National Cancer Institute

Office of Cancer Complementary and Alternative Medicine

Annual Report on Complementary and Alternative Medicine

Fiscal Year 2008

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Director's Message

The research the National Cancer Institute (NCI) supports, both in our own laboratories and at institutions worldwide, is focused on the ultimate goal of helping cancer patients. That mission – achieved through rigorous science – extends, as well, to NCI's complementary and alternative medicine program, also known as CAM.

It is with great pleasure and pride that we once again provide NCI's research partners, physicians, the advocacy community, policymakers and cancer patients with this fourth annual review of NCI's extensive accomplishments in advancing evidence-based CAM interventions and therapies.

While the study of CAM is challenging, we are fortunate to have many partners in this endeavor, as demonstrated in the brief research profiles you'll find featured in this report.

A significant new CAM partnership commenced in July 2008 when U.S. Department of Health and Human Services and the Chinese Health Ministry signed a landmark memorandum of understanding to foster collaboration between researchers who study integrative and traditional Chinese medicine in both countries.

One of the first and most promising of these projects is a partnership between the Kunming Institute of Botany of China Academy of Sciences and NCI. The Kunming Institute supplies rare and promising specimens, while NCI's Natural Products Branch of the Developmental Therapeutics Program screens them in their system of 60 human cancer cell lines.

NCI's Office of Cancer Complementary and Alternative Medicine does an excellent job of coordinating the endeavors that resulted from our agreement with the Chinese researchers and in developing the Institute's CAM research portfolio and partnerships with extramural researchers as well as within NCI's intramural programs. This effort expands our ability to extend the search for effective therapies into areas outside the mainstream of conventional biomedical research.

I hope you find this report helpful and informative. I also hope that it will generate an enhanced dialogue – especially between patients and health care professionals – about the appropriate uses of CAM interventions in conjunction with conventional medicine. Cancer patients deserve credible, unbiased information about any intervention or treatment regimen that they are considering. It is our duty to conduct the science that makes wise and informed decisions possible.

John E. Niederhuber, M.D.
Director
National Cancer Institute

The following acronyms are used throughout this report:

NCI	National Cancer Institute
CAM	complementary and alternative medicine
OCCAM	Office of Cancer Complementary and Alternative Medicine
DCB	Division of Cancer Biology
DCTD	Division of Cancer Treatment and Diagnosis
CCR	Center for Cancer Research
DCEG	Division of Cancer Epidemiology and Genetics
FY	fiscal year
RDSP	Research Development and Support Program
PAP	Practice Assessment Program
BCS	Best Case Series
COP	Communications and Outreach Program
NCCAM	National Center for Complementary and Alternative Medicine
NIH	National Institutes of Health
CARRA	Consumer Advocates in Research and Related Activities
MOU	Memorandum of Understanding
TCM	Traditional Chinese Medicine
CRTA	Cancer Research Training Award
PDQ	Physicians Data Query
CIS	Cancer Information Service
FASEB	Federation of American Societies for Experimental Biology
CBT	cognitive behavioral therapy
ACCC	Arizona Comprehensive Cancer Center
UA	University of Arizona
FOA	Funding Opportunity Announcement
RFA	Request for Applications
PA	physical activity
HDAC	histone deacetylases
PPT	Polyp Prevention Trial
ESCC	esophageal squamous cell carcinoma
PAH	polycyclic aromatic hydrocarbons
PanINs	pancreatic intraepithelial neoplasias
EGCG	epigallocatechin-3-gallate
CSC	cancer stem cells
DIM	diindolylmethane
PDGF	platelet derived growth factor
QOL	quality of life
TCC	Tau Chi Chuan
PMID	PubMed Indentifier

Contents

Figure 1. Major Categories of CAM Therapies

Alternative Medical Systems

Definition: Alternative medical systems are built upon complete systems of theory and practice. Often, these systems have evolved apart from and earlier than the conventional medical approach used in the United States.

Examples: Acupuncture, Ayurveda, Homeopathy, Naturopathy, Traditional Chinese Medicine, Tibetan Medicine

Energy Therapies

Definition: Energy therapies involve the use of energy fields. There are two types:

- **Biofield therapies** are intended to affect energy fields that purportedly surround and penetrate the human body. The existence of such fields has not yet been scientifically proven.

  Examples: Qi gong, Reiki, Therapeutic touch

- **Electromagnetic-based therapies** involve the unconventional use of electromagnetic fields, such as pulsed fields, magnetic fields, or alternating current or direct current fields.

  Examples: Pulsed electromagnetic fields, Magnet therapy

Exercise Therapies

Definition: Exercise therapies include health-enhancing systems of exercise and movement.

Examples: T'ai chi, Yoga asanas

Manipulative and Body-Based Methods

Definition: Manipulative and body-based methods in CAM are based on manipulation and/or movement of one or more parts of the body.

Examples: Chiropractic, Therapeutic massage, Osteopathy, Reflexology

Mind-Body Interventions

Definition: Mind-body medicine uses a variety of techniques designed to enhance the mind's capacity to affect bodily function and symptom.

Examples: Meditation, Hypnosis, Art therapy, Biofeedback, Imagery, Relaxation therapy, Support groups, Music therapy, Cognitive-behavioral therapy, Aromatherapy

Nutritional Therapeutics

Definition: Nutritional therapeutics are an assortment of nutrients and non-nutrients, bioactive food components used as chemo-preventive agents, and specific foods or diets used as cancer prevention or treatment strategies.

Examples: Macrobiotic diet, Vegetarianism, Gerson therapy, Kelley/Gonzalez regimen, Vitamins, Soy phytoestrogens, Antioxidants, Selenium, Coenzyme Q10

Pharmacological and Biologic Treatments

Definition: Pharmacological and biologic treatments include the off-label use of prescription drugs, hormones, complex natural products, vaccines, and other biological interventions not yet accepted in mainstream medicine.

Examples: Antineoplastions, 714X, Low dose naltrexone, Immunoaugmentative therapy, Laetrile, Hydrazine sulfate, Melatonin

Complex Natural Products

Definition: Complex natural products are an assortment of plant samples (botanicals), extracts of crude natural substances, and un-fractionated extracts from marine organisms used for healing and treatment of disease.

Examples: Herbs and herbal extracts, Mistletoe, Mixtures of tea polyphenols, Shark cartilage

Spiritual Therapies

Definition: Spiritual therapies are therapies that focus on deep, often religious beliefs and feelings, including a person's sense of peace, purpose, connection to others, and beliefs about the meaning of life.

Examples: Intercessory prayer, Spiritual healing

Introduction

Each year, Congress requests a report of the National Cancer Institute's (NCI) annual expenditures in complementary and alternative medicine* (CAM) research. To give more meaning to the numbers provided to Congress, a more detailed account of the Institute's investment in CAM has been produced for the last three years. The reports, (including last year's *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2007)*, are intended as a way for NCI to communicate its progress in this area of medical research, not only to Congress, but also to other interested stakeholders including cancer researchers, CAM practitioners, health care providers, advocacy organizations, cancer patients, and the general public.

This year, the NCI's Office of Cancer Complementary and Alternative Medicine (OCCAM) is proud to present the latest such report, *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2008*. Similar to the previous reports, this publication provides an overview of NCI-supported work in this field along with details on selected CAM projects relating to research, communication, and training and conferences.

This report highlights projects, grants, and cooperative agreements supported by each of the Institute's extramural grant funding divisions – Division of Cancer Biology (DCB), Division of Cancer Control and Population Sciences, Division of Cancer Prevention, and the Division of Cancer Treatment and Diagnosis (DCTD), along with projects from NCI's intramural laboratories – Center for Cancer Research (CCR) and the Division of Cancer Epidemiology and Genetics (DCEG). These projects represent a variety of CAM categories, cancer types, research types, and grant mechanisms. For the first time, this year's report includes an analysis of the different types of training grant awards in NCI's CAM research portfolio and summaries of some of these grants. In fiscal year (FY) 2008, NCI's research expenditures for CAM are an estimated $121,264,507 for the funding of 444 CAM research projects.

As this report on cancer CAM indicates, we at the NCI are committed to an integrated approach to marshalling all of the many resources and approaches necessary to make cancer a condition that is – at worst – a manageable, chronic illness similar to heart disease and diabetes. We believe that evidence-based CAM techniques, systems, and products can have an important role in helping us reach that worthwhile goal.

* CAM is often defined as any medical system, practice, or product that is not thought of as "western medicine" or standard medical care. Complementary medicine means it is used along with standard medicine, also called conventional medicine. Alternative medicine is used in place of standard treatments. CAM treatments may include dietary supplements, megadose vitamins, herbal preparations, acupuncture, massage therapy, magnet therapy, spiritual healing, and meditation. (See Figure 1, on page 4 for the major categories of CAM therapies.)

Office of Cancer Complementary and Alternative Medicine

NCI's OCCAM is a coordinating office responsible for: identifying gaps in the science and creating corresponding funding opportunities for cancer CAM research; partnering with NCI program staff and other governmental and nongovernmental organizations to increase the testing of CAM approaches for cancer prevention, diagnosis, treatment, symptom management, and rehabilitation; developing communication products for various audiences concerning the investigation and use of these approaches; and helping to build bridges between CAM practitioners and the cancer research community.

OCCAM is part of DCTD. The division's mission is to improve the lives of the American public by discovering and conducting better ways to diagnose, assess, treat, and cure cancer through stimulating, coordinating, and funding a national program of cancer research. OCCAM's programs and activities complement DCTD's mission and are enhanced by the other major programs and branches within DCTD.

OCCAM Programs

Research Development and Support Program

As previously noted, NCI sponsored more than 444 cancer CAM research projects in FY 2008, each of which is managed within the various Divisions and Centers of the Institute. OCCAM's Research Development and Support Program (RDSP) staff manages a portion of this portfolio and works with other program staff throughout NCI, assists investigators in identifying funding opportunities, and provides guidance in the pre- and post-review periods of grant application. The RDSP staff also coordinates programs and initiatives designed to stimulate research in cancer CAM as well as activities to develop the foundation of the science in cancer CAM research. RDSP also works with other NCI program staff to fund new grants and supplements to existing grants.

For example, OCCAM awarded a grant supplement during FY 2008 to Yale University researcher Dr. Yung-Chi Cheng for his study on "Nucleoside Analogs as Anti-cancer Compounds" (R01CA063477). The supplement supported research on the interaction of the herbal supplement PHY906 with the chemotherapy drug irinotecan.

In addition, OCCAM awarded the following research grants to:

- Dr. Rakesh Srivastava at the University of Texas Health Center at Tyler for his project "Chemoprevention of Pancreatic Cancer by EGCG." (R01CA125262)
- Dr. Fazlul Sarkar at Wayne State University in Detroit, Michigan for his project "A Novel and Targeted Approach to Inhibit Invasion and Angiogenesis." (R01CA131151)
- Dr. Shengmin Sang at North Carolina Central University, Kannapolis for his project "Ginger Extract Bioavailability Study and Lung Cancer Preventive Effect." (R21CA138277)

Journal Article on Survey of CAM Researchers

OCCAM staff published the article "Survey of cancer researchers regarding complementary and alternative medicine" in the *Journal of the Society for Integrative Oncology* (Winter 2008; 16(1) 2-12). About 85% of the respondents had participated in cancer CAM research. For all CAM categories, the percentage of respondents who would like to conduct research was greater than the percentage of those who have already done so. About two-thirds of the respondents rated research in pharmacologic and biologic treatments and nutritional therapeutics for cancer treatment and symptom/side-effect management as high-priority areas.

Practice Assessment Program

OCCAM's Practice Assessment Program (PAP) reviews retrospective and prospective data on cancer patients treated with alternative therapies. PAP manages the NCI Best Case Series (BCS) Program, which provides an opportunity for CAM practitioners to submit medical data regarding cancer CAM treatments used in their settings. Practitioners are asked to submit patient records for evaluation by experts in clinical assessment and cancer treatment research. Results of the NCI BCS Program are used to inform decisions regarding NCI-initiated research and to share well-documented best cases with interested members of the scientific community in order to stimulate research.

Communications and Outreach Program

OCCAM's Communications and Outreach Program (COP) develops and disseminates information about NCI program initiatives and funding opportunities, workshops and other events, and educational materials through OCCAM's Web site (http://www.cancer.gov/cam) and publications.

This program also assesses the opinions, interests, and informational needs of cancer researchers, CAM practitioners, and cancer patients regarding CAM research through surveys, public comment sessions, and focus groups. Results from these explorations are used to guide outreach efforts to these communities.

COP also developed the following publications in FY 2008:

- *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2007*
- *NCI CAM News* – Spring 2008
- *NCI CAM News* – Fall 2008

National Institutes of Health Yoga Week

In FY 2008, OCCAM's COP partnered with the National Heart, Lung, and Blood Institute; the Office of Research Services; the National Center for Complementary and Alternative Medicine (NCCAM); and the National Institutes of Health (NIH) Recreation and Welfare Association to host NIH's first annual Yoga Week. The five-day series of events took place May 19-23, 2008 and highlighted the science and practice of yoga. The events were planned to serve NIH employees and the public, allowing participants to learn about the benefits of yoga and experience them first-hand through stretching and poses.

Yoga week included presentations by leading yoga instructors, lectures by current NIH grantees conducting research on yoga, including Dr. Lorenzo Cohen, director of the Integrative Medicine Program at the University of Texas M.D. Anderson Cancer Center, and a discussion of NCI's yoga research portfolio by OCCAM Director Dr. Jeffrey D. White. Yoga classes were taught by local instructors throughout the week.

Some participants brought donations of non-perishable foods for Manna Food Center in Rockville, Maryland and the Safra Family Lodge at NIH. Lectures and practice sessions at facilities outside of NIH's main campus in Bethesda, Maryland (Rockledge I and II and 6001 Executive Blvd., in Rockville) allowed off-campus NIH staff to experience yoga.

In addition, COP expanded OCCAM's outreach efforts through exhibiting or sending publications to numerous professional meetings during FY 2008:

- Society for Integrative Oncology International Conference – November 2007
- Evidence-based CAM for Cancer Patients – January 2008
- Oncology Nursing Society – May 2008
- American Association of Naturopathic Physicians/ American Holistic Medical Association Annual Meeting – August 2008
- Fourth International Conference on Holistic Health and Medicine – September 2008

Working with Advocates

In FY 2008, cancer patient advocates were involved in the review of NCI's CAM Annual Report. COP solicited feedback from four Consumer Advocates in Research and Related Activities (CARRA) members who agreed to review a draft of the FY 2007 report. These members provided comments on whether the document was easy to read, contained relevant information to the cancer patient community, or omitted topics of patient interest. Feedback from CARRA members improved the quality of the NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2007.

Cancer CAM Researchers Directory

In FY 2008, COP launched OCCAM's searchable directory of cancer CAM researchers. This resource assists researchers in this growing field to identify others with similar or related research interests. In order to be included in the online directory, researchers must register and demonstrate that they have published original research on a cancer and CAM topic by providing a literature citation. Once registered, users have full access to information provided by other registered users. The Cancer CAM Researcher Directory is located online at http://www.cancer.gov/cam/research_directory.html

OCCAM Highlights

United States and China Accord on Traditional Chinese Medicine

On July 16, 2008, the U.S. Department of Health and Human Services and the Chinese Health Ministry signed a Memorandum of Understanding (MOU) agreement to foster collaboration between researchers studying integrative and Traditional Chinese Medicine (TCM) in both countries. The MOU follows an earlier agreement, signed in 2006, between NCCAM and the Chinese Ministry of Science and Technology. The new agreement encompasses a much larger number of interested institutions in the United States, including NCI, and those in China.

The 2008 MOU on TCM was signed at the beginning of a two-day research roundtable held at NIH that highlighted research in areas of TCM and displayed examples of opportunities for future collaborations between U.S. and Chinese researchers. The presenters discussed diagnostic approaches that might help identify subgroups of cancer patients with different reactions to conventional treatments, as well as quality control of herbal medicines and how to standardize herbal approaches in a way that would make research results more reproducible.

CAM Researchers and Practitioners Conference

In October 2007, OCCAM hosted the conference, *Cancer Researchers and CAM Practitioners: Fostering Collaborations; Advancing the Science,* to bring together people who work in a myriad of varying fields of cancer research, ranging from apoptotic cancer cells to acupuncture. The goal of the conference was to facilitate one of the most important factors in science– teamwork.

OCCAM has long recognized that building and sustaining strong interdisciplinary partnerships is a critical factor in the success of some cancer CAM research endeavors. To promote this, OCCAM Director Dr. Jeffrey D. White and his staff organized the two-day conference at the NIH Natcher Conference Center for over 100 participants from around the world. Conference sessions included "Developing CAM for Cancer: U.S. Regulations," "Understanding and Designing Clinical Case Reports," and "Research Basics and Training Opportunities for CAM Practitioners."

Videocasts from the conference are archived at http://www.cancer.gov/cam/news_occamconferences.html.

OCCAM's Participation at Major Professional Conferences

OCCAM staff members are active in both domestic and international professional conferences through presentations and engaging in dialog with cancer CAM researchers, practitioners, and patient advocacy groups.

During FY 2008, this encompassed several important meetings:

- Drs. Jeffrey D. White and Libin Jia attended the International Traditional Chinese Medicine Conference for Cooperation in Science and Technology in Beijing, China, November 28-29, 2007.
- Dr. Jeffrey D. White attended the 3rd International Congress on Complementary Medicine Research in Sydney, Australia, March 29-31, 2008.
- Dr. Libin Jia participated in an "NCI Meet the Experts" session during the American Association of Cancer Research meeting in San Diego, CA, April 12-16, 2008.
- Drs. Jeffrey D. White and Dan Xi attended the Society of Integrative Oncology's Shanghai International Symposium: Integrative Oncology Theory, Research, and Practice in China, April 25-26, 2008.
- Ms. Lauren Rice attended the National Conference on Health Communication, Marketing, and Media in Atlanta, GA, August 12-14, 2008.
- Dr. Oluwadamilola Olaku presented at the Research Working Group on Case Reports in Heidelberg, Germany, September 5, 2008.
- Dr. Farah Zia presented at the Insulin Potentiation Therapy Conference in San Diego, CA, September 26-28, 2008.

