of the retinoblastoma tumor suppressor gene. It is a nuclear phosphoprotein hypothesized to normally act as an inhibitor of cell proliferation. Rb protein is absent in retinoblastoma cell lines. It also has been shown to form complexes with the adenovirus E1A protein, the SV40 T antigen, and the human papilloma virus E7 protein. [NIH]

Retinoid: Vitamin A or a vitamin A-like compound. [NIH]

Retrospective: Looking back at events that have already taken place. [NIH]

Retrospective Studies: Studies used to test etiologic hypotheses in which inferences about an exposure to putative causal factors are derived from data relating to characteristics of persons under study or to events or experiences in their past. The essential feature is that some of the persons under study have the disease or outcome of interest and their characteristics are compared with those of unaffected persons. [NIH]

Retrospective study: A study that looks backward in time, usually using medical records and interviews with patients who already have or had a disease. [NIH]

Retroviral vector: RNA from a virus that is used to insert genetic material into cells. [NIH]

Rheumatism: A group of disorders marked by inflammation or pain in the connective tissue structures of the body. These structures include bone, cartilage, and fat. [NIH]

Rheumatoid: Resembling rheumatism. [EU]

Rheumatoid arthritis: A form of arthritis, the cause of which is unknown, although infection, hypersensitivity, hormone imbalance and psychologic stress have been suggested as possible causes. [NIH]

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]

Rubella: An acute, usually benign, infectious disease caused by a togavirus and most often affecting children and nonimmune young adults, in which the virus enters the respiratory tract via droplet nuclei and spreads to the lymphatic system. It is characterized by a slight cold, sore throat, and fever, followed by enlargement of the postauricular, suboccipital, and cervical lymph nodes, and the appearances of a fine pink rash that begins on the head and spreads to become generalized. Called also German measles, roetln, röteln, and three-day measles, and rubeola in French and Spanish. [EU]

Rutin: 3-((6-O-(6-Deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl)oxy)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-1-benzopyran-4-one. Found in many plants, including buckwheat, tobacco, forsythia, hydrangea, pansies, etc. It has been used therapeutically to decrease capillary fragility. [NIH]

Saccule: The smaller of the 2 sacs within the vestibule of the ear. [NIH]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Salivation: 1. The secretion of saliva. 2. Ptyalism (= excessive flow of saliva). [EU]

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

Satellite: Applied to a vein which closely accompanies an artery for some distance; in cytogenetics, a chromosomal agent separated by a secondary constriction from the main body of the chromosome. [NIH]

Scalpel: A small pointed knife with a convex edge. [NIH]

Sciatica: A condition characterized by pain radiating from the back into the buttock and posterior/lateral aspects of the leg. Sciatica may be a manifestation of sciatic neuropathy; radiculopathy (involving the L4, L5, S1 or S2 spinal nerve roots; often associated with intervertebral disk displacement); or lesions of the cauda equina. [NIH]

Scleroproteins: Simple proteins characterized by their insolubility and fibrous structure. Within the body, they perform a supportive or protective function. [NIH]

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

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

Secondary tumor: Cancer that has spread from the organ in which it first appeared to another organ. For example, breast cancer cells may spread (metastasize) to the lungs and cause the growth of a new tumor. When this happens, the disease is called metastatic breast cancer, and the tumor in the lungs is called a secondary tumor. Also called secondary cancer. [NIH]

Secretion: 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

Secretory: Secreting; relating to or influencing secretion or the secretions. [NIH]

Segmental: Describing or pertaining to a structure which is repeated in similar form in successive segments of an organism, or which is undergoing segmentation. [NIH]

Segmentation: The process by which muscles in the intestines move food and wastes through the body. [NIH]

Seizures: Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

Selenium: An element with the atomic symbol Se, atomic number 34, and atomic weight 78.96. It is an essential micronutrient for mammals and other animals but is toxic in large amounts. Selenium protects intracellular structures against oxidative damage. It is an essential component of glutathione peroxidase. [NIH]