NCI participation at other conferences and events can be found in the Training and Conferences section on pg. 18).

OCCAM Staff List: FY 2008

Jeffrey D. White, M.D.	Director, OCCAM
Christina Armstrong	Administrative Program Specialist
Akia Samuda	Administrative Assistant
April Woodfork	Administrative Assistant
Dan Xi, Ph.D.	Program Officer
Oluwadamilola Olaku, M.D., M.P.H.	Scientific Program Analyst
Libin Jia, M.D.	Health Scientist Administrator
Obianuju Igbokwe, M.S.	Cancer Research Training Award (CRTA) Fellow
Shadia Kawa, M.S.	CRTA Fellow
Farah Zeba Zia, M.D.	Director, Practice Assessment Program
Colleen Lee, CDR (U.S. PHS), M.S., CRNP, AOCN®	Coordinator, Practice Assessment Program
Shea Buckman, M.A.	Coordinator, Communications and Outreach Program
Lauren Rice, M.S.	Communications Analyst
Jennifer Frazier, M.P.H.	Health Communications Intern
Vera Rosenthal, M.P.H.	Health Communications Intern

NCI CAM Communications Programs

NCI directs communications programs that are committed to providing current and credible information resources about CAM to its stakeholders.

Providing Information Online

OCCAM's Web site (http://www.cancer.gov/cam) serves as NCI's information hub on CAM issues. It provides a wealth of information resources and timely updates about the Institute's CAM research portfolio, grant opportunities, and other news.

Included on the OCCAM site are links to other information sources such as the Physician Data Query (PDQ®), NCI's comprehensive cancer database. PDQ produces a registry of clinical trials and summaries covering topics such as cancer treatment, prevention, screening, and CAM.

Most Frequently Accessed PDQ CAM Summaries

NCI tracks of the number of page views for both patient and health professional versions of each PDQ CAM summary on Cancer.gov. The number of page views is determined by the number of views/visits to the first page of each PDQ summary.

In FY 2008, the patient version summary with the highest number of page views was Coenzyme Q10, with 30,163 page views. The second highest number of page views was for the patient version of Essiac/Flor-Essence, with 25,581 page views. Third in the rankings was the Mistletoe patient summary, with 18,442 page views.

Note: NCI's Web sites do not offer personalized medical advice to individuals about their condition or treatment, and the resources on the sites should not be used as a substitute for professional medical care.

Figure 2. PDQ CAM Summaries

Patient summary page views

	714X	Acupuncture	Antineoplastons	Aromatherapy	Cancell/Entelev	Cartilage	Coenzyme Q10	Essiac/Flor-Essence	Gerson Therapy
Totals	4242	11596	2663	8306	3725	9347	30163	25581	10885

Health professional summary page views

	714X	Acupuncture	Antineoplastons	Aromatherapy	Cancell/Entelev	Cartilage	Coenzyme Q10	Essiac/Flor-Essence	Gerson Therapy
Totals	1772	3871	2055	4581	1334	2067	5743	3932	2451

During FY 2008, the highest number of page views received for a health professional version of a PDQ CAM summary was 6,997 for Mistletoe. Coenzyme Q10 had the second most page views for a health professional version with 5,743 page views. The Aromatherapy professional summary, with 4,581 page views, had the third most page views.

Figure 2 shows the total number of page views during FY 2008 for all of the PDQ CAM summaries.

PDQ CAM Clinical Trials

NCI sponsors clinical studies on CAM approaches for cancer. On the OCCAM Web site, there is a table which organizes CAM clinical trials by cancer types and types of symptoms. Clicking on an entry in the table triggers a search of NCI's PDQ Cancer Clinical Trials Registry, which includes abstracts of approximately 4,500 protocols that are open and approved to accept patients as well as trials that are closed. The Registry is available on the NCI Web site at http://www.cancer.gov/clinicaltrials/search/. In FY 2008, there were 111 cancer CAM clinical trials. (See appendix on page 67 for the complete list.)

For the current list of CAM clinical trials by cancer type and to access the CAM clinical trials table, go to http://www.cancer.gov/cam/clinicaltrials_list.html.

The NCI fact sheet "Complementary and Alternative Medicine in Cancer Treatment: Questions and Answers" was viewed 23,981 times in FY 2008. To view this publication, please visit http://www.cancer.gov/cancertopics/factsheet/therapy/cam.

Gonzalez Regimen	Hydrazine Sulfate	Laetrile/Amygdalin	Milk Thistle	Mistletoe Extracts	Newcastle Disease Virus	PC-SPES	Selected Vegetables/ Sun's Soup	Spirituality in Cancer Care
3158	6007	18101	11972	18442	5255	5670	479	6174

Gonzalez Regimen	Hydrazine Sulfate	Laetrile/Amygdalin	Milk Thistle	Mistletoe Extracts	Newcastle Disease Virus	PC-SPES	Selected Vegetables/ Sun's Soup	Spirituality in Cancer Care
2071	1084	2988	3459	6997	2014	3193	152	7581

Producing Publications

In addition to the OCCAM Web site, various offices within NCI provide educational materials on CAM in print format to health professionals, people affected with cancer, and consumers.

NCI's Annual Reports on CAM

OCCAM published NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2007, which documented NCI's participation in and support of a wide range of CAM activities. The report highlights the contributions of communications programs, training and conferences, and cancer CAM research in addressing the NCI strategic areas to support the elimination of suffering and death due to cancer.

The report can be viewed and downloaded from http://www.cancer.gov/cam/attachments/CAMAnnualReportFY2007.pdf.

In FY 2008, NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2006 was selected from over 2,300 entries for the RX Club Award of Excellence. The NCI CAM report was displayed at the 22nd Annual RX Club Show. The RX Club honors the creative aspects of healthcare product advertising and promotion, provides an independent forum for the worldwide healthcare advertising community to exchange ideas, showcases their best creative projects, and brings forth innovative ideas in the expanding healthcare market place.

Newsletter on NCI's CAM Activities

OCCAM's newsletter NCI CAM News provides the latest information on NCI-sponsored research, funding opportunities, meetings and workshops, as well as educational information on cancer and CAM.

The following issues of NCI CAM News were made available online during FY 2008:

- **Spring 2008**
  http://www.cancer.gov/cam/newsletter/2008-spring/home.html

- **Fall 2008**
  http://www.cancer.gov/cam/newsletter/2008-fall/home.html

CAM in NCI Newsletters and Publications

The *NCI Cancer Bulletin* is a biweekly online newsletter designed to provide useful, timely information about cancer research to the cancer research community. During FY 2008, numerous cancer CAM studies were featured in the NCI Cancer Bulletin:

- Probing the Effects of Circadian Rhythms on Cancer (February 19, 2008)
- Herbal Therapy for Brain Cancer (April 15, 2008)
- Vitamin D Not Associated with Decreased Prostate Cancer Risk (May 27, 2008)
- Vitamin C Injections Slow Tumor Growth in Mice (August 19, 2008)

Likewise, in FY 2008, cancer CAM was the topic of stories in other NCI and NIH publications:

- Liver Cancer Chemoprevention Trial, DCEG *Linkage* (March 2008)
- Vitamin D and Cancer Mortality, DCEG *Linkage* (March 2008)
- Red and Processed Meat Intake, DCEG *Linkage* (March 2008)
- NCI Collaborates with China on Esophageal Cancer Research, DCEG *Linkage* (March 2008)
- Visiting Scholar Mimi Yu, DCEG *Linkage* (March 2008)
- NIH Marks First Annual Yoga Week, *NIH Record* (June 13, 2008)
- Mediterranean Diet in a U.S. Population, DCEG *Linkage* (July 2008)
- Effects of Physical Activity, DCEG *Linkage* (July 2008)
- Amanda Cross Investigates Red Meat and Cancer Risk, DCEG *Linkage* (July 2008)
- The Natural Products Repository: A National Drug Development Resource, *CCR Connections* (Volume 2, No. 2, 2008)
- The Mediterranean Diet Reduces the Risk of Dying from Chronic Diseases, *Diet and Health Study News,* NIH-AARP (Fall 2008)

Responding to CAM Cancer Inquiries

The Cancer Information Service (CIS) serves as NCI's link to the public by interpreting and explaining research findings in a clear and understandable manner and providing personalized responses to specific questions about cancer. Highly trained cancer information specialists are available via phone, live online chat, mail, and e-mail to answer questions about cancer treatment and clinical trials, including CAM therapies. During FY 2008, CIS responded to 1,493 inquiries regarding CAM approaches for cancer prevention and treatment.

Access the CIS by calling 1-800-4-CANCER (1-800-422-6237), or by using the LiveHelp instant-messaging service at https://cissecure.nci.nih.gov/livehelp/welcome.asp.

Training and Conferences

NCI provides an array of training support programs on aspects of CAM research including grant writing work shops and scientific conference sponsorships.

Training Opportunities at OCCAM

During FY 2008, OCCAM hosted two CRTA fellows, Ms. Obianuju Igbokwe, M.S. and Ms. Shadia Kawa, M.S., who were mentored by Dr. Jeffrey D. White, OCCAM director. The fellows' goals were to learn about the NIH grant process and explore approaches to cancer CAM research. During the course of the fellowship, the CRTAs assisted with tasks including coding the CAM modality for projects in the NCI CAM research portfolio, providing support to the OCCAM programs, and working on literature review projects that may be submitted for publication.

In addition, OCCAM also hosted two Health Communications Interns, Ms. Jennifer Frazier, M.P.H., and Ms. Vera Rosenthal, M.P.H., who were mentored by Ms. Shea Buckman, M.A., coordinator of the COP. The interns helped organize and execute a scientific conference, write articles for the newsletter NCI CAM News, write and edit publications and other promotional materials, and assisted with the management of OCCAM's Web site. These interns also participated in professional meetings and NIH-sponsored training seminars.

CAM Researcher Honored

Dr. Jie Li, a visiting postdoctoral fellow in NCI's CCR was honored with the Outstanding Poster Presentation Award for his presentation – "Inhibitory Effect of Sheng Qi Formula on Gr-1+CD11b+ Myeloid Immunosuppressor Cells in the 4T1 Murine Mammary Cancer Model" – at the Eighth Annual NCI/CCR Fellows and Young Investigators Colloquium on March 3, 2008. Dr. Li's research was supported by OCCAM, NCI's Laboratory of Molecular Immunoregulation, and the Office of International Affairs as part of a collaboration with Guang An Men Hospital, a component of the China Academy of Chinese Medical Sciences in Beijing.

NCI Lectures and Workshops on CAM

NCI provides educational opportunities for its scientific program staff, fellows, other staff members, and the public on topics related to cancer. In FY 2008, the following seminars and lectures relevant to CAM research were held:

Division of Cancer Prevention

Stars in Nutrition & Cancer – Genetic and Nutritional Modulation of Intestinal Tumorigenesis
October 4, 2007
http://prevention.cancer.gov/newsandevents/eventsarchive/20071004

Intestinal Homeostasis, Inflammation and Neoplasia: Dietary Chemoprevention Strategies
February 13, 2008

Frontiers in Cellular Energetics, Diet and Cancer Prevention
March 12, 2008
http://prevention.cancer.gov/CEDCP

Nutrition and Cancer Prevention Research Practicum
March 17-21, 2008
http://prevention.cancer.gov/newsandevents/eventsarchive/20080317-21

Nutrition and Cancer: From Genotype to Phenotype
March 18, 2008
http://dcp.cancer.gov/newsandevents/eventsarchive/20080318

Cancer Prevention: Discovery and Development of Ethnobotanicals from the Developing World
May 14, 2008
http://dcp.cancer.gov/newsandevents/eventsarchive/20080514

Division of Cancer Control and Population Sciences

Biobehavioral Influences on Tumor Biology: Preclinical Models of Neuroendocrine Regulation
June 24-26, 2008
http://guest.cvent.com/EVENTS/Info/Summary.aspx?e=08625354-009b-4ff5-a902-8e8efe9eea1b

CAM Monthly Lecture Series at NCI

The OCCAM Monthly Lecture Series informs the NCI community about recent and ongoing research projects in cancer CAM. These hour-long lectures feature a fifty-minute presentation on a cancer CAM topic and allow 10 minutes for questions. The lectures are open to the public and also are archived as videocasts on the OCCAM Web site at http://www.cancer.gov/cam/news_lectures.html.

During FY 2008, the series included the following lectures on:

- Endothelial Lineage Cells in Cancer: A Potential Target for Green Tea Derived Catechins
- Bringing Evidence to CAM Approaches for Supportive Care in Children with Cancer
- Why and How to Globalize Traditional Chinese Medicine: A Case Study Looking at the Potential of PHY 906 as an Effective Anti-cancer Adjuvant Therapy
- Personalized Phytococktail for the Management of Prostate Cancer
- A Pilot Trial of Acupuncture for Cancer-related Fatigue: Lessons Learned
- Effects of Phytochemicals on Prostate Cancer Stem Cells
- The Deconstruction of Ginseng – What is the Sum of Its Parts in Breast Cancer Treatment?
- Omega-3 Fatty Acids and Ovarian Cancer
- Curcumin Suppression of Head and Neck Cancer
- Energy Medicine Research in an Oncology Setting

Support of Scientific Conferences

In FY 2008, NCI helped financially support the following conferences, all of which included CAM-related content.

Conference Title	Date	Location	Grant Number
American Association for Cancer Research-Transdisciplinary Research on Energetics and Cancer-National Institutes of Health Think Tank Conference: Energy Balance and Cancer; Mechanism and Mediators	February 24-26, 2008	Lansdowne, VA	1R13CA134016-01
Gordon Research Conference on Marine Natural Products 2008	February 24-29, 2008	Ventura, CA	1R13CA132218-01
14th Biennial Federation of American Societies for Experimental Biology (FASEB) Summer Research Conference on Retinoids	June 15-20, 2008	New Haven, CT	1R13DK081216-01
Molecular Mechanisms Involved in the Nutrient Control of Cellular Function and Metabolism	July 20-25, 2008	Carefree, AZ	5R21DK071458-04
FASEB Summer Conference: Folic Acid, Vitamin B12, and One Carbon Metabolism	August 10-15, 2008	Il Ciocco, Italy	5R13DK076513-03
FASEB Summer Research Conference 2008-Melatonin Receptors: Actions and Therapeutics	August 15-18, 2008	Snowmass, CO	1R13NS063489-01
2008 International Symposium (joint meeting of the Eighth International Skin Carcinogenesis Conference and the Third International Hormel Institute Frontiers in Cancer Research Symposium)	October 4-7, 2008	Austin, MN	1R13CA135806-01
33rd Annual Conference of the American Society of Preventative Oncology	March 8-10, 2009	Tampa, FL	2R13CA094927-07
Society of Behavioral Medicine Annual Meeting and Scientific Sessions	April 22-25, 2009	Montreal, Canada	5R13CA091918-08
North American Research Conference on Complementary and Integrative Medicine	May 12-15, 2009	Minneapolis, MN	1R13AT005049-01
Annual Mentoring Program in PsychoNeuro-Immunology Research	May 28-31, 2009	Madison, WI	1R13CA134006-01
6th International Conference of the Society for Integrative Oncology	November 12-13, 2009	New York City, NY	7R13CA126426-03

Bioactive Food and Chemoprevention Symposium Held in FY 2008

The first-ever, international symposium on "Bioactive Food Components, Alternative Medicine, and Cancer Chemoprevention," held in Greece in October 2007, was supported, in part, by an FY 2007 R13 conference grant* from OCCAM and NCCAM. The two-day meeting drew almost 150 attendees and included presentations and discussions on recent advances in the field including studies on prostate cancer chemoprevention with genistein and resveratrol, anti-inflammatory and antioxidant agents present in dietary and medicinal plants, and recent advances in mechanisms of cancer chemoprevention by grape seed extract.

John Milner, Ph.D., chief of NCI's Nutritional Sciences Research Group, delivered a presentation on "Frontiers in Cancer Prevention by Bioactive Food Components." Dr. Milner also co-chaired the symposium's opening session with conference organizer Shivendra Singh, Ph.D., professor at the University of Pittsburgh School of Medicine and co-leader of the Cancer Biochemoprevention rogram at the University of Pittsburgh Cancer Institute. The grant from OCCAM and NCCAM helped partially cover travel costs of the organizers, invited speakers, and young investigators, as well as pay for publicity for the meeting. Papers from the conference will be published in *Nutrition and Cancer.*

***Grant Number: 1R13CA132241-01**

Highlights from NCI's CAM Training Projects

The highlights on the following pages are selected from the 32 CAM training projects that NCI supported during FY 2008 at laboratories and clinics throughout the United States and the world. NCI's programs allow students and professionals at all stages of their careers to develop the skills necessary to conduct basic, clinical, and cancer con trol research of CAM therapies and interventions.

Abstracts for the CAM training projects featured in the report can be found by searching the NIH RePORTer database at http://projectreporter.nih.gov/reporter.cfm.

Nurses Trained to Do Presurgery Hypnosis for Breast Cancer Patients

Cancer Training Branch

Nurse anesthetists in two different hospital settings are being trained to perform a brief hypnosis intervention for breast cancer patients just prior to surgery. In an earlier clinical study*, the technique had been shown to reduce pain, nausea, and fatigue in a sample of 200 breast cancer surgical patients. The benefits of hypnosis also resulted in a cost savings for the institution of $772 per patient.

"Based on those findings, we asked ourselves, how do we get this beneficial technique out to more people beyond the academic medicine setting?" noted Principal Investigator Guy H. Montgomery, Ph.D., associate professor and director of the Integrative Behavioral Medicine Program at Mount Sinai School of Medicine in New York City. "We thought one way would be by working with nurses. They're in the clinical setting and directly involved in symptom control and management, so they are a good way to get this to patients in the 'real world'."

Funded by an NCI Cancer Education grant,** Dr. Montgomery and his colleagues are conducting and evaluating a research dissemination program to train more than 25 nurses at Mt. Sinai Medical Center – a private research and teaching hospital – and also at Kings County Hospital, a public hospital in Brooklyn. "We believe that it is important to disseminate information on this kind of intervention so it is not just being offered to patients coming to private hospitals like Mt. Sinai. We're also trying to get it out there to public hospital patients, as well," he noted.