Self-Examination: The inspection of one's own body, usually for signs of disease (e.g., breast self-examination, testicular self-examination). [NIH]

Sella: A deep depression in the shape of a Turkish saddle in the upper surface of the body of the sphenoid bone in the deepest part of which is lodged the hypophysis cerebri. [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]

Senescence: The bodily and mental state associated with advancing age. [NIH]

Sentinel lymph node: The first lymph node that cancer is likely to spread to from the

primary tumor. Cancer cells may appear first in the sentinel node before spreading to other lymph nodes. [NIH]

Sequester: A portion of dead bone which has become detached from the healthy bone tissue, as occurs in necrosis. [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]

Serous: Having to do with serum, the clear liquid part of blood. [NIH]

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

Sex Characteristics: Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

Sex Determination: The biological characteristics which distinguish human beings as female or male. [NIH]

Shedding: Release of infectious particles (e. g., bacteria, viruses) into the environment, for example by sneezing, by fecal excretion, or from an open lesion. [NIH]

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]

Sigmoid: 1. Shaped like the letter S or the letter C. 2. The sigmoid colon. [EU]

Sigmoid Colon: The lower part of the colon that empties into the rectum. [NIH]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

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

Sil: The arithmetical average of the octave band sound pressure levels of a noise, centered on the frequencies 425, 850 and 1700 Hz together with the frequency 212 of the SIL in this band exceeds the others by 10 dB or more. [NIH]

Skeleton: The framework that supports the soft tissues of vertebrate animals and protects many of their internal organs. The skeletons of vertebrates are made of bone and/or cartilage. [NIH]

Skull: The skeleton of the head including the bones of the face and the bones enclosing the brain. [NIH]

Small 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]

Smooth muscle: Muscle that performs automatic tasks, such as constricting blood vessels. [NIH]

Sneezing: Sudden, forceful, involuntary expulsion of air from the nose and mouth caused by irritation to the mucous membranes of the upper respiratory tract. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Social Support: Support systems that provide assistance and encouragement to individuals with physical or emotional disabilities in order that they may better cope. Informal social support is usually provided by friends, relatives, or peers, while formal assistance is provided by churches, groups, etc. [NIH]

Sodium: An element that is a member of the alkali group of metals. It has the atomic symbol Na, atomic number 11, and atomic weight 23. With a valence of 1, it has a strong affinity for oxygen and other nonmetallic elements. Sodium provides the chief cation of the extracellular body fluids. Its salts are the most widely used in medicine. (From Dorland, 27th ed) Physiologically the sodium ion plays a major role in blood pressure regulation, maintenance of fluid volume, and electrolyte balance. [NIH]

Sodium Iodide: Sodium iodide (NaI). A compound forming white, odorless deliquescent crystals and used as iodine supplement, expectorant or in its radioactive (I-131) form as an diagnostic aid, particularly for thyroid function determinants. [NIH]

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

Soft tissue sarcoma: A sarcoma that begins in the muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. [NIH]

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

Solvent: 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving; the component of a solution that is present in greater amount. [EU]

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]

Somatostatin: A polypeptide hormone produced in the hypothalamus, and other tissues and organs. It inhibits the release of human growth hormone, and also modulates important physiological functions of the kidney, pancreas, and gastrointestinal tract. Somatostatin receptors are widely expressed throughout the body. Somatostatin also acts as a neurotransmitter in the central and peripheral nervous systems. [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]

Spermidine: A polyamine formed from putrescine. It is found in almost all tissues in association with nucleic acids. It is found as a cation at all pH values, and is thought to help stabilize some membranes and nucleic acid structures. It is a precursor of spermine. [NIH]

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]