The nurses receive four training sessions on the 15-minute hypnosis technique, using role play and feedback. They are also provided with journal articles, information about hypnosis, and data on its effectiveness in the clinical setting. "They love doing the intervention," Dr. Montgomery reported. "It's been a learning curve for us in finding out how can we fit the training program into nurses' busy schedules and make sure that people get the information they need."

Over the next three years, the researchers will study the impact of the hypnosis intervention on patient outcomes and institutional costs. "It's a simple intervention that people can easily adopt and that can potentially have large benefits, both for the patients in symptom reduction and for institutions and society at large," Dr. Montgomery said.

*Montgomery GH, Bovbjerg DH, Schnur JB, David D, Goldfarb A, Weltz CR, Schechter C, Graff-Zivin J, Tatrow K, Price DD, Silverstein JH. A randomized clinical trial of a brief hypnosis intervention to control side effects in breast surgery patients. Journal of the National Cancer Institute, September 5, 2007; 99(17):1304-12. Epub August 28, 2007.

**Grant Number: 5R25CA129094-02

Psychologist Helps Breast Cancer Patients Cope with Radiation Treatment

Cancer Training Branch

Clinical psychologist Julie B. Schnur, Ph.D., is using an NIH Career Development Award* to study a promising cognitive-behavioral therapy (CBT) in combination with hypnosis to help breast cancer patients deal with the pain and emotional distress from skin damage caused by radiation treatment.

"I've always been interested in working with cancer patients," noted Dr. Schnur who is an assistant professor in the Department of Oncological Sciences, Integrative Behavioral Medicine Program, at the Mount Sinai School of Medicine in New York City. Her first research project as an undergraduate was a qualitative study on childhood cancer survivors and their parents and the predictors of PTSD (post-traumatic stress disorder). She continued to pursue cancer research through her post-doctoral fellowship at Mount Sinai. "It's a great experience to be able to continue to learn more about research and also use my clinical skills interacting with patients," she said.

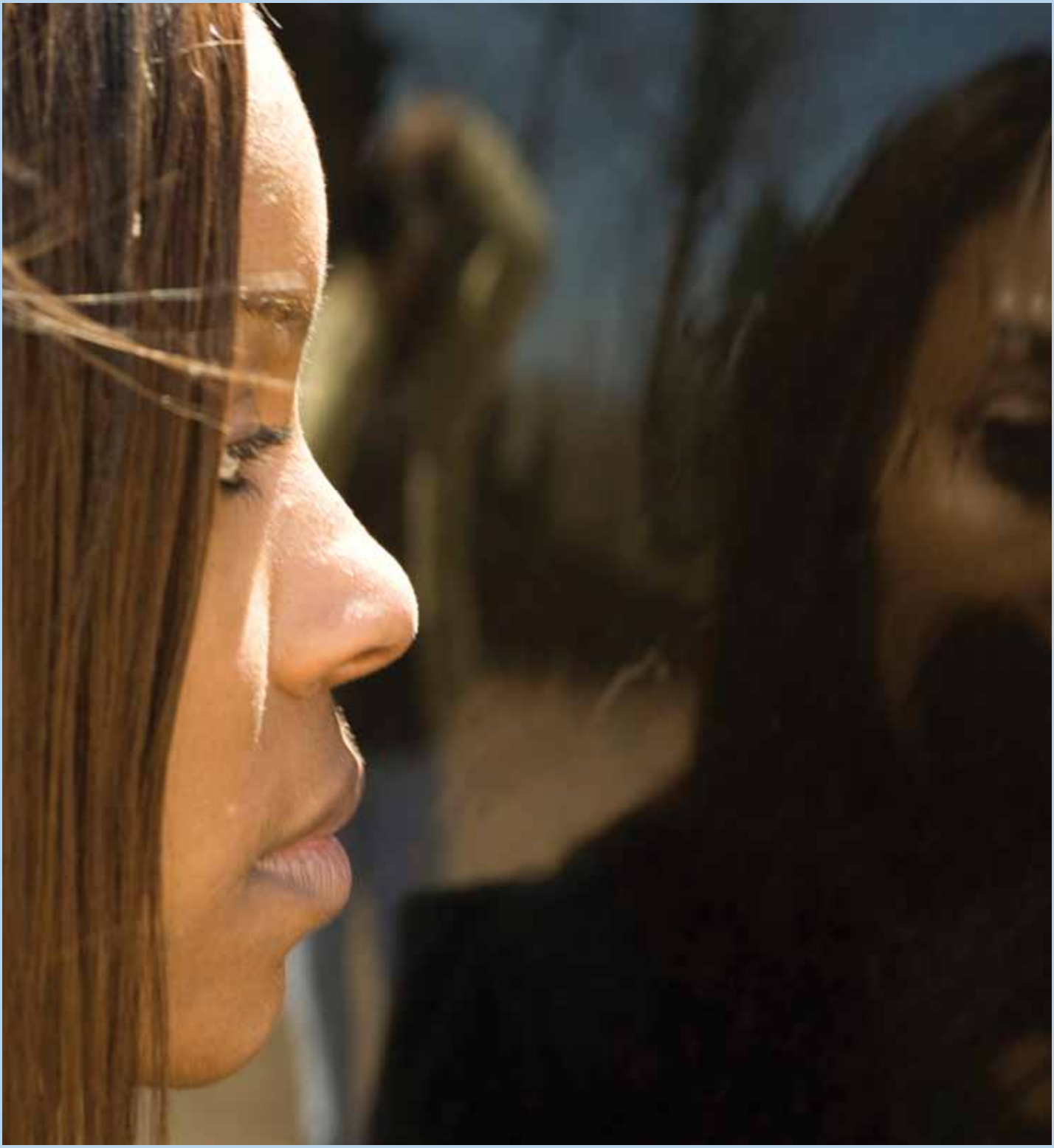
Dr. Schnur worked with her post-doctoral mentor Guy Montgomery, Ph.D., on his study of the CBT/hypnosis intervention to treat fatigue in breast cancer patients (see related story, page 26). Dr. Montgomery told her about the NIH career award program. "As I was talking with these patients about fatigue, they also started talking to me about the radiation-induced skin changes, how ugly they felt, how it interfered with their sleep, and how it hurt," she recalled. Finding little information about the problem in medical literature, Dr. Schnur applied for the NIH grant to test the CBT/hypnosis method to combat the effects of acute skin toxicity in patients undergoing radiation.

The CBT involves teaching patients to identify negative thoughts and learn how to "debate" those thoughts – to ask themselves if negative thinking is helping them or causing them more stress – and helping the patients to exchange those thoughts for more helpful, positive thoughts. In twice-weekly sessions with the patients, Dr. Schnur discusses their CBT workbook entries and conducts brief hypnosis sessions to provide suggestions to reduce their overall stress levels and focus on coolness, "because the skin damage can feel like a burn", as well as healing, reduced pain, and comfort.

She has completed the initial qualitative phase of the study, interviewing 20 breast cancer patients to develop a better description of the skin problems related to radiation toxicity. Dr. Schnur plans to enroll 144 women into a randomized clinical trial of CBT/hypnosis compared to a control group of patients who will receive non-therapeutic, twice-weekly consultations with her.

If the intervention proves effective, it could be a "terrific complement to current medical treatments for these patients," Dr. Schnur said. "All of the distress and psychological reactions to this problem aren't dealt with by a purely medical approach."

*Grant Number: 1K07CA131473-01



Expressive Writing Program May Help Advanced Breast Cancer Patients

Cancer Training Branch

Often patients with advanced breast cancer receive relatively little support in dealing with the serious psycho-social concerns they face from their growing dependence on others, cognitive and physical decline, and issues related to the end-of-life. Teaching these patients to write expressively and disclose their deepest thoughts and feelings about their condition may reduce their emotional and physical distress by providing them opportunities to share their cancer experiences and find meaning in their situations.

Clinical psychologist Catherine E. Mosher, Ph.D., was awarded an NIH fellowship grant* to study the impact of an expressive writing program on women with metastatic breast cancer. "There was a study in metastatic, renal-cell carcinoma patients where they found expressive writing had sleep-related health benefits," noted Dr. Mosher, a postdoctoral research fellow at Memorial Sloan-Kettering Cancer Center Department of Psychiatry & Behavioral Sciences. "I wondered if I could replicate that finding in breast cancer patients."

She is well on the way to enrolling 98 patients in the study, which will compare the expressive writing method against a control group of patients who will write only about their daily activities.
Dr. Mosher conducts four weekly phone sessions with each patient. "I call them on the phone and ask them to write about their moods," she reported. Women in the expressive writing group use a workbook to "write about their deepest thoughts and feelings regarding their cancer experience," she explained.

"I strongly believe that home-based interventions like this are needed, particularly for advanced cancer patients," Dr. Mosher added. "Not all of them can travel to hospitals for group or individual therapy sessions."

The study will primarily assess the impact of expressive writing on the patients' levels of distress (i.e., depressive symptoms and feeling disheartened). It will also monitor effects on other outcomes, including a sense of meaning in life and peace, pain severity, sleep disturbance, fatigue, and functional impairment.

Dr. Mosher heard about the NIH fellowship program during her doctoral health psychology internship at Duke University Medical School. She successfully applied to the program and has found it "a tremendous opportunity to collaborate with multiple laboratories, to mentor student volunteers who help with my study, and to write grant proposals. It's been a really good two years."

*Grant Number: 5F32CA130600-02

Career Mentors Bring Young Investigator into Promising Skin Cancer Prevention Work

Cancer Training Branch

Native Americans in the Southwest call Arizona the "land of the endless sky," yet out of that sky rains a continuous stream of UVB radiation. This type of radiation causes DNA damage that can lead to non-melanoma skin cancer, the most common cancer in the United States accounting for almost two in every five cancer diagnoses.

David Alberts, M.D., director of the Arizona Comprehensive Cancer Center (ACCC) at the University of Arizona (UA), and his colleagues G. Timothy Bowden, Ph.D., deputy director, and Steve Stratton, Ph.D., drug development core leader, are all renowned researchers in the field and work as co-investigators on a Skin Cancer Program Project grant from the NCI. Part of their leadership includes mentoring young investigators that come to work in Tucson, such as Sally Dickinson, Ph.D.

"That's part of what is so great about the ACCC," Dr. Dickinson said. "There are about 35 post-docs working here, and we enjoy a high level of access to training and support systems both at the Cancer Center and throughout UA as a whole. The support from and contact with senior investigators is a priority, and so we benefit from a lot of valuable networking."

Dr. Dickinson has just received her research assistant professorship at UA and is focusing on sulforaphane – a bioactive ingredient in cruciferous vegetables such as broccoli and cauliflower – which Dr. Bowden's lab is actively investigating as a cancer preventive agent. "One of the standard explanations for sulforaphane's early experimental success has been activation of the Nrf2 gene," Dr. Dickinson explained. Nrf2 is widely accepted as an essential transcription factor in protecting humans from oxidative stress-related diseases including UVB-induced damage.

This path from graduate student to assistant professor and cancer biologist at UA has been aided by Dr. Dickinson's receipt of a Career Development Award (K07 grant) from NCI.* She has been aided by a team of outstanding mentors at ACCC in skin cancer research, mouse studies, drug formulation, bioethics, biostatistics, and clinical trial management.

"Moving into the active community of researchers looking at sulforaphane is really exciting," Dr. Dickinson noted, while mentioning contacts and discussions she had at the 2009 annual meeting of the American Association for Cancer Research. "We think sulforaphane is a powerful agent with potential for the prevention of cancers in many other tissues as well as skin," she added. "I think the NCI award has opened up the path for me to investigate what looks like a truly vital opportunity in cancer prevention."

***Grant Number: 1K07CA132956-01A1**

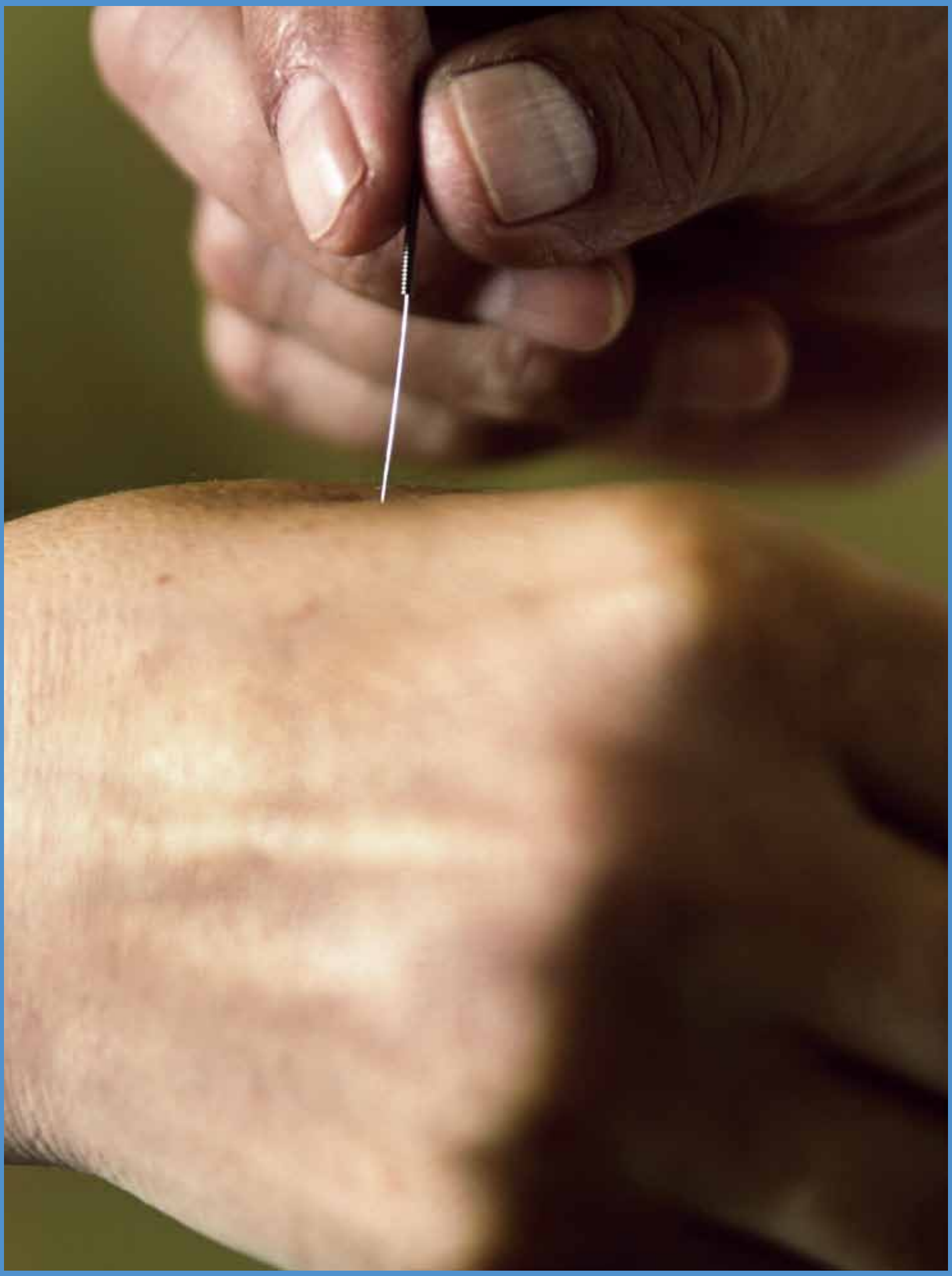
NCI Research in Complementary and Alternative Medicine

The CAM Portfolio Analysis Process

How much money does NCI spend on CAM research each year? This is one of the questions most frequently posed to OCCAM. Researchers, cancer patient advocates, proponents of CAM, and Congress are interested in the answer, and OC CAM is responsible for gathering the data needed to report the total CAM expenditures budget figure each year.

It is a common misconception that OCCAM man ages all of the CAM projects for NCI. The vast majority of CAM projects are managed by other programs and labora tories throughout the Institute. After the close of the fiscal year, NCI's Division of Extramural Activities provides OC CAM with a list of funded grants and cooperative agreements that were coded as containing some component of CAM re search. Similarly, NCI's two intramural components, CCR and DCEG, provide lists of their potentially relevant projects. Also, a list of contracts identified as potentially containing CAM research is provided. OCCAM reviews each project to confirm those projects which are accurately classified as CAM research. OCCAM also classifies each CAM project into a sub category to further define the purpose of the research.

NCI's total CAM expenditure figure includes money awarded for intramural projects (projects conducted with in NIH facilities and labs), extramural grants, cooperative agreements, contracts, and supplements. It is important to note that the reported figure for total NCI CAM expenditures for a fiscal year does not include projects for which NCI is not the primary funder.



NCI CAM Research Portfolio Analysis: FY 2008

Total Estimated Cancer CAM Research Expenditure

In FY 2008, NCI invested $121,264,507 for 444 intramural and extramural research projects relevant to CAM. For the purpose of the FY 2008 analysis, the following types of funding are included: intramural projects and extramural grants, cooperative agreements, contracts, and supplements. (See Figure 3.)

For the first time in this annual report, the portfolio analysis includes CAM training grants, both training (T) and fellowship (F) awards, as well as career (K) and cancer education (R25) grants listed in Figure 4.

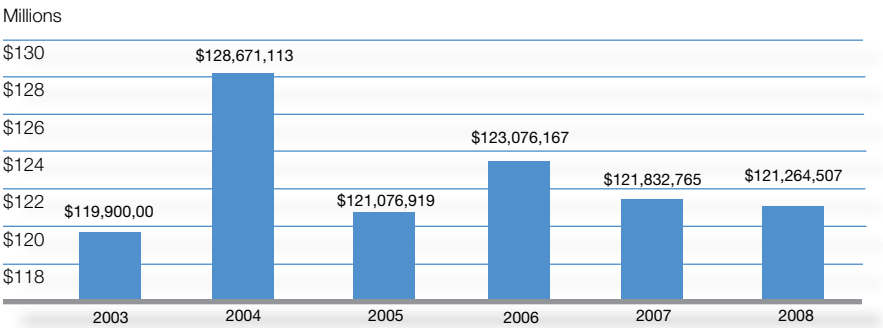
Grant Awards by Funding Opportunity Announcement

In FY 2008, there were 70 funding opportunity announcements (FOA) that yielded cancer CAM grants. The program announcement "Research Project Grants/Parent R01" (PA-07-070) was the most productive mechanisms for attracting new CAM grants to NCI. A total of 36 of the 210 CAM grants awarded through FOAs in FY 2008 came to NCI through this announcement. (See Figure 5.)