Spinal Nerve Roots: The paired bundles of nerve fibers entering and leaving the spinal cord at each segment. The dorsal and ventral nerve roots join to form the mixed segmental spinal nerves. The dorsal roots are generally afferent, formed by the central projections of the spinal (dorsal root) ganglia sensory cells, and the ventral roots efferent, comprising the axons of spinal motor and autonomic preganglionic neurons. There are, however, some exceptions to this afferent/efferent rule. [NIH]

Spinous: Like a spine or thorn in shape; having spines. [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]

Sprains and Strains: A collective term for muscle and ligament injuries without dislocation or fracture. A sprain is a joint injury in which some of the fibers of a supporting ligament are ruptured but the continuity of the ligament remains intact. A strain is an overstretching or overexertion of some part of the musculature. [NIH]

Sprue: A non febrile tropical disease of uncertain origin. [NIH]

Squamous: Scaly, or platelike. [EU]

Squamous cell carcinoma: Cancer that begins in squamous cells, which are thin, flat cells resembling fish scales. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts. Also called epidermoid carcinoma. [NIH]

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Squamous cells: Flat cells that look like fish scales under a microscope. These cells cover

internal and external surfaces of the body. [NIH]

Stabilization: The creation of a stable state. [EU]

Stabilizer: A device for maintaining constant X-ray tube voltage or current. [NIH]

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

Standardize: To compare with or conform to a standard; to establish standards. [EU]

Stimulant: 1. Producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. An agent or remedy that produces stimulation. [EU]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

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

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

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Stress Fibers: Bundles of actin filaments (microfilaments) and myosin-II that span across the cell attaching to the cell membrane at focal adhesions and to the network of intermediate filaments that surrounds the nucleus. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Stroma: The middle, thickest layer of tissue in the cornea. [NIH]

Stromal: Large, veil-like cell in the bone marrow. [NIH]

Stromal Cells: Connective tissue cells of an organ found in the loose connective tissue. These are most often associated with the uterine mucosa and the ovary as well as the hematopoietic system and elsewhere. [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]

Submaxillary: Four to six lymph glands, located between the lower jaw and the submandibular salivary gland. [NIH]

Submucous: Occurring beneath the mucosa or a mucous membrane. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

Support group: A group of people with similar disease who meet to discuss how better to cope with their cancer and treatment. [NIH]

Supportive care: Treatment given to prevent, control, or relieve complications and side effects and to improve the comfort and quality of life of people who have cancer. [NIH]

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

Suppressive: Tending to suppress : effecting suppression; specifically : serving to suppress activity, function, symptoms. [EU]

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]

Sympathomimetic: 1. Mimicking the effects of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. 2. An agent that produces effects similar to those of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. Called also adrenergic. [EU]

Symphysis: A secondary cartilaginous joint. [NIH]

Synaptic: Pertaining to or affecting a synapse (= site of functional apposition between neurons, at which an impulse is transmitted from one neuron to another by electrical or chemical means); pertaining to synapsis (= pairing off in point-for-point association of homologous chromosomes from the male and female pronuclei during the early prophase of meiosis). [EU]

Synaptic Transmission: The communication from a neuron to a target (neuron, muscle, or secretory cell) across a synapse. In chemical synaptic transmission, the presynaptic neuron releases a neurotransmitter that diffuses across the synaptic cleft and binds to specific synaptic receptors. These activated receptors modulate ion channels and/or second-messenger systems to influence the postsynaptic cell. Electrical transmission is less common in the nervous system, and, as in other tissues, is mediated by gap junctions. [NIH]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Synthetic retinoid: A substance related to vitamin A that is produced in a laboratory. [NIH]

Systemic: Affecting the entire body. [NIH]

Systemic disease: Disease that affects the whole body. [NIH]

Systemic therapy: Treatment that uses substances that travel through the bloodstream, reaching and affecting cells all over the body. [NIH]

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

Telomerase: Essential ribonucleoprotein reverse transcriptase that adds telomeric DNA to the ends of eukaryotic chromosomes. Telomerase appears to be repressed in normal human somatic tissues but reactivated in cancer, and thus may be necessary for malignant transformation. EC 2.7.7.-. [NIH]

Temporal: One of the two irregular bones forming part of the lateral surfaces and base of the skull, and containing the organs of hearing. [NIH]

Terminator: A DNA sequence sited at the end of a transcriptional unit that signals the end of transcription. [NIH]

Testicular: Pertaining to a testis. [EU]

Testosterone: A hormone that promotes the development and maintenance of male sex characteristics. [NIH]

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

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

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

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

Thoracic: Having to do with the chest. [NIH]

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]

Thromboembolism: Obstruction of a vessel by a blood clot that has been transported from a distant site by the blood stream. [NIH]

Thrombolytic: 1. Dissolving or splitting up a thrombus. 2. A thrombolytic agent. [EU]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thrombus: An aggregation of blood factors, primarily platelets and fibrin with entrapment of cellular elements, frequently causing vascular obstruction at the point of its formation. Some authorities thus differentiate thrombus formation from simple coagulation or clot formation. [EU]

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]

Time Factors: Elements of limited time intervals, contributing to particular results or situations. [NIH]

Tin: A trace element that is required in bone formation. It has the atomic symbol Sn, atomic number 50, and atomic weight 118.71. [NIH]

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

Tissue Culture: Maintaining or growing of tissue, organ primordia, or the whole or part of an organ in vitro so as to preserve its architecture and/or function (Dorland, 28th ed). Tissue culture includes both organ culture and cell culture. [NIH]

Tissue Distribution: Accumulation of a drug or chemical substance in various organs (including those not relevant to its pharmacologic or therapeutic action). This distribution depends on the blood flow or perfusion rate of the organ, the ability of the drug to penetrate organ membranes, tissue specificity, protein binding. The distribution is usually expressed as tissue to plasma ratios. [NIH]

Tomography: Imaging methods that result in sharp images of objects located on a chosen plane and blurred images located above or below the plane. [NIH]

Tooth Preparation: Procedures carried out with regard to the teeth or tooth structures preparatory to specified dental therapeutic and surgical measures. [NIH]

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

Topoisomerase inhibitors: A family of anticancer drugs. The topoisomerase enzymes are responsible for the arrangement and rearrangement of DNA in the cell and for cell growth and replication. Inhibiting these enzymes may kill cancer cells or stop their growth. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxicology: The science concerned with the detection, chemical composition, and pharmacologic action of toxic substances or poisons and the treatment and prevention of toxic manifestations. [NIH]

Toxins: Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

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

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

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

Transfer Factor: Factor derived from leukocyte lysates of immune donors which can transfer both local and systemic cellular immunity to nonimmune recipients. [NIH]

Transferases: Transferases are enzymes transferring a group, for example, the methyl group or a glycosyl group, from one compound (generally regarded as donor) to another compound (generally regarded as acceptor). The classification is based on the scheme "donor:acceptor group transferase". (Enzyme Nomenclature, 1992) EC 2. [NIH]

Translating: Conversion from one language to another language. [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]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

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

Transversion: A base-pair substitution mutation in which a purine-pyrimidine pair is replaced by the equivalent pyrimidine-purine pair, i. e. A-T becomes T-A. [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]

Tropism: Directed movements and orientations found in plants, such as the turning of the sunflower to face the sun. [NIH]

Trypsin: A serine endopeptidase that is formed from trypsinogen in the pancreas. It is converted into its active form by enteropeptidase in the small intestine. It catalyzes hydrolysis of the carboxyl group of either arginine or lysine. EC 3.4.21.4. [NIH]

Tryptophan: An essential amino acid that is necessary for normal growth in infants and for nitrogen balance in adults. It is a precursor serotonin and niacin. [NIH]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [NIH]

Tuberous Sclerosis: A rare congenital disease in which the essential pathology is the appearance of multiple tumors in the cerebrum and in other organs, such as the heart or kidneys. [NIH]