Project Distribution by Research Type

The accompanying pie-chart (Figure 6) shows the distribution of the projects according to research type: prevention, treatment, symptom/side effects management, epidemiology, and conferences. In FY 2008, 60.9% of cancer CAM-related research project funds went to various cancer prevention efforts, while treatment, symptom/side effects management, epidemiology, and conferences received 20.7%, 10.6%, 7.8%, and 0.05% respectively.

Figure 3. NCI CAM Expenditures: FY 2003-2008



* Footnote: Includes grants, cooperative agreements, intramural projects, and contracts. Grants and cooperative agreements are only included when NCI is the primary funding agency. Excludes training grants (Ts, Fs, Ks, and R25s) Total projects include all active projects in FY 2008.

Figure 4. NCI CAM Training Projects

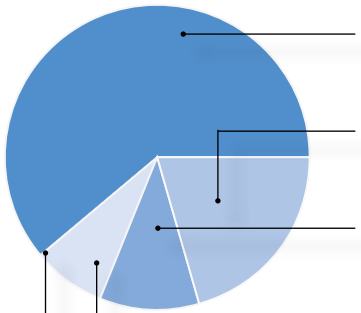
Training Grant Mechanisms	Number of Grants	Total Funding
F (31, 32)	4	$ 112,679
K (01, 05, 07, 22, 23, 24)	20	$1,627,828
R25	5	$ 753,054
T32	3	$ 188,753
TOTAL	**32**	**$2,682,314**

Figure 5. Number of Grant Awards by Funding Opportunity Announcement

*AT03-002	2	*CA07-025	6	PA05-040	1	PA06-351	2	PA07-175	2	PAR03-010	3	PAR06-505	1
*CA02-007	1	*ES02-009	1	PA05-059	1	PA06-400	6	PA07-176	1	PAR03-153	4	PAR08-055	3
*CA03-001	3	*ES05-007	1	PA05-125	2	PA06-412	3	PA07-177	1	PAR04-011	1	PAR99-167	1
*CA03-003	6	*OD03-008	1	PA05-141	1	PA06-413	2	PA07-257	2	PAR04-147	10	PAS02-009	1
*CA03-006	1	PA02-001	1	PA06-041	1	PA06-414	2	PA07-280	2	PAR04-159	2		
*CA04-001	1	PA04-046	1	PA06-042	1	PA06-440	1	PA07-320	1	PAR05-156	4	Solicited	210
*CA04-002	1	PA04-053	8	PA06-120	1	PA06-510	7	PA07-356	1	PAR06-073	2	Unsolicited	185
*CA04-004	6	PA04-068	1	PA06-283	1	PA07-007	2	PA07-362	2	PAR06-294	5	**Total Grants Awarded**	**395**
*CA04-008	1	PA04-099	2	PA06-303	3	PA07-070	36	PA08-050	1	PAR06-313	23		
*CA05-013	2	PA04-108	2	PA06-314	1	PA07-100	1	PAR01-110	1	PAR06-451	2		
*CA05-014	1	PA05-027	1	PA06-315	5	PA07-174	1	PAR03-009	1	PAR06-458	2		

* Request for Applications (RFA).

Figure 6. NCI CAM Research Projects by Research Type*



Prevention
$73,822,456
60.9%

Treatment
$25,044,245
20.7%

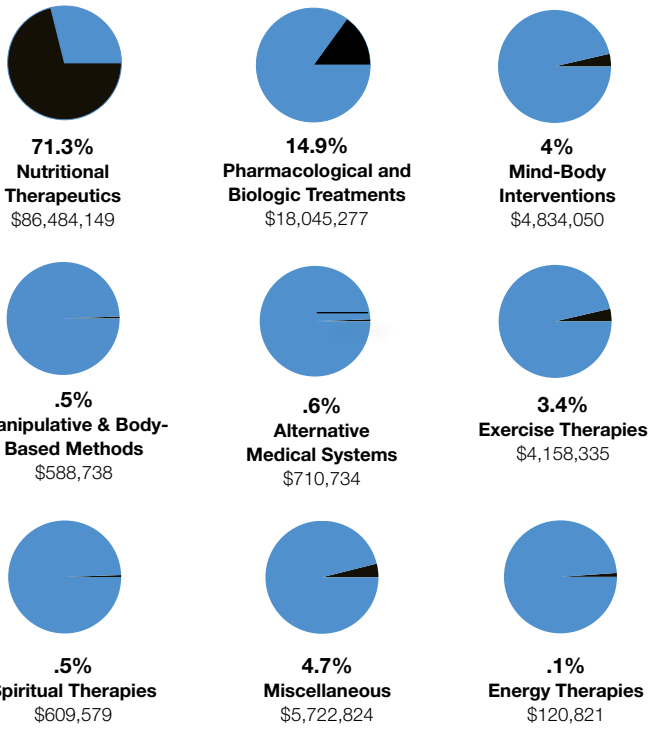
Symptom/Side-Effect Management
$12,845,699
10.6%

Epidemiology
$9,495,005
7.8%

Conferences
$57,202
0.05%

* Includes grants, cooperative agreements, intramural projects, and contracts. Grants and cooperative agreements are only included when NCI is the primary funding agency. Excludes training grants (Ts, Fs, Ks, and R25s) Total projects include all active projects in FY 2008.

Figure 7. NCI CAM Research Projects by CAM Category*



71.3%
Nutritional Therapeutics
$86,484,149

14.9%
Pharmacological and Biologic Treatments
$18,045,277

4%
Mind-Body Interventions
$4,834,050

.5%
Manipulative & Body-Based Methods
$588,738

.6%
Alternative Medical Systems
$710,734

3.4%
Exercise Therapies
$4,158,335

.5%
Spiritual Therapies
$609,579

4.7%
Miscellaneous
$5,722,824

.1%
Energy Therapies
$120,821

Project Distribution by CAM Category

In FY 2008, NCI performed or supported research addressing a variety of CAM therapies (Figure 7). These CAM therapies fall into nine groups: alternative medicine systems, exercise therapies, manipulative and body-based methods, mind-body interventions, nutritional therapeutics, pharmacological and biologic treatments, energy therapies, spiritual therapies, and miscellaneous. (See page 4 for definitions of CAM categories.)

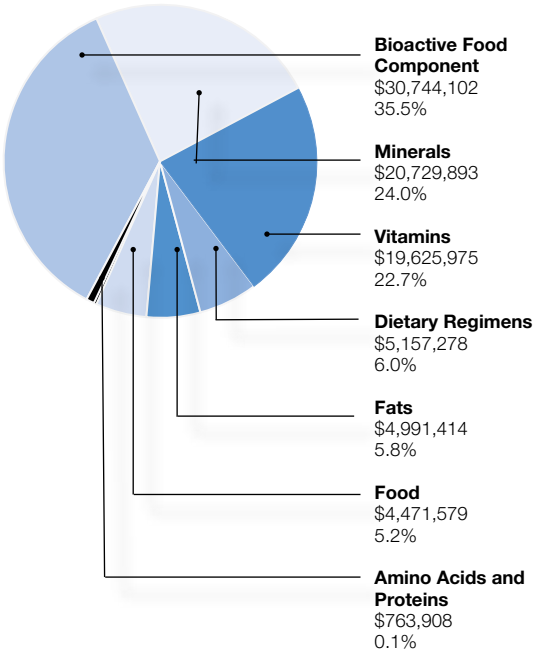
The largest percentage (71.3%) of CAM research funding went to projects that investigated nutritional therapeutics, which can be further broken out into subcategories of research on: foods (e.g., broccoli and berries); minerals (e.g., calcium and selenium); vitamins (e.g., vitamins C and D); bioactive food components (e.g., isoflavones and carotenoids); dietary regimens (e.g., caloric restriction and high fruits and vegetables); fats (e.g., linoleic acid and omega-3); and amino acids and proteins (e.g., N-acetyl cysteine and glycine). Figure 8 shows the distribution of projects according to the subcategory of nutritional therapeutics.

Project Distribution by Cancer Type

The research projects that make up NCI's FY 2008 CAM research portfolio address 19 categories of cancer types. Among the various categories, prostate, breast, colorectal, and lung cancers received the largest amounts of cancer CAM research funding. Nearly one-quarter (23%) of NCI's cancer CAM research funding was allotted for "multiple types" of cancer within the same project.

For a complete listing of the cancer type categories and estimated funding amounts, please see Figure 9 below.

Figure 8. NCI CAM Nutritional Therapeutics Projects by Category*



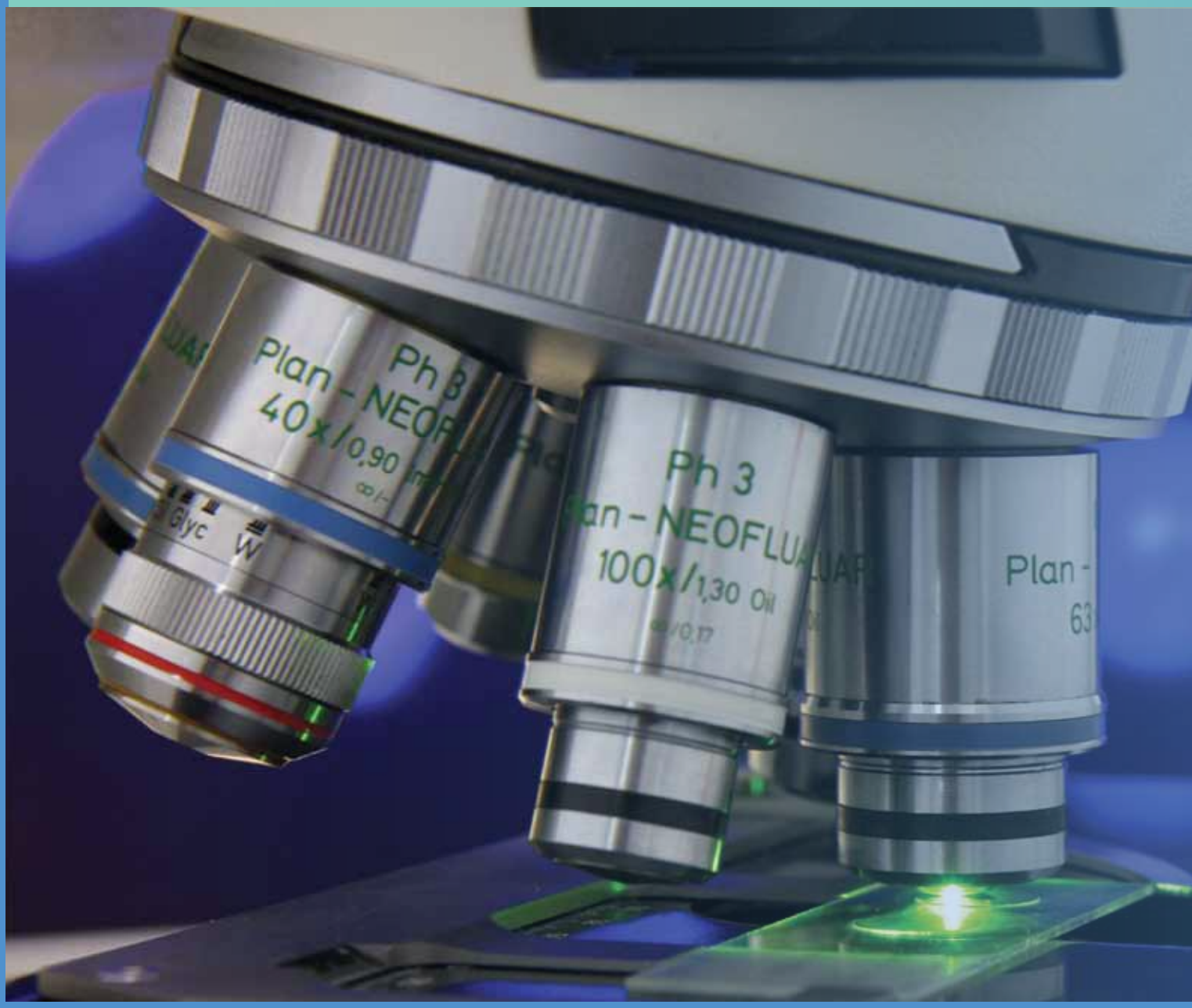
* Includes grants, cooperative agreements, intramural projects, and contracts. Grants and cooperative agreements are only included when NCI is the primary funding agency. Excludes training grants (Ts, Fs, Ks, and R25s) Total projects include all active projects in FY 2008.

Figure 9. NCI CAM Research Projects by Cancer Type*

Bladder	$980,937
Brain	$174,424
Breast	$16,774,338
Cervical	$1,364,913
Childhood	$238,184
Colorectal	$15,377,660
Esophageal	$871,533
Gastric	$1,731,659
Head and Neck	$2,884,084
Hematologic	$1,285,793
Kidney	$35,556
Liver	$579,474
Lung	$13,500,476
Multiple Types	$27,973,073
Ovarian	$322,882
Pancreatic	$3,807,957
Prostate	$25,723,501
Skin: Non-Melanoma and Melanoma	$7,561,560
Small Intestines	$76,503
TOTAL:	**$121,264,507**

* Includes grants, cooperative agreements, intramural projects, and contracts. Grants and cooperative agreements are only included when NCI is the primary funding agency. Excludes training grants (Ts, Fs, Ks, and R25s) Total projects include all active projects in FY 2008.

Highlights from NCI's Wide-Ranging CAM Research



The following research highlights are selected from the 444 CAM research projects that NCI supported during FY 2008 at laboratories within the Institute and throughout the United States and the world. These research projects are organized under several categories reflecting NCI's comprehensive re search focus into understanding the underlying mechanisms of cancer causation, prevention, treatment, and symptom management and palliation of the disease.

Abstracts for the research projects featured in the report can be found by searching the NIH RePORTer database at http://projectreporter.nih.gov/reporter.cfm.

Understanding the Causes and Mechanisms of Cancer

Cancer is a complex set of diseases that scientists are striving to understand from multiple perspectives. Research that improves our understanding of its causes and the mechanisms that underlie its development – from assessing cancer risk to explaining the process of metastasis – is essential to our ability to develop and apply interventions to preempt cancer initiation and progression.

Chickens Studied for Ways to Prevent and Detect Ovarian Cancer

Division of Cancer Prevention

Ovarian cancer is known as the "silent killer," because researchers have been unable to develop a test or screening tool to reliably detect it in the early, more treatable stages. There has also been little progress on prevention of the disease. Dale Buchanan Hales, Ph.D., chair of the Physiology Department at Southern Illinois University School of Medicine, is trying to find ways to prevent or detect the disease sooner.

With NCI funding*, Dr. Hales is continuing his research using *Gallus domesticus* or the common American chicken. Since publication of a landmark paper in 1971, the study of ovarian cancer has benefited from this unusual animal model, said Dr. Hales, because chickens develop a lot of spontaneous ovarian cancer, even more than humans.

Most scientists believe this higher risk of ovarian cancer in domesticated chickens can be explained by the *incessant ovulation hypothesis*. "In an effort to maximize their egg production, farmers breed them to ovulate about five days out of seven," Dr. Hales explained. "With each ovulation comes inflammation and oxidative stress to the cells of the ovarian surface epithelium (OSE), which is where ovarian cancers develop in hens and women." Over just a few years of reproductive life, chicken hens ovulate up to 500 times, which is comparable to the number of times women ovulate over 30-40 years.

"Women have about four weeks to recover from the oxidative stress and inflammation of each cycle, while the chicken must endure a chronic higher inflammatory load," Dr. Hales commented. "I'm pretty sure this explains chickens' high rate of ovarian cancer."

Based on previous research in breast cancer, Dr. Hales believes that ovarian cancer is also driven by both estrogen and cyclooxygenase-1 (COX-1) that can fuel OSE carcinogenesis by producing too much prostaglandin. This hormone and enzyme are essential to ovarian function at normal levels, but when overproduced, they can fuel unwanted cell growth.

Researchers have known for years that fruits and vegetables – in particular, cruciferous vegetables such as cauliflower, cabbage, broccoli, and Brussels sprouts – can impede or prevent some cancers from developing in animals. Dr. Hales' laboratory is testing whether two compounds, found naturally in broccoli, can interfere with OSE carcinogenesis in chickens. The first compound sulforaphane is an antioxidant that affects many steps in the development of cancer, but it cannot be easily produced synthetically so plant extracts are the primary source.

"Testing dietary strategies always presents a challenge, because the amount of activity can vary significantly from plant to plant," Dr. Hales noted. He works with the University of Illinois, which is producing broccoli under strict growth conditions and freeze dries the plants to get rid of the 90 percent water content. "This gives us a pretty reliable source of sulforaphane," he added.

The second compound, indole-3-carbinol (I3C), is another phytoactive ingredient in broccoli, which can be produced synthetically. "It has been studied extensively, and we know it increases production of enzymes that affect the estrogen metabolism process, and some that also eliminate some carcinogens from the system," Dr. Hales explained.

The researchers are feeding hens broccoli-based diets enriched with these two ingredients and are testing whether either compound alone, or the two together, has an impact on ovarian cancer. Then the researchers will wait to see which hens will develop ovarian cancer spontaneously. Dr. Hales and his colleagues also plan to develop ways to look at cells in the hens' OSE as they begin to mutate from normal to carcinogenic.

Because the chicken model of ovarian cancer is close to the human model of ovarian cancer, the tests that researchers are trying to develop might lead to creation of a cancer screening tool that could be used to look for early signs of ovarian cancer in the blood or urine of women "Ovarian cancer is not nearly as lethal when we catch it early, and we really need a better way to do that," Dr. Hales said.

***Grant Number: 1R03CA133915-1**

Physical Activity Levels Studied in China for Impact on Cancer Risk

Division of Cancer Epidemiology and Cancer Genetics

A growing body of evidence demonstrates that the level of physical activity (PA) may be related to the risk of certain cancers. Most of these studies have been conducted in developed, urbanized Western societies, including the United States, but little is known about PA levels in China and other developing nations which are rapidly "westernizing" their economies and lifestyles.

To address this knowledge gap, researchers from NCI's DCEG have joined with scientists from Vanderbilt University and the Shanghai Cancer Institute to assess PA levels in the city of Shanghai, China. They are also studying how the PA habits of Chinese adults affect the blood plasma levels of certain inflammatory biomarkers associated with increased cancer risk.

Steven C. Moore, Ph.D., a research fellow in DCEG's Nutritional Epidemiology Branch noted, "We had epidemiologic research ongoing within Shanghai already, so we decided to monitor the PA of a subset of study participants using devices that measure motion, known as accelerometers." The accelerometers provide researchers a minute-by-minute assessment of a participant's physical activity. "Such data will allow us to examine PA at different intensity levels among men and women living in Shanghai and whether their PA levels are comparable to those of men and women in the United States," he added.

The researchers conducted their studies among subsets (300 individuals each) of healthy adults from the Shanghai Women's Cohort and Shanghai Men's Cohort. In previous work among these populations, self-reported data on PA levels suggested that Shanghai women engaged in much more physical activity than U.S. women, Dr. Moore said. Moreover, contrary to what has been found in the United States, older and/or heavier Shanghai residents reported a greater level of PA than younger and/or lighter individuals.

Intrigued, the researchers took a closer look using a specially-designed PA questionnaire and the accelerometers, which each of the study participants wore for a full week, once every three months during the year-long study period. "One of our study goals was to develop a PA questionnaire that is culturally appropriate to China, so that we could better understand patterns of physical activity there," Dr Moore explained. "We developed a questionnaire that emphasizes participation in everyday routine activities, such as light household work and activity as part of an occupation. We also included much greater representation of those exercise activities that are common among Shanghai residents." The researchers validated this questionnaire against the objective accelerometer data and their initial analysis has been submitted for publication to a peer-reviewed medical journal.

The scientists also collected blood and urine samples from the study subjects to determine the levels of several biomarkers related to chronic low-grade inflammation and also to cancer risk. The researchers will analyze whether different types and intensities of physical activity, measured objectively by the accelerometers, are associated with circulating levels of these inflammation markers. The researchers will also analyze the bio-samples for potential biomarkers of short-term and long-term PA levels.

Project Number: Z01 CP010197

Treating Metabolic Syndrome is Studied to Reduce Pancreatic Cancer Risk

Division of Cancer Biology

Two decades ago, the term "metabolic syndrome" was adopted by researchers and clinicians to describe the cluster of disease risk factors, including resistance to insulin, that develop as people accumulate excess weight. "Knowing these specific processes and targets in the body, we can begin to develop and evaluate ways to prevent and treat metabolic syndrome" as a way to reduce the risk of certain cancers (such as breast and prostate), as well as type 2 diabetes and cardiovascular disease, noted Jin-Rong Zhou, Ph.D., director of the Nutrition/Metabolism Laboratory at Beth Israel Deaconess Medical Center in Boston and assistant professor of surgery at Harvard Medical School.

In 2007, Dr. Zhou was the co-director of a Harvard symposium on "Metabolic Syndrome and the Onset of Cancer," where Dr. Zhou described NCI-supported work in his lab showing that a combination of dietary soy and green tea dramatically reduced four of the risk factors for metabolic syndrome in mice.

So far, Dr. Zhou and others have provided evidence for this link only in breast and prostate cancer. He is now trying to determine whether the syndrome also increases the risk of pancreatic cancer. "We don't really know what causes pancreatic cancer and have not been able to develop effective treatments," he said. Pancreatic cancer is now the fourth leading cause of cancer death, which is why Dr. Zhou believes that finding preventive approaches is crucial.

"We are seeing increases in both metabolic syndrome and pancreatic cancer in the population," Dr. Zhou explained. "If one is causing the other, and we can treat the development of metabolic syndrome, it could prevent a lot of disease that we really don't know how to otherwise effectively treat."

With funding from NCI*, Zhou's lab is exploring whether green and black tea can prevent metabolic syndrome in mice that are genetically-engineered to develop pancreatic cancer. By feeding the mice a diet high in fat and white sugars, the researchers can track elements of the metabolic syndrome to see which may be contributing directly to the appearance and growth of the cancer. "The pancreas is the major organ producing insulin," Dr. Zhou noted. "We think that one of the core risk factors for metabolic syndrome – insulin resistance – could be a factor in pancreatic cancer development."

In his earlier work using a mouse model with prostate cancer, Zhou found that mice given compounds extracted from both teas had significantly lowered body weight when compared to mice not given the tea extracts, although the groups consumed the same number of calories. Other biomarkers for metabolic syndrome were also reduced. The new study in pancreatic cancer mice will allow the researchers to evaluate how the diet might impact some of the other risk factors that comprise metabolic syndrome, including hypertension, low HDL cholesterol, and high triglycerides in the blood. Dr. Zhou's research team will try to correlate changes in these risk factors with the development of pre-cancerous, pancreatic lesions in the mice.

Many people drink green and black tea with minimum side effects, Dr. Zhou commented. Positive results from the mouse studies could lead directly to clinical trials in people, testing a preventive strategy for pancreatic cancer that is practical and safe.

NCI Program Director Ming Lei, Ph.D., commented, "Dr. Zhou's pilot study represents an increasingly important component of DCB's cancer cell metabolism portfolio. Using well-controlled animal models, the research will provide high-quality experimental evidence that is critical for assessing the role of metabolic disorders in pancreatic cancer development, and the efficiency of natural products such as green tea as cancer prevention remedies."

***Grant Number: 1R21CA127794-02**

Accelerating Progress in Cancer Prevention

Prevention is our first line of defense against cancer. Efforts to prevent cancer focus on understanding and modifying behaviors that increase risk, mitigating the influence of genetic and environmental risk factors, and interrupting cancer causing processes through early medical intervention.

Kava Root Compound Shows Promise for the Prevention of Bladder Cancer

Division of Cancer Prevention

Exposure to carcinogens from both tobacco and those associated with working in some industries are known risk factors for bladder cancer. Bladder cancer researchers are interested in certain chemicals in foods or dietary supplements that may help protect against tumor formation and those that naturally concentrate in the urine and pass through the bladder.

Xiaolin Zi, Ph.D., associate professor of urology at the University of California, Irvine, is examining a compound found in kava root called flavokawain A as a potential bladder cancer preventative.

"In the western Pacific islands, where people drink kava beverages like we drink wine, incidences of bladder cancer are low despite high smoking rates," Dr. Zi noted. "I've been investigating whether kava extracts, specific chemical components in kava extracts, or combinations of kava chemicals have anti-bladder cancer activity, and if so, how specific kava compounds can be used for preventing bladder cancers in smokers or even for reducing the risk of bladder cancer recurrence."

In earlier studies,* Dr. Zi and his colleagues performed extensive laboratory analyses of the chemical components of kava root extract, including several belonging to a chemical family called the chalcones. The chalcone flavokawain A had the strongest antiproliferative effect (reducing cell division) and apoptotic effect (causing cell death) in human bladder cancer cell lines derived from several different stages of the disease.

Further studies** showed that the effects of flavokawain A are dependent on a gene called *p53*, a known tumor-suppressor gene that is mutated in many tumor types. Bladder cancer cells with defective *p53* were actually more sensitive to growth inhibition by flavokawain A. The kava compound appears to induce apoptosis by re-activating several genes normally controlled by *p53* through a complex cell-signaling pathway, Dr. Zi explained.

Flavokawain A also reduced tumor growth by 64 percent in mice implanted with bladder cancer cells in these studies. With NCI funding,*** Dr. Zi is currently exploring flavokawain A's anti-cancer effects in several more complex mouse models of bladder cancer, in a series of experiments expected to conclude in 2012.

In one of these models, mice are exposed to the carcinogen 4-hydroxybutyl (butyl) nitrosamine (OH-BBN), which causes tumors that mimic bladder cancer development in smokers. "This model will be used to test the usefulness of flavokawain A for preventing the occurrence of bladder cancer in heavy smokers," explained Dr. Zi.

Two additional transgenic mouse models of bladder cancer will also be used. "These models recapitulate two different molecular pathways leading to two different types of bladder cancer," said Dr. Zi. "We'll use these models to test if flavokawain A can decrease the recurrence of bladder cancer or prevent the progression of bladder cancer into invasive disease, what's sometimes called secondary prevention."

Dr. Zi noted, "Available treatments for preventing bladder cancer recurrences are associated with significant toxicities. We hope that flavokawain A or its derivatives will be a non- or less-toxic oral agent for preventing bladder cancer recurrence, and also for bladder cancer prevention in heavy smokers and people working in a number of high-risk industries."

NCI Program Director for the study Vernon Steele, Ph.D., M.P.H., commented, "Preventing bladder cancer recurrence and bladder cancer prevention are important goals in the field of cancer prevention. This is especially true in heavy smokers and people working in high-risk occupations. Hopefully, flavokawain A or its analogues will be non- or less-toxic oral agents for preventing bladder cancer recurrence and prevention. Positive animal results in a cancer prevention model will help support further development of these agents."

*Zi X, Simoneau AR. Flavokawain A, a novel chalcone from kava extract, induces apoptosis in bladder cancer cells by involvement of Bax protein-dependent and mitochondria-dependent apoptotic pathway and suppresses tumor growth in mice. *Cancer Research*, April 15, 2005; 65(8):3479-86.

**See page 66 for the reference.

***Grant Number: 1R01CA122558-2

Dietary Compounds that Affect the Epigenome Tested for Cancer Prevention

Division of Cancer Prevention

The list of known genetic mutations that can lead to cancer grows daily. In addition, scientists have discovered another layer of complexity driving abnormal gene expression in the disease: epigenetics. Epigenetic changes are changes to a chromosome's structure that do not change the genetic sequence itself, but nonetheless change the way genes are expressed within cells.

For example, a type of epigenetic change – called histone acetylation – controls whether or not a gene can be transcribed into RNA. If too many acetyl groups are removed by enzymes called histone deacetylases (HDACs), the DNA becomes wound too tight and cannot physically be reached by a cell's transcription factors (proteins that control the translation of DNA into RNA). If this complex sequence of events results in "silencing" a tumor suppressor gene, the result can be a cancer cell.

A group of compounds called HDAC inhibitors, which stop the removal of acetyl groups, have shown promise for the treatment of several cancer types. Roderick Dashwood, Ph.D., director of the Cancer Chemoprotection Program at the Linus Pauling Institute at Oregon State University, is exploring the use of HDAC inhibitor compounds found in foods as potential chemopreventive agents for colorectal cancer.

His work so far has concentrated primarily on sulforaphane, a compound found in cruciferous vegetables such as broccoli. Researchers had previously focused on sulforaphane as an inducer of cells' natural detoxification enzymes, which can add polar groups to carcinogens and help remove them from the cells.

"In some studies, carcinogens were given to animals and then followed later by doses of sulforaphane. Tumor suppressor effects were still noted," Dr. Dashwood explained. "If the entire protection was related to induction of detoxification enzymes and enhanced carcinogen excretion, that wouldn't explain why, in an animal that has already been exposed to a colon carcinogen, sulforaphane would still be effective." He added, "When we treated colon cancer cells with sulforaphane, we saw certain genes being turned on in a way that resembled the effects of some HDAC inhibitor drugs, such as vorinostat," which is approved for the treatment of cutaneous T-cell lymphoma.

In a previous study*, Dr. Dashwood and his colleagues first showed that metabolites of sulforaphane act as HDAC inhibitors and can re-activate a gene called p21, which arrests the cell cycle. They also showed that sulforaphane in the diet suppressed colon tumor formation in a mouse model and that the compound both increased acetylation of the histones and expression of p21.

In a human pilot study, a single large serving of broccoli sprouts – a food naturally high in glucoraphanin, the precursor of sulforaphane – was enough to cause significant HDAC inhibition as measured in the participants' peripheral blood mononuclear cells, within 3 hours after eating the broccoli sprouts.

With NCI funding **, Dr. Dashwood's research team is currently expanding their studies of sulforaphane and other potential dietary HDAC inhibitors. In cell cultures, Dashwood's team is investigating which individual HDACs (HDAC1, HDAC2, etc.) control the expression of p21 and which are affected either by sulforaphane or organosulfur compounds from garlic, including the metabolite allyl mercaptan.

However, a detailed understanding of the molecular pathways affected by dietary HDAC inhibitors is needed before moving to clinical trials, Dr. Dashwood cautioned. "We still don't really know precisely what group of genes and downstream pathways specific HDACs are regulating in colon cancer cells versus prostate cancer cells." By studying weaker dietary HDAC inhibitors, "we hope to provide new insights into ways to avoid serious side effects while maintaining therapeutic efficacy," he added.

NCI Program Director Sharon Ross, Ph.D., M.P.H., commented, "NCI's Division of Cancer Prevention believes this project is significant because it will enhance our understanding of how dietary factors in broccoli and garlic, working through epigenetic mechanisms, may increase the expression of tumor suppressor genes, thereby halting aberrant proliferation and/or inducing death of abnormal cells. These studies should inform future dietary intervention trials for cancer prevention."

*Myzak MC, Karplus PA, Chung FL, Dashwood RH. A novel mechanism of chemoprotection by sulforaphane: inhibition of histone deacetylase. *Cancer Research,* August 15, 2004; 64(16):5767-74.

**Grant Number: 1R01CA122959-1

Dietary Flavonols Tested for Colorectal Cancer Prevention

Center for Cancer Research

The NCI Polyp Prevention Trial (PPT) was a multicenter, randomized clinical trial, with almost 2,000 individuals, that tested whether a diet (high-fiber, low-fat, and high in fruits and vegetables) could prevent the recurrence of precancerous adenomas (polyps) in the colon and rectum. However, the researchers found no preventive effect of the healthy diet on polyp recurrence, even after long-term follow up.

Gerd Bobe, Ph.D., a research fellow in NCI's Laboratory of Cancer Prevention, decided to take a closer look at the data from the PPT, focusing on the study participants' intake of flavonols. Flavonols are bioactive compounds in plant-derived foods found in high concentrations in beans, onions, apples, and tea.

"Two recent case-control studies* had shown a protective effect of flavonols against colorectal cancer, and another analysis, specifically of fruit and vegetable intake of the PPT participants, had shown that food groups rich in flavonols were more protective," said Dr. Bobe.

He and his NCI colleagues discovered that a high intake of flavonols by some PPT participants was associated with a significantly decreased risk of advanced adenoma recurrence compared with study participants who had a very low intake of the compounds.

At NCI**, Dr. Bobe is currently testing several individual flavonol compounds for colorectal cancer prevention in a two-stage mouse model of carcinogenesis. The mice are first exposed to a known carcinogen, azoxymethane, and then a colon irritant, dextran sodium sulfate, to specifically initiate tumors in the gastrointestinal tract. Then, they are given different flavonol compounds to test the effects.

These experiments will go beyond identifying the most effective flavonols and the best dosage levels for preventing the formation of colorectal tumors in the mice. Dr. Bobe and his colleagues also hope to identify the molecular targets for the most promising flavonols. The researcher team will also attempt to determine if there are any reliable biomarkers in the blood that can indicate whether a flavonol compound is hitting the molecular target and suppressing tumor formation in the mice.

Dr. Bobe and his colleagues have already demonstrated in previous studies*** the effectiveness of navy beans as colon cancer preventives. They were able to show that cooked navy beans and their residue or extracts reduced the formation of colon lesions in obese mice exposed to azoxymethane. They found that the navy bean diet altered a panel of genes associated with inflammation and identified two proteins that could potentially serve as biomarkers of the diet's anti-carcinogenic effect.

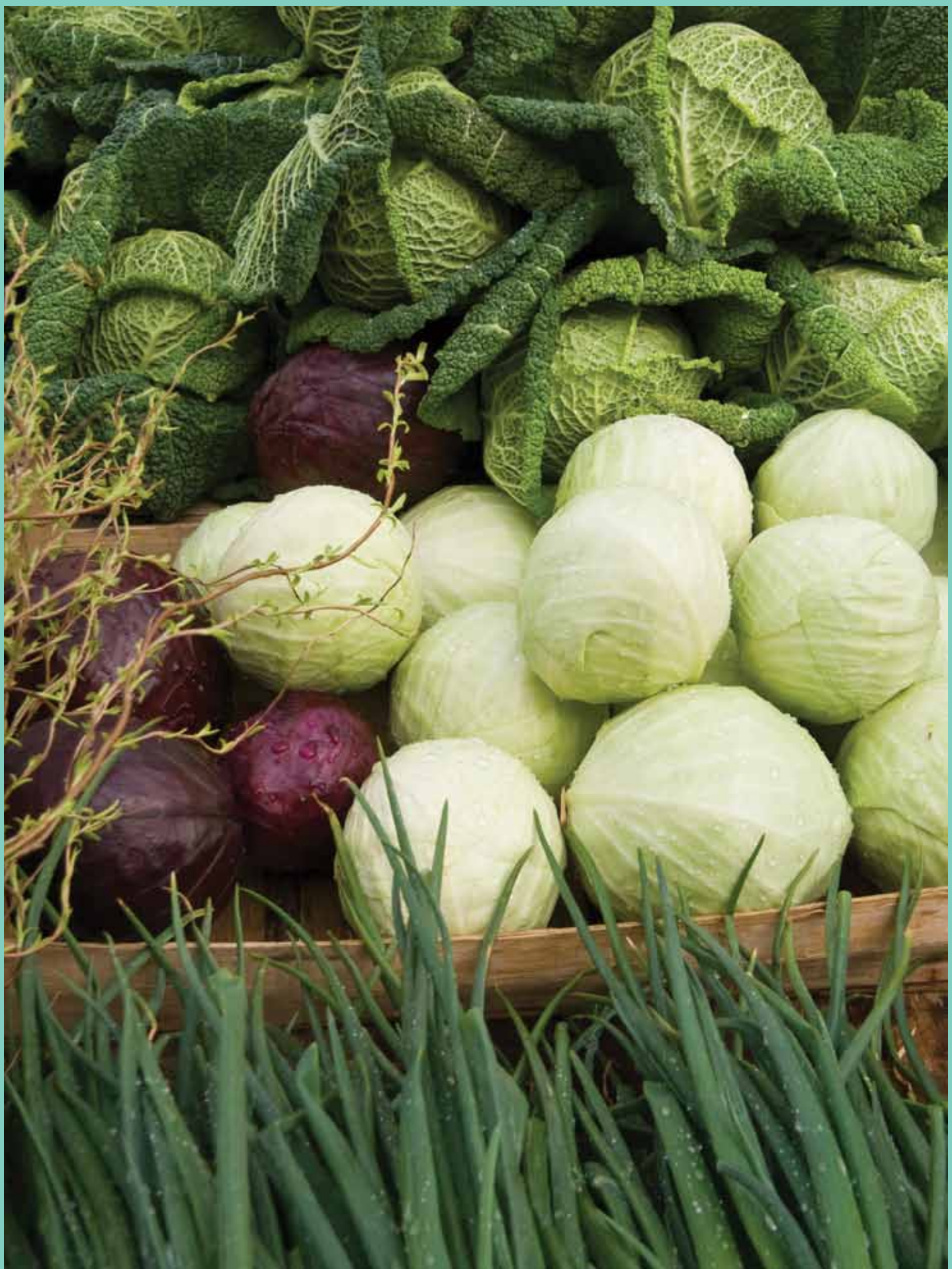
After performing similar experiments with flavonols in their two-step mouse model of colorectal tumor formation, "we're going to go back to analyze the data from the PPT," explained Dr. Bobe. "We have serum samples stored from the trial and detailed dietary data, and we'll look to see whether we can relate the dietary data to levels of the serum biomarkers we identify in our animal studies."

He and Nancy Colburn, Ph.D., director of the NCI Laboratory of Cancer Prevention, hope to eventually conduct a short-term feeding study in about 30 or 40 human volunteers, who would receive a flavonol supplement for four weeks and would be monitored for inflammation by changes in biomarkers. This planned experiment will depend upon preclinical data that validates biomarkers for flavonols' ability to hit their putative molecular targets successfully.

* Bobe G, Sansbury LB, Albert PS, Cross AJ, Kahle L, Ashby J, Slattery ML, Caan B, Paskett E, Iber F, Kikendall JW, Lance P, Daston C, Marshall JR, Schatzkin A, Lanza E. Dietary flavonoids and colorectal adenoma recurrence in the Polyp Prevention Trial. *Cancer Epidemiology, Biomarkers & Prevention,* June 2008; 17(6):1344-53.

*** Mentor-Marcel RA, Bobe G, Barrett KG, Young MR, Albert PS, Bennink MR, Lanza E, Colburn NH. Inflammation-associated serum and colon markers as indicators of dietary attenuation of colon carcinogenesis in ob/ob mice. *Cancer Prevention Research,* January 2009; 2(1):60-9.

**Project Number: Z01BC010025



Environmental and Nutritional Links to Esophageal Cancer Found Globally

Division of Cancer Epidemiology and Genetics

Christian Abnet, Ph.D., M.P.H., has literally traveled around the world in search of answers to questions about what causes esophageal and gastric (stomach) cancers. The investigator from NCI's Nutritional Epidemiology Branch has focused his research sleuthing on high-risk populations for these diseases in China, Iran, Ireland, South America, and Africa.

The populations in those regions have little in common ethnically, culturally, or genetically, so Dr. Abnet tries to identify any "unifying theme" that might tie their high rates of cancer to shared risk factors. For example, people living in certain areas of China, Iran, and Brazil have moderate to very high rates of esophageal squamous cell carcinoma (ESCC). The connecting thread among these far-flung pockets of the disease may be high levels of human exposure to a group of compounds called polycyclic aromatic hydrocarbons (PAH), including the known carcinogen benzo[a]pyrene.

"In Linxian, China, the PAH exposures are from both cooking and heating," Dr. Abnet explained. "They use coal and unventilated stoves, so they're exposed directly to PAHs from breathing the coal smoke. They're exposed indirectly from smoke deposits on their food."

He and his colleagues are still trying to determine the source of high exposure to PAHs in northern Iran. However, in their studies in Brazil, where there are moderately high rates of ESCC, PAH exposure was surprisingly linked to drinking the popular regional beverage, maté– an herbal tea. "We've done some work to show that the amount of benzo[a]pyrene and other PAHs in maté is actually quite high," Dr. Abnet said. With maté drinkers typically consuming one or more liters a day, their exposure levels can be substantial.

Dr. Abnet's research is intended to have public health impact through prevention programs in areas of the world where resources for treating cancer and other serious diseases are limited.

"In China, there is the possibility for change in the way people cook and heat their homes, such as adding chimneys for their stoves," he noted. In South America, "we found variations in the amount of PAHs in the different brands of maté," Dr. Abnet recalled. "So it seems possible to find ways to process the plant leaves in a way that would lower PAH exposure in drinkers, or people may want to avoid drinking maté."

Based on his and his colleagues' earlier research in China, "We have clinical trial and observational epidemiological studies suggesting that the lack of selenium in the diet is a critical determinant of the high risk for ESCC in certain regions. Selenizing salt may be beneficial," Dr. Abnet believes. "We've been discussing with our Chinese research colleagues whether or not it's time for at least a demonstration project where they would selenize salt and look at how it affects the population's levels of selenium and the subsequent cancer rates."

To conduct this wide-ranging research, Dr. Abnet and his collaborators have "built population resources in different parts of the world where we've collected, either through case-control or cohort studies, large datasets and biospecimens for studying cancers in high-risk populations," he said. "We have quite a few ongoing studies looking at several nutrients in addition to selenium. For example, in our study in China, we're in the middle of a project to look at serum vitamin C status in relation to the risk of both ESCC and gastric cancer."

Project Numbers: Z01-CP000185 and Z01-CP000112

Green Tea Shows Promise in Preventing Pancreatic Cancer

Office of Cancer Complementary and Alternative Medicine
Division of Cancer Treatment and Diagnosis

Pancreatic cancer is highly resistant to current chemotherapy and radiotherapy treatments, and therefore, it presents one of the most difficult challenges for cancer clinicians and patients. These challenges provide researchers a strong mandate to develop better treatments than currently exist.

"We really need new [treatment] options," said Rakesh Srivastava, Ph.D., at the University of Texas Health Science Center at Tyler. Pancreatic cancer is difficult to detect in its early stages, he explained. However, when researchers study the disease's progression in the laboratory and in precancerous lesions, pancreatic intraepithelial neoplasias (PanINs), these conditions are usually much more treatable than the usually lethal cancer that will present itself clinically in later stages.

With funding from NCI*, Dr. Srivastava's biochemistry lab is pursuing a lead that has powerful implications from epidemiological studies in China and Japan. A great deal of green tea is consumed daily in those regions, which also have the lowest rates of prostate and stomach cancer in the world. These populations may be benefiting from epigallocatechin-3-gallate (EGCG), a polyphenolic ingredient in green tea that previous laboratory research shows to be an effective anti-cancer component in that beverage.

Dr. Srivastava is trying to chart the mechanisms involved in green tea's preventive effect, as well as trying to determine whether EGCG also works against PanINs. He and his colleagues will develop an oral dose of EGCG for mice and track the molecular impact of the compound on the animals' early signs of pancreatic cancer.

One of the earliest genetic steps on the path to development of PanINs is mutations in the K-ras gene, "which we see highly expressed in more than 90 percent of invasive carcinomas," Dr. Srivastava explained. Based on work from previous studies, the researchers are demonstrating how EGCG inhibits this particular altered metabolic pathway.

"EGCG's effect on pancreatic cancer appears to be multi-pronged," Dr. Srivastava added. Early-stage cancer cells proliferate by going through a series of cycles, but EGCG induces some specific inhibitors to interfere with this process. In addition, he has long been focused on the study of apoptosis, a form of programmed cell death, which cancer cells generally find ways to evade. He has found that EGCG blocks some of the cellular processes that inhibit apoptosis in cancer cells.

"What is promising about EGCG is the redundancy of its protective effects," said Dr. Srivastava. "As a potential non-toxic, dietary preventive, green tea seems to carry a whole program of anti-cancer tools."

OCCAM Program Director Dan Xi, Ph.D., commented, "This study is highly significant, because pancreatic adenocarcinoma still ranks as the most challenging of human malignancies, with an overall five-year survivorship of only three percent."

***Grant Number: 1R01CA125262-1**

Ginger Extract to Be Tested for Lung Cancer Prevention

Office of Cancer Complementary and Alternative Medicine
Division of Cancer Treatment and Diagnosis

Lung cancer currently causes the greatest number of cancer-related deaths in the United States, and no drugs are available to help prevent the disease. Shengmin Sang, Ph.D., assistant professor in the Human Nutrition Research Program at the North Carolina Central University, is studying whether several compounds isolated from the herb ginger could potentially be used to prevent the development of lung cancer.

"Ginger is currently one of the popular dietary supplements in the U.S. market, and it has recently started receiving attention from researchers due to its potential antioxidant, anti-inflammatory, and anti-cancer activity," said Dr. Sang.

In earlier laboratory studies*, Dr. Sang and his colleagues showed that a compound isolated from dried ginger, 6-shogaol, inhibited the growth of human cancer cells and induced apoptosis (cell death) in a colorectal cancer cell line by destroying the mitochondria, the organelles that produce cellular energy.

Much of the previous work testing ginger as an anti-cancer agent has focused on compounds called gingerols, which are found in fresh ginger. Shogaols are formed when ginger is dehydrated. "In our studies, we have found that shogaols have much stronger anti-inflammatory and anti-carcinogenic activity than gingerols," explained Dr. Sang.

One of the challenges for research using botanicals and dietary supplements, explained Dr. Sang, is that there are many compounds with biological activity in any one product. The levels of these compounds can also vary from batch-to-batch in commercial products. When Dr. Sang tested several ginger preparations purchased from a supermarket, the levels of shogaols and gingerols varied substantially among different products.

With funding from the NCI,** Dr. Sang's laboratory is creating a standardized ginger extract high in shogaols. They plan to quantify the levels of shogaols and gingerols in the extract, identify any other bioactive compounds in the final product, and determine the bioavailability of any compounds with anti-cancer activity.

Once they have developed a standardized ginger extract, they will test it in a mouse model of lung carcinogenesis. In this model, mice will be exposed to a lung carcinogen called 4-(Methylnitrosamino-1-(3-pyridyl)-1-butanone (called NNK), which is found in tobacco. Different groups of mice will receive either the standardized ginger extract or extract from fresh ginger before, or after, carcinogen exposure. A third group of mice will not receive ginger. Tumor development will be compared between mice that did or did not receive the ginger extracts.

"The development of a standardized and more-active ginger extract preparation will facilitate future pre-clinical and clinical studies on the health benefits of ginger," said Dr. Sang. "If a standardized ginger extract can be developed into a lung cancer preventive agent, the public health benefit would be tremendous."

* Pan MH, Hsieh MC, Kuo JM, Lai CS, Wu H, Sang S, Ho CT. 6-Shogaol induces apoptosis in human colorectal carcinoma cells via ROS production, caspase activation, and GADD 153 expression. *Mol Nutr Food Res,* 2008 May; 52(5):527-37.

**Grant Number: 1R21CA138277-01A2

Developing Effective and Efficient Treatments

The development of more efficient and effective cancer treatments – that target cancer cells while leaving surrounding healthy tissue unharmed – is at the heart of NCI's research agenda. We strive to develop well tolerated, individualized therapies that are tailored to specific features of a patient's cancer.

Plant Compounds Show Effects Against Prostate Cancer Stem Cells

Center for Cancer Research

Scientists at NCI's CCR are finding early evidence that some plant-based compounds (phytochemicals) – specifically parthenolide, from the Chinese herbal medicine feverfew and gossypol, a compound isolated from cotton-seed oil – can inhibit or eliminate cancer stem cells (CSCs). CSCs are increasingly viewed as the driving force behind relapse and chemotherapy resistance in prostate and other cancers.

A growing body of evidence has identified CSCs, also called tumor-initiating cells, as the major cause of tumor progression, explained William Farrar, Ph.D., head of CCR's Cancer Stem Cell Section and an investigator for the phytochemical study on prostate cancer which is supported by OCCAM.*

Cancer stem cells are believed to be a small subpopulation of cells within a tumor that are able to self-renew as well as give rise to more differentiated tumor cells. It is thought that these stem cells survive initial therapies (such as chemotherapy and hormone therapy) and then generate new tumor cells that are resistant to standard treatments. If prostate cancer stem cells could be identified and characterized, it might be possible to design treatments that prevent resistance.

CSCs are distinct from the cancer "progeny cells," which are created by CSCs and make up the bulk of most tumors. Current cancer treatments focus on destroying the progeny cells "but in many cases, even after the tumor is reduced or seemingly eliminated, it grows back and becomes resistant to further treatment," Dr. Farrar added. Many researchers now believe that the CSCs often survive initial treatment and act like "evil seeds" that regrow new, more treatment-resistant progeny cells.

In the study of parthenolide,** the researchers found that the compound killed more than 90% of CSCs in several prostate cancer cell lines and in primary prostate cancer cells. These findings were validated in mice that were grafted (xenografts) with prostate CSCs and treated with parthenolide. Previous research showed the compound was also effective against CSCs for certain leukemias, which may be the focus of the first human clinical trial of parthenolide, Dr. Farrar noted.

In future studies, Dr. Farrar's lab will expand its library of phytochemicals, including curcumin and quercetin, and isolate CSCs to determine the effectiveness of plant compounds for other cancers. "Besides just killing CSCs, we want to look at whether we can block their ability to metastasize," he said. "We want to get particularly aggressive with researching CSCs' impact on pancreatic cancers."

**Kawasaki BT, Hurt EM, Kalathur M, Duhagon MA, Milner Ja, Kim YS, Farrar WL. Effects of the sesquiterpene lactone parthenolide on prostate tumor-initiating cells: An integrated molecular profiling approach. *The Prostate*, June 1, 2009; 69(8): 827-37.

*Project Number: Z01BC010794

Traditional Chinese Medicine Treatment May Enhance Chemotherapy

Center for Cancer Research

An herbal mixture used in traditional Chinese medicine for over 1,700 years for gastrointestinal problems including diarrhea, nausea, and vomiting has been reformulated in the U.S. This reformulation –PHY 906 – interested U.S. researchers looking for new and better ways to treat the often severe gastrointestinal side effects that can result from chemotherapy.

Yung-Chi Cheng, Ph.D., Henry Bronson Professor of Pharmacology at the Yale University School of Medicine, first looked at the ability of PHY 906 to lessen the gastrointestinal side effects of chemotherapy nine years ago. In an early small clinical study, the compound was successful in reducing the side effects in colon cancer patients receiving the drugs irinotecan and 5-FU.

In animal studies, Dr. Cheng and his colleagues observed a synergistic anti-cancer effect of the compound when given in combination with irinotecan. Although PHY 906 had no effect on animal tumors when given alone, irinotecan plus PHY 906 had greater anti-tumor activity than irinotecan alone.

"Initially, we didn't expect antitumor activity. We were testing PHY 906 purely for relieving side effects," said Dr. Cheng.

PHY 906 is being tested for potential anti-cancer activity in combination with chemotherapy drugs in three different clinical trials: irinotecan for advanced colon cancer resistant to first-line treatment; capecitabine in liver cancer; and capecitabine in pancreatic cancer resistant to first-line gemcitabine. In the pancreatic study, the hope is that reducing the side effects with PHY 906 will allow greater doses of the drug to be given.

So far, preliminary results from all three studies have been promising. In the study with liver cancer patients, the combination appeared to provide a significant survival advantage (compared to historical controls) in Asian patients but not Caucasian patients, although the number of participants was too small to draw definitive conclusions. In the pancreatic cancer study, the addition of PHY 906 allowed for a 50% dose escalation of capecitabine without an increase in side-effects.

One concern with any natural product preparation is consistency, as the levels of active compounds in herbs or other plants can vary from batch to batch and year to year. Dr. Cheng and his colleagues have been able to show that a consistent preparation of PHY 906 can be achieved* by using the tools of mass spectrometry and RNA fingerprinting, which allow different herbal mixtures' effects on RNA expression to be compared.

"The next question was, how exactly does PHY 906 enhance the anti-cancer activity of chemotherapy drugs?" noted Dr. Cheng. In 2008, his laboratory collaborated with Francesco Marincola, M.D., chief of the Infectious Disease and Immunogenetics Section at the NIH Clinical Center**. Dr. Marincola's laboratory has extensive experience using RNA technology to look at the tumor microenvironment under different treatment conditions.

Dr. Marincola is now using whole mouse genome arrays to look at global RNA expression after PHY 906 and chemotherapy drug administration. "We were initially looking for immune altering effects of PHY 906," he explained. "That was our hypothesis of how it worked."

His lab analyzed tumor samples, comparing untreated animals with those treated with chemotherapy only, PHY 906 alone, or the combination. The analysis demonstrated that the herbal formula, when used alone, has potent anti-inflammatory activity that lessens the chronic inflammatory process caused by cancer cells. The combination of PHY 906 and chemotherapy causes a potent inflammatory response similar to that observed during rejection of allografts or of cancer cells during immunotherapy, Dr. Marincola added. "These findings suggest that the PHY 906 may enhance the effects of chemotherapy by adding an anti-cancer immune response."

Future work will look at whether the combination of the herbs and chemotherapy impacts tissues other than those affected by cancer, and if so, what the effects might be.

*Ye M, Liu SH, Jiang Z, Lee Y, Tilton R, Cheng YC. Liquid chromatography/mass spectrometry analysis of PHY906, a Chinese medicine formulation for cancer therapy. *Rapid Communications in Mass Spectrometry,* 2007; 21(22):3593-607.

**Project Number: 5R01CA063477-13

Cruciferous Vegetables Studied for Prevention and Treatment of Pancreatic Cancer

Office of Cancer Complementary and Alternative Medicine
Division of Cancer Treatment and Diagnosis

Pancreatic cancer is one of the most aggressive and lethal solid tumor diseases. Four in five patients live for less than a year after diagnosis and less than five percent reach the five-year benchmark often used to assess cancer survival rates. Researchers are pursuing various approaches to address the urgent need for new and targeted therapeutics for pancreatic cancer.

Among the treatments that have shown early promise in pre-clinical studies is 3,3--diindolylmethane (DIM), a bioactive metabolic component of indole-3-carbinol (I3C) found in cruciferous vegetables like broccoli, Brussels sprouts, and cauliflower. Many cancer researchers studying this compound use a special formulation manufactured by BioResponse, Inc. called B-DIM. In several experiments, B-DIM has inhibited mTOR and Akt, two important molecular pathways in cell proliferation and invasion.

Fazlul Sarkar, Ph.D., professor of pathology at Wayne State University School of Medicine, is experimenting in cell cultures and with mice to demonstrate how B-DIM might effectively prevent as well as treat pancreatic cancer. "With many tumors, there is a switch that seems to unleash the cancer process," he explained. The culprit in pancreatic cancer may be a recently discovered member of the platelet-derived growth factor (PDGF) family known as PDGF-D. "We find it prominently expressed in many of the tumors," Dr. Sarkar added.

This NCI-supported research* is designed to study what happens to the development of pancreatic cancer cells when PDGF-D production is slowed (turned down) by B-DIM, focusing in particular on the impact on cancer stem-like cells. Cancer stem-like cells are the cells in pancreatic and other cancers that drive the reproduction and treatment resistance of cancer cells.

The first prominent effect on pancreatic cells in culture is interference with the expression of a gene called *Notch-1*, which has a role in cell growth. When *Notch-1* is activated, so too is another of the main factors driving tumor progression and metastasis, NF--B, which could be reduced by B-DIM, Dr. Sarkar noted. In turn, two of NF--B's downstream gene targets are also impaired by B-DIM: MMP-9, a matrix metallopeptidase, which also helps cells to spread in the body and aids in bringing a new blood supply (angiogenesis) to the developing pancreatic tumor; and vascular endothelial growth factor, which also spurs angiogenesis, as well as other major steps in the cancer process.

All of these cancer-promoting factors are reduced when PDGF-D is turned down. "We're confident of the results from B-DIM administration in cell culture," said Dr. Sarkar, "because when we went the other way and turned up the PDGF-D production, all of these genes and carcinogenic effects increased."

The next step, now underway, is to confirm that the same set of cellular processes actually happens in mice that are genetically altered to develop and mimic human pancreatic cancer. If that animal disease model proves responsive, Dr. Sarkar and his colleagues will test B-DIM as a way to turn down the PDGF-D production in the mice. The final step in this research strategy would be human clinical trials to test whether B-DIM could actually work as a non-toxic, dietary chemopreventive agent. "It may also be used in conjunction with conventional therapeutics to improve survival of patients diagnosed with this devastating disease," he said.

NCI Program Director Isis Mikhail, M.D., M.P.H., Dr.P.H., commented, "I am very pleased with Dr. Sarkar's progress on his innovative research project on B-DIM. The identification of novel therapeutics from this natural product fits well within OCCAM's Research Development and Support Program portfolio. The findings have promising translational results for the prevention as well as treatment of pancreatic cancer, moving it from bench to bedside."

***Grant Number: 1R01CA131151-02**

Improving the Quality of Life for Cancer Patients, Survivors, and their Families

Advances in our ability to detect, treat, and support cancer patients have turned this disease into one that is chronic, or readily managed, for many and curable for increasing numbers. While the ultimate goal of eliminating cancer altogether continues to be our long term commitment, the capacity to dramatically reduce the suffering caused by cancer is within our immediate grasp.

Traditional Chinese Mind-Body Practice May Relieve Cancer Stress and Improve Quality of Life

Division of Cancer Prevention

Researchers at M.D. Anderson Cancer Center are studying the traditional Chinese mind-body practice of *qigong* (pronounced CHEE-gong) among rectal cancer patients receiving radiation treatments. The researchers are examining qigong as a way to address the considerable distress, impaired quality of life (QOL), and reduced physical function rectal cancer patients experience.

Qigong is an ancient practice in which individuals learn to channel their qi (internal energy flow) to benefit their physical, emotional, mental, or spiritual health. It incorporates stress-reduction techniques including regulated breathing, visual imagery, meditation, and various gentle movements, explained Lorenzo Cohen, Ph.D., director of the Integrative Medicine Program at M.D. Anderson Cancer Center in Houston, Texas.

The qigong technique will be combined with the Chinese slow movement meditation practice of Tai Chi Chuan (TCC). The reason for this addition is the mixed results of a previous study. "Some NCI-funded research that we conducted in China in women with breast cancer used a very similar qigong program," noted Dr. Cohen. "Our initial analysis found the intervention useful for helping to decrease levels of depression." However, "it really had no other beneficial effects for relieving any of the physical side effects of treatment."

"We proposed to NCI* that we add on a TCC component to the qigong program for the rectal cancer study to increase the physical aspects of the intervention," in hopes of getting beneficial results on the physical side effects of the treatment, he added.

The patients will be taught a shortened form of TCC which consists of eight "very simple movements that are all linked together in flowing fashion," Dr. Cohen said. He will compare the qigong/TCC group to a second study arm of patients who will be doing "what we call light exercise." The addition of the exercise group is important, he explained, because "at the end of the study, we should be able to know if is there something about just physical activity and the extra attention you get by participating in one of these interventions, or whether there is actually something a bit more unique about the qigong program that's useful for improving QOL."

There will also be a third group of patients, acting as a control, who receive no intervention. Each of the three study arms will enroll 50 rectal cancer patients. Participants in the qigong and exercise groups will attend practice sessions three days a week throughout their six-week radiotherapy schedule. QOL measures will be assessed among all patients at the beginning of the study and again at one and three months after radiation treatment ends.

If the study is positive, showing unique effects of qigong/TCC, the researchers will conduct future studies to determine "what it is about qigong that improves these outcomes relative to exercise alone," Dr. Cohen said. There may be other, simpler techniques more familiar to Western society that could produce similar results. "However, if we find that the qigong is better than a generic light exercise and relaxation program, it starts to open up a better understanding of these concepts from ancient Chinese medicine," he added.

NCI Program Director Ann O'Mara, Ph.D., commented, "Focusing this intervention on rectal cancer patients is laudatory, since rectal cancer is very understudied, in part, because of its rarity. This is the only project in our portfolio examining ways to mitigate the morbidities associated with rectal cancer and associated treatment."

***Grant Number: 5R21CA129201-02**

Breathing Exercises Studied to Ease Hot Flashes in Breast Cancer

Division of Cancer Control and Population Sciences

Hot flashes associated with treatment-induced menopause in breast cancer survivors can cause stress, sleep disturbances, and otherwise negatively affect the quality of life for many women. The current medications and hormone therapies used to alleviate this bothersome condition are often not particularly effective or may not be a medical option for some survivors. This has led to an increase in research for nonpharmacological interventions for hot flashes.

Slow, deep breathing has previously been recommended as a first-line treatment for hot flashes by the North American Menopause Society. However, the recommendation was based on two, small clinical studies in healthy women. "We thought we should repeat the studies on a larger scale, looking at a similar intervention in the breast cancer survivor community rather than just in menopausal women," noted Janet S. Carpenter, Ph.D., R.N., professor of adult health at Indiana University School of Nursing.

Under a grant from NCI*, Dr. Carpenter is conducting a randomized, controlled clinical study to evaluate a simple CD-ROM/DVD-based at-home training and practice program for a breathing intervention to relieve hot flashes. The study is enrolling 91 breast cancer survivors and 91 healthy women who are randomly assigned to one of the three study arms: 1) breathing program 1 (40% of enrollees); 2) breathing program 2 (40%); or 3) a non-treatment group (20%).

The previous clinical studies showed that if women practiced the technique for 15 minutes, twice-a-day and also applied the technique at the time of a hot flash, the frequency and severity of hot flashes decreased. "This effect may be due to the technique's impact on balancing the parasympathetic and sympathetic nervous systems. We may apply for a supplement to our grant in order to determine how the intervention might be working," Dr. Carpenter said

All of the women in the study are assessed when they enroll in the study and at 8- and 16 weeks after the intervention ended. For a subset of women, a portable respiratory monitor will help evaluate if they are correctly applying the breathing technique. The women will also wear a small device that will serve as an electronic "diary" in which they will record the frequency and severity of hot flashes they have during the study period.

"My early research shows that hot flashes result in negative mood, interference with daily life, and sleep disturbances," Dr. Carpenter noted. "So we're also measuring all of those outcomes in this study. What we're hoping to do is get to a point where we've tested a series of interventions, so we can actually direct women to the best interventions for their cluster of symptoms."

***Grant Number: 5R01CA132927-02**

Scientific Publications

This is a selected list of some of the most important peer-reviewed scientific articles about the findings and analyses of NCI-supported CAM research studies published during FY 2008. The articles are classified and grouped according to research type: cancer prevention, cancer treatment, and cancer side effect/symptom management.

Abstracts of all the articles are available online through the National Library of Medicine's "PubMed" database at http://www.pubmed.gov. A PubMed Identifier (PMID) number is provided for each of the citations.

Prevention

Cho KN, Sukhthankar M, Lee SH, Yoon JH, Baek SJ. Green tea catechin (-)-epicatechin gallate induces tumour suppressor protein ATF3 via EGR-1 activation. *European Journal of Cancer,* November 2007; 43(16):2404-12. Epub Aug. 30, 2007. PMID: 17764926.

Deeb D, Gao X, Dulchavsky SA, Gautam SC. CDDO-Me inhibits proliferation, induces apoptosis, down-regulates Akt, mTOR, NF-kappaB and NF-kappaB-regulated antiapoptotic and pro-angiogenic proteins in TRAMP prostate cancer cells. *Journal of Experimental Therapeutics and Oncology,* 2008; 7(1):31-9. PMID: 18472640.

Guo Y, Xie J, Rubin E, Tang YX, Lin F, Zi X, Hoang BH. Frzb, a secreted Wnt antagonist, decreases growth and invasiveness of fibrosarcoma cells associated with inhibition of Met signaling. *Cancer Research,* May 2008; 68(9):3350-60. PMID: 18451162.

Katiyar SK. Grape seed proanthocyanidines and skin cancer prevention: inhibition of oxidative stress and protection of immune system. *Molecular Nutrition and Food Research,* June 2008; 52 Suppl 1:S71-76. PMID: 18384090.

Kim MH. Protein phosphatase 1 activation and alternative splicing of Bcl-X and Mcl-1 by EGCG + ibuprofen. *Journal of Cellular Biochemistry,* July 2008; 104(4):1491-99. PMID: 18348186.

Kim MH, Chung J. Synergistic cell death by EGCG and ibuprofen in DU-145 prostate cancer cell line. *Anticancer Research,* November-December 2007; 27(6B):3947-56. PMID: 18225555.

Lee JC, Bhora F, Sun J, Cheng G, Arguiri E, Solomides CC, Chatterjee S, Christofidou-Solomidou M. Dietary flaxseed enhances antioxidant defenses and is protective in a mouse model of lung ischemia-reperfusion injury. *American Journal of Physiology-Lung Cellular and Molecular Physiology,* February 2008; 294(2):L255-65. Epub Dec. 14, 2007. PMID: 18083772.

Lee SH, Cekanova M, Baek SJ. Multiple mechanisms are involved in 6-gingerol-induced cell growth arrest and apoptosis in human colorectal cancer cells. *Molecular Carcinogenesis,* March 2008; 47(3):197-208. PMID: 18058799.

Mallery SR, Zwick JC, Pei P, Tong M, Larsen PE, Shumway BS, Lu B, Fields HW, Mumper RJ, Stoner GD. Topical application of a bioadhesive black raspberry gel modulates gene expression and reduces cyclooxygenase 2 protein in human premalignant oral lesions. *Cancer Research,* June 2008; 68(12):4945-57. PMID: 18559542.

Meeran SM, Katiyar SK. Proanthocyanidins inhibit mitogenic and survival-signaling in vitro and tumor growth in vivo. *Frontiers in Bioscience,* January 2008; 13:887-97. PMID: 17981597.

Piyanuch R, Sukhthankar M, Wandee G, Baek SJ. Berberine, a natural isoquinoline alkaloid, induces NAG-1 and ATF3 expression in human colorectal cancer cells. *Cancer Letters,* December 2007; 258(2):230-40. Epub Oct. 25, 2007. PMID: 17964072.

Sukhthankar M, Yamaguchi K, Lee SH, McEntee MF, Eling TE, Hara Y, Baek SJ. A green tea component suppresses posttranslational expression of basic fibroblast growth factor in colorectal cancer. *Gastroenterology,* June 2008; 134(7):1972-80. Epub March 8, 2008. PMID: 18549879.

Shumway BS, Kresty LA, Larsen PE, Zwick JC, Lu B, Fields HW, Mumper RJ, Stoner GD, Mallery SR. Effects of a topically applied bioadhesive berry gel on loss of heterozygosity indices in premalignant oral lesions. *Clinical Cancer Research,* April 2008; 14(8):2421-30. PMID: 18413833.

Treatment

Billam M, Mukhi S, Tang L, Gao W, Wang JS. Toxic response indicators of microcystin-LR in F344 rats following a single-dose treatment. *Toxicon,* May 2008; 51(6):1068-80. Epub Feb, 6, 2008. PMID: 18339415.

Coleman MC, Asbury CR, Daniels D, Du J, Aykin-Burns N, Smith BJ, Li L, Spitz DR, Cullen JJ. 2-deoxy-D-glucose causes cytotoxicity, oxidative stress, and radiosensitization in pancreatic cancer. *Free Radical Biology and Medicine,* February 2008 ; 44(3):322-31. Epub Oct. 16, 2007. PMID: 18215740.

Funahashi H, Satake M, Hasan S, Sawai H, Newman RA, Reber HA, Hines OJ, Eibl G. Opposing effects of n-6 and n-3 polyunsaturated fatty acids on pancreatic cancer growth. *Pancreas,* May 2008; 36(4):353-62. PMID: 18437081.

Ghosh R, Garcia GE, Crosby K, Inoue H, Thompson IM, Troyer DA, Kumar AP. Regulation of Cox-2 by cyclic AMP response element binding protein in prostate cancer: potential role for nexrutine. *Neoplasia,* November 2007; 9(11):893-9. PMID: 18030357.

Lu M, Xia L, Hua H, Jing Y. Acetyl-keto-beta-boswellic acid induces apoptosis through a death receptor 5-mediated pathway in prostate cancer cells. *Cancer Research,* February 2008; 68(4):1180-86. PMID: 18281494.

Lyon DE, McCain NL, Walter J, Schubert C. Cytokine comparisons between women with breast cancer and women with a negative breast biopsy. *Nursing Research,* January-February 2008; 57(1):51-58. PMID: 18091292.

Ma Y, Yu WD, Hershberger PA, Flynn G, Kong RX, Trump DL, Johnson CS. 1alpha, 25-Dihydroxyvitamin D3 potentiates cisplatin antitumor activity by p73 induction in a squamous cell carcinoma model. *Molecular Cancer Therapeutics,* September 2008; 7(9):3047-55. PMID: 18790784.

McAllister SD, Christian RT, Horowitz MP, Garcia A, Desprez PY. Cannabidiol as a novel inhibitor of Id-1 gene expression in aggressive breast cancer cells. *Molecular Cancer Therapeutics,* November 2007; 6(11):2921-7. PMID: 18025276.

Ostberg JR, Dayanc BE, Yuan M, Oflazoglu E, Repasky EA. Enhancement of natural killer (NK) cell cytotoxicity by fever-range thermal stress is dependent on NKG2D function and is associated with plasma membrane NKG2D clustering and increased expression of MICA on target cells. *Journal of Leukocyte Biology,* November 2007; 82(5):1322-31. Epub Aug. 21, 2007. PMID: 17711975.

Wang X, Patet R, Studzinski GP. hKSR-2, a vitamin D-regulated gene, inhibits apoptosis in arabinocytosine-treated HL60 leukemia cells. *Molecular Cancer Therapeutics,* September 2008; 7(9):2798-806. PMID: 18790760.

Side Effect/Symptom Management

Deng G, Vickers A, Yeung S, D'Andrea GM, Xiao H, Heerdt AS, Sugarman S, Troso-Sandoval T, Seidman AD, Hudis CA, Cassileth B. Randomized, controlled trial of acupuncture for the treatment of hot flashes in breast cancer patients. *Journal of Clinical Oncology,* December 2007; 25(35):5584-90. Erratum in: *Journal of Clinical Oncology,* March 2008; 26(9):1572. D'Andrea GM [added]; Xiao H [added]; Heerdt AS [added]; Sugarman S [added]; Troso-Sandoval T [added]; Seidman AD [added]; Hudis CA [added]. PMID: 18065731.

Nelson EL, Wenzel LB, Osann K, Dogan-Ates A, Chantana N, Reina-Patton A, Laust AK, Nishimoto KP, Chicz-DeMet A, du Pont N, Monk BJ. Stress, immunity, and cervical cancer: biobehavioral outcomes of a randomized clinical trial [corrected]. *Clinical Cancer Research,* April 2008; 14(7):2111-8. Erratum in: Clinical Cancer Research, May 2008; 14(9):2892. PMID: 18381952.

Zhang RX, Li A, Liu B, Wang L, Ren K, Zhang H, Berman BM, Lao L. IL-1ra alleviates inflammatory hyperalgesia through preventing phosphorylation of NMDA receptor NR-1 subunit in rats. *Pain,* April 2008; 135(3):232-9. Epub Aug. 6, 2007. PMID: 17689191.

Zhang RX, Li A, Liu B, Wang L, Ren K, Qiao JT, Berman BM, Lao L. Electroacupuncture attenuates bone cancer pain and inhibits spinal interleukin-1 beta expression in a rat model. *Anesthesia and Analgesia,* November 2007; 105(5):1482-88. PMID: 17959986.

Publication from Featured Research

**Tang Y, Simoneau AR, Xie J, Shahandeh B, Zi X. Effects of the kava chalcone flavokawain A differ in bladder cancer cells with wild-type versus mutant p53. *Cancer Prevention Research,* November 2008; 1(6):439-51. (From page 47, Kava Root Compound Shows Promise for the Prevention of Bladder Cancer)

Appendix

An NCI-sponsored clinical trial meets one or more of the following criteria: the protocol (1) has been reviewed and approved by NCI's CTEP Protocol Review Committee or by an approved NCI-designated Cancer Center Protocol Review and Monitoring System and/or (2) receives support through an NCI grant, contract, or cooperative agreement.

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Pediatric Trials					
Phase III Randomized Study of a Therapeutic Music Video Intervention Versus Listening and Discussing Books on Tape for Increased Resilience and Quality of Life of Adolescents and Young Adults Undergoing Myeloablative Autologous or Allogeneic Transplantation for Cancer	COG-ANUR0631	Educational/ Counseling/Training	11 to 24	NINR; NCI	Phase III
Phase III Randomized Study of Glutamic Acid in Reducing Vincristine-Related Peripheral Neurotoxicity in Young Patients Undergoing Vincristine-Containing Treatment for Wilms' Tumor, Rhabdomyosarcoma, Acute Lymphoblastic Leukemia, or Non-Hodgkin's Lymphoma	HLMCC-0402	Supportive care; Treatment	3 to 20	NCI	Phase III
Phase I Study of Beta-Glucan and Rituximab in Pediatric Patients with Relapsed or Progressive CD20-Positive Lymphoma or Leukemia or Post-Allogeneic Stem Cell Transplant-Related Lymphoproliferative Disorder	MSKCC-03095	Treatment	Under 22	NCI	Phase I
Phase I Study of Beta-Glucan and Monoclonal Antibody 3F8 in Patients with Metastatic Neuroblastoma	MSKCC-05073	Treatment; Biomarker/ Laboratory analysis	Any age	NCI	Phase I
Pilot Study of Educational and Promotional Materials Development for Use in Promoting Physical Activity in Community-Based After-School Programs by Multiethnic, Urban Adolescents	MSUHNS-0003669	Prevention; Educational/ Counseling/Training	11 to 14	NCI	No phase specified

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Pediatric Trials					
Randomized Study of Electroacupuncture for Treatment of Delayed Chemotherapy-Induced Nausea and Vomiting in Patients with Newly Diagnosed Pediatric Sarcoma, Neuroblastoma, Nasopharyngeal Carcinoma, Germ Cell Tumors, or Hodgkin Lymphoma	NCCAM-02-AT-0172	Supportive care	5 to 35	NCCAM; NCI	No phase specified
Adult Trials					
Bladder					
Phase II Randomized Study of Neoadjuvant Genistein in Patients Undergoing Surgical Resection for Bladder Cancer	WCCC-CO-04307	Biomarker/Laboratory analysis; Treatment	18 and over	NCI	Phase II
Phase II Randomized Study of Neoadjuvant Polyphenon® E (Defined Green Tea Catechin Extract) in Patients with Nonmetastatic Bladder Cancer	WCCC-UWI06-8-01	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Brain					
Phase II Randomized Study of Adjuvant Boswellia serrata and Standard Treatment Versus Standard Treatment Alone in Patients with Newly Diagnosed or Recurrent High-Grade Gliomas	CASE-CCF-7348	Treatment	18 and over	NCI	Phase II
Pilot Study of a Stress Reduction Program in Patients with Malignant Brain Tumors and Their Family Caregivers	CASE-CCF-2306-CC052	Supportive care	18 and over	NCI	No phase specified
Breast					
Phase III Randomized Study of the Effects of Dietary Soy on Estrogens in Breast Fluid, Serum, and Urine Samples from Healthy Women	UHM-CHS-4116	Prevention; Biomarker/ Laboratory analysis	30 to 45	NCI	Phase III
Phase II Randomized Study of Genistein in Women at High Risk for Breast Cancer	NU-NWU03-1-04	Prevention	25 and older	NCI	Phase II
Phase II Randomized Study of Soy Protein in Postmenopausal Women with Breast Disease Taking Tamoxifen and Experiencing Hot Flashes	CALGB-79805	Supportive care	Postmenopausal (20 and over)	NCI	Phase II

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Phase II Study of Hypericum Perforatum (St. John's wort) in Postmenopausal Women with Non-Metastatic Breast Cancer Suffering from Hot Flashes	CCCWFU-98301	Supportive care	18 and over	NCI	Phase II
Phase II Randomized Study of Three Different Programs of Paced Breathing in Women with Hot Flashes	MAYO-MC06C8	Supportive care	18 and over	NCI	Phase II
Phase II Randomized Study of Acupuncture Versus Standard-of-Care Analgesics in Reducing Pain in Post-Menopausal Women with Breast Cancer and Aromatase Inhibitor-Associated Arthralgia	UARIZ-07-0792-04	Supportive care; Biomarker/Laboratory analysis	Not specified	NCI	Phase II
Phase II Randomized Study of Acupuncture in Reducing Musculoskeletal Symptoms in Women Receiving Aromatase Inhibitors for Stage 0-III Breast Cancer	JHOC-J07110	Supportive care; Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Phase II Study of Gemcitabine Hydrochloride and Genistein in Women with Stage IV Breast Cancer	WSU-C-2597	Treatment	18 and over	NCI	Phase II
Phase II Randomized Study of Omega-3 Fatty Acids in Women with Newly Diagnosed Ductal Carcinoma In Situ and/or Atypical Ductal Hyperplasia	OHSU-3872	Treatment; Biomarker/ Laboratory analysis	Over 21	NCI	Phase II
Phase I/II Randomized Study of Physical Activity Versus Usual Care in Preventing Weight Gain in Women with Newly Diagnosed Stage I or II Breast Cancer Undergoing Adjuvant Chemotherapy	FCCC-FCRB-05-009	Supportive care	18 and over	NCI	Phase I; Phase II
Phase I Pilot Chemoprevention Study of IH636 Grape Seed Proanthocyanidin Extract in Healthy Postmenopausal Women at High Risk of Developing Breast Cancer	CHNMC-IRB-03178	Prevention	40 to 75	NCI	Phase I
Phase I Study of White Button Mushroom Extract in Preventing the Recurrence of Breast Cancer in Postmenopausal Women Who Are Breast Cancer Survivors	CHNMC-07213	Treatment; Biomarker/ Laboratory analysis	21 and over	NCI	Phase I

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Phase I Randomized Study of Green Tea Catechin Extract (Polyphenon E) in Women with a History of Hormone Receptor-Negative Stage I-III Breast Cancer	MDA-MDA04-4-01	Treatment; Prevention; Biomarker/Laboratory analysis	21 to 65	NCI	Phase I
Pilot Study of Standardized Freeze-Dried Table Grape Powder on Plasma Estrogen Levels in Postmenopausal Women Participating in the Mayo Mammography Health Study	MAYO-MC0536	Biomarker/Laboratory analysis; Prevention	18 and over	NCI	No phase specified
Randomized Pilot Study of Flaxseed in Premenopausal Women at Risk of Developing a Primary Breast Cancer	RPCI-I-81906	Prevention; Biomarker/ Laboratory analysis	21 to 50	NCI	No phase specified
Randomized Study of the Effect of a Reduced-Calorie Diet and/or Exercise Program on Risk Factors for Breast Cancer Development in Overweight or Obese Postmenopausal Women	FHCRC-PHS-1960.00	Prevention; Biomarker/ Laboratory analysis; Behavioral study	50 to 75	NCI	No phase specified
Randomized Study of Exercise in Preventing Breast Cancer in Healthy Young Women	UMN-0505M69867	Prevention; Diagnostic	18 to 30	NCI	No phase specified
Randomized Pilot Study of Hypnosis in Controlling Hot Flashes in Women Who are Breast Cancer Survivors	S-WHITE-8165	Supportive care	Over 18	NCI	No phase specified
Randomized Pilot Study of the Effect of Healing Touch in Women with Breast Cancer Experiencing Radiotherapy-Induced Fatigue	VU-VICC–SUPP-0633	Supportive care	21 to 75	NCI	No phase specified
Pilot Study of Pre-Operative Hypnosis to Reduce Post-Operative Pain and Anesthesia-Related Side-Effects in Women Undergoing Surgery for Breast Cancer	CHNMC-08029	Supportive care	18 and over	NCI	No phase specified
Randomized Pilot Study of the Mindful Movement Program in Older Female Breast Cancer Survivors	CHNMC-08061	Supportive care	50 and over	NCI	No phase specified
Randomized Study of Hatha Yoga in Improving Physical Activity, Inflammation, Fatigue, and Distress in Female Breast Cancer Survivors	OSU-2007C0004	Supportive care; Biomarker/Laboratory analysis	21 and over	NCI	No phase specified

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Randomized Study of Education with or without Exercise and Counseling in Preventing Lymphedema in Women with Stage I-III Breast Cancer Who Are Undergoing Axillary Lymph Node Dissection	CALGB-70305	Supportive care; Treatment	18 and over	NCI	No phase specified
Randomized Pilot Study of Neoadjuvant Therapy Comprising Flaxseed and/or Anastrozole in Postmenopausal Women Undergoing Surgery for Newly Diagnosed, Estrogen Receptor-Positive, Stage I or II Breast Cancer	RPCI-I-99507	Treatment; Biomarker/ Laboratory analysis	18 to 85	NCI	No phase specified
Cervix					
Phase II Randomized Study of Green Tea Extract (Polyphenon E) for the Prevention of Cervical Cancer in Patients with Human Papillomavirus (HPV) and Low-Grade Cervical Intraepithelial Neoplasia (CIN 1)	UARIZ-UAZ03-1-02	Prevention	18 and over	NCI	Phase II
Phase II Study of Folic Acid Supplementation in Women Infected with HPV-16 and Diagnosed with Grade 1 or Less Cervical Intraepithelial Neoplasia	UAB-F060511015	Prevention; Biomarker/ Laboratory analysis	19 and over	NCI	Phase II
Phase I Randomized Study of Leucine-Enhanced Essential Amino Acid Supplement and/or Testosterone for Cancer-Related Cachexia in Patients with Advanced or Recurrent Cervical Carcinoma	UTMB-06073	Supportive care; Biomarker/Laboratory analysis	18 to 59	NCI	Phase I
Randomized Study of Mindfulness-Based Stress Reduction Versus General Health Education in Improving Immune Response to Human Papilloma Virus in Patients with Cervical Dysplasia	FCCC-06851	Behavioral study; Educational/Counseling/ Training; Biomarker/ Laboratory analysis	18 and over	NCI	No phase specified
Colon/Rectum					
Phase III Study of the Effect of Vitamin E and/or Selenium on Adenomatous Colorectal Polyps in Men Enrolled on SELECT Trial SWOG-S0000	SWOG-S0000D	Natural history/ Epidemiology; Prevention	50 and over	NCI	Phase III

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Phase III Randomized Study of Selenium in Patients with Adenomatous Colorectal Polyps	UARIZ-00-0430-01	Prevention	40 to 80	NCI	Phase III
Phase II Randomized Chemoprevention Study of Atorvastatin Versus Oligofructose-Enriched Inulin (Raftilose Synergy 1) Versus Sulindac in Patients at Increased Risk of Developing Sporadic Colorectal Neoplasia	MAYO-030103	Prevention; Biomarker/ Laboratory analysis	40 and over	NCI	Phase II
Phase II Randomized Study of Acupuncture in Reducing Postoperative Ileus in Patients Who Have Undergone Segmental or Subtotal Colectomy for Colorectal Cancer	MSKCC-06145	Supportive care	Over 18	NCI	Phase II
Phase I Study of Resveratrol in Patients with Resectable Colorectal Cancer	CCUM-TASK2B	Treatment; Biomarker/ Laboratory analysis	Over 18	NCI	Phase I
Pilot Randomized Study of Cholecalciferol and Calcium Carbonate in Patients with Resected Colon Cancer	RPCI-I-78706	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	No phase specified
Esophagus					
Phase IB Randomized Study of Green Tea Extract (Polyphenon E) in Preventing Esophageal Cancer in Patients with Barrett's Esophagus	MDA-03101	Prevention	18 and over	NCI	Phase I
Head and Neck					
Phase III Randomized Study of Acupuncture Versus Standard of Care in Treating Pain and Dysfunction in Patients with Head and Neck Cancer Who Have Undergone Neck Dissection	MSKCC-03131A	Supportive care	Not specified	NCI	Phase III
Phase II/III Randomized Study of Acupuncture-Like Transcutaneous Electrical Nerve Stimulation (ALTENS) Versus Pilocarpine Hydrochloride in Head and Neck Cancer Patients with Early Radiotherapy-Induced Xerostomia	RTOG-0537	Supportive care	18 and over	NCI	Phase II; Phase III
Phase II Randomized Study of Fruit and Vegetable Extracts in Patients with Stage I-IVB Head and Neck Cancer	CCCWFU-0112	Treatment	18 and over	NCI	Phase II

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Phase I Randomized Study of Antioxidant-Deficient Diet in Controlling Cachexia in Patients with Oropharyngeal Cancer Receiving Chemoradiotherapy	UNC-LCCC-0523	Supportive care; Biomarker/Laboratory analysis; Treatment	Over 18	NCI	Phase I
Randomized Pilot Study of Electroacupuncture for Chronic Radiation-Induced Xerostomia in Patients with Head and Neck Cancer	MAYO-MCS285	Supportive care	21 to 89	NCI	No phase specified
Hematologic					
Phase III Randomized Study of American Ginseng Extract to Prevent Respiratory Infection and Reduce Antibiotic Use in Patients with Chronic Lymphocytic Leukemia	CCCWFU-98308	Supportive care	18 and over	NCI	Phase III
Phase I/II Study of Green Tea Extract (Polyphenon E) in Patients with Previously Untreated Stage 0-II Chronic Lymphocytic Leukemia	MAYO-MC0419	Treatment	18 and over	NCI	Phase I; Phase II
Lung					
Phase III Randomized Chemoprevention Study of Selenium in Participants with Previously Resected Stage I Non-Small Cell Lung Cancer	ECOG-5597	Prevention	18 and over	NCI	Phase III
Phase II Randomized Study of Defined Green Tea Catechin Extract in Former or Current Heavy Smokers with Abnormal Sputum Score	BCCA-H03-61083	Prevention; Biomarker/ Laboratory analysis	45 to 74	NCI	Phase II
Phase II Randomized Study of Green Tea or Polyphenon E in Preventing Lung Cancer in Former Smokers with Chronic Obstructive Pulmonary Disease	UARIZ-HSC-0353	Prevention; Biomarker/ Laboratory analysis	40 to 80	NCI	Phase II
Phase II Chemoprevention Study of Curcumin in Current Smokers with Aberrant Crypt Foci	UCIRVINE-UCI04-2-01	Prevention; Biomarker/ Laboratory analysis	40 and over	NCI	Phase II
Phase II Randomized Study of Polyphenon E, A Defined Green Tea Catechin Extract, in Current or Former Smokers with Bronchial Dysplasia	BCCA-H07-02401	Prevention; Biomarker/ Laboratory analysis	45 to 74	NCI	Phase II

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Phase I Pilot Study of Calcitriol in Smokers or Former Smokers with Squamous Metaplasia or Squamous Dysplasia of the Lungs	RPCI-I-90206	Prevention; Biomarker/ Laboratory analysis	40 to 79	NCI	Phase I
Phase I Study of Beta-Glucan MM-10-001in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer	CHNMC-07243	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI; Pharmaceutical/ Industry	Phase I
Chemoprevention Study of Broccoli Sprout Extract in Smokers	JHOC-J0427	Prevention	Over 18	NCI	No phase specified
Multiple					
Pilot Randomized Study of Cognitive-Behavioral Therapy Versus Standard Care in Patients with Advanced Gastrointestinal Cancer or Lung Cancer	MGH-2007-P-000368	Educational/ Counseling/Training; Supportive care	Over 18	NCI	No phase specified
Non-Cancer					
Phase I Randomized Study of Nutritional-Grade, Absorption-Enhanced Diindolylmethane (BR-DIM) in Healthy Volunteers	KUMC-HSC-9139-3	Biomarker/Laboratory analysis; Prevention	18 to 70	NCI	Phase I
Phase I Study of Resveratrol in Healthy Adult Participants	UARIZ-BIO-07-0376-04	Biomarker/Laboratory analysis; Prevention	18 and over	NCI	Phase I
Phase I Randomized Study of Garlic Supplements to Modulate Opioid Effects in Healthy Volunteers	FHCRC-2040.00	Natural history/ Epidemiology; Biomarker/Laboratory analysis	21 to 45	NCI	Phase I
Phase I Randomized Study of a New Formulation of Bowman-Birk Inhibitor Concentrate in Healthy Male Participants	UPCC-805938	Prevention; Biomarker/ Laboratory analysis	18 to 65	NCI	Phase I
Randomized Study of a Patient-Directed Lifestyle Change and Health Promotion Program Versus Usual Care in Low-Income, Uninsured Participants in Los Angeles County, California	UCLA-G-060801501A	Behavioral study; Educational/Counseling/ Training; Health services research	18 and over	NCI	No phase specified
Pilot Study of a Combination Nutritional Supplement Capsule Containing Curcumin, Green Tea Extract, Polygonum cuspidatum Extract, and Soybean Extract in Healthy Participants	WSU-2007-109	Biomarker/Laboratory analysis; Prevention	18 and over	NCI	No phase specified

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Prostate					
Phase III Randomized Study of Soy Protein/Isoflavones and Venlafaxine on Vasomotor Symptoms in Patients with Prostate Cancer Undergoing Hormonal Manipulation	CCCWFU-97405	Supportive care	21 and over	NCI	Phase III
Phase III Randomized Study of Pomegranate Extract in Patients with Rising Prostate-Specific Antigen Levels After Surgery or Radiotherapy for Localized Prostate Cancer	ROLL-GUP-0205-1	Treatment	18 and over	NCI; Pharmaceutical/ Industry	Phase III
Phase II/III Randomized Study of Adjuvant Soy Protein Isolate in Preventing Recurrence in Patients Who Have Undergone Radical Prostatectomy for Stage II Prostate Cancer	UIC-2006-0706	Treatment; Biomarker/ Laboratory analysis	40 to 75	NCI	Phase II; Phase III
Phase II Randomized Chemoprevention Study of Calcitriol in Patients with High-Grade Prostatic Intraepithelial Neoplasia	CINJ-080404	Prevention	18 and over	NCI	Phase II
Phase II Randomized Pilot Study of Calcitriol and Dexamethasone Before Radical Prostatectomy in Patients with Localized Adenocarcinoma of the Prostate	RPCI-RP-0212	Treatment	18 and over	NCI	Phase