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

Tumor model: A type of animal model which can be used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Tumor Necrosis Factor: Serum glycoprotein produced by activated macrophages and other mammalian mononuclear leukocytes which has necrotizing activity against tumor cell lines and increases ability to reject tumor transplants. It mimics the action of endotoxin but differs from it. It has a molecular weight of less than 70,000 kDa. [NIH]

Tumor suppressor gene: Genes in the body that can suppress or block the development of cancer. [NIH]

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

Tumour: 1. Swelling, one of the cardinal signs of inflammations; morbid enlargement. 2. A new growth of tissue in which the multiplication of cells is uncontrolled and progressive; called also neoplasm. [EU]

Tyrosine: A non-essential amino acid. In animals it is synthesized from phenylalanine. It is also the precursor of epinephrine, thyroid hormones, and melanin. [NIH]

Ulcer: A localized necrotic lesion of the skin or a mucous surface. [NIH]

Ulceration: 1. The formation or development of an ulcer. 2. An ulcer. [EU]

Ulcerative colitis: Chronic inflammation of the colon that produces ulcers in its lining. This condition is marked by abdominal pain, cramps, and loose discharges of pus, blood, and mucus from the bowel. [NIH]

Unconscious: Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

Urea: A compound (CO(NH2)2), formed in the liver from ammonia produced by the deamination of amino acids. It is the principal end product of protein catabolism and constitutes about one half of the total urinary solids. [NIH]

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

[NIH]

Urge urinary incontinence: Urinary leakage when the bladder contracts unexpectedly by itself. [NIH]

Urinary: Having to do with urine or the organs of the body that produce and get rid of urine. [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]

Urokinase: A drug that dissolves blood clots or prevents them from forming. [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]

Vascular endothelial growth factor: VEGF. A substance made by cells that stimulates new blood vessel formation. [NIH]

Vasodilation: Physiological dilation of the blood vessels without anatomic change. For dilation with anatomic change, dilatation, pathologic or aneurysm (or specific aneurysm) is used. [NIH]

Vasodilator: An agent that widens 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]

Venous: Of or pertaining to the veins. [EU]

Venous Thrombosis: The formation or presence of a thrombus within a vein. [NIH]

Ventral: 1. Pertaining to the belly or to any venter. 2. Denoting a position more toward the belly surface than some other object of reference; same as anterior in human anatomy. [EU]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Vertebrae: A bony unit of the segmented spinal column. [NIH]

Vestibule: A small, oval, bony chamber of the labyrinth. The vestibule contains the utricle and saccule, organs which are part of the balancing apparatus of the ear. [NIH]

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

Vimentin: An intermediate filament protein found in most differentiating cells, in cells grown in tissue culture, and in certain fully differentiated cells. Its insolubility suggests that it serves a structural function in the cytoplasm. MW 52,000. [NIH]

Vinblastine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. It is a mitotic inhibitor. [NIH]

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

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

Viral Load: The quantity of measurable virus in the blood. Change in viral load, measured in plasma, is used as a surrogate marker in HIV disease progression. [NIH]

Virulence: The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the tissues of the host. [NIH]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

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

Vital Statistics: Used for general articles concerning statistics of births, deaths, marriages, etc. [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]

Warts: Benign epidermal proliferations or tumors; some are viral in origin. [NIH]

Watchful waiting: Closely monitoring a patient's condition but withholding treatment until symptoms appear or change. Also called observation. [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]

Wound Healing: Restoration of integrity to traumatized tissue. [NIH]

Xenobiotics: Chemical substances that are foreign to the biological system. They include naturally occurring compounds, drugs, environmental agents, carcinogens, insecticides, etc. [NIH]

Xenograft: The cells of one species transplanted to another species. [NIH]

Xerostomia: Decreased salivary flow. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

X-ray therapy: The use of high-energy radiation from x-rays to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. X-ray therapy is also called radiation therapy, radiotherapy, and irradiation. [NIH]

Yeasts: A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

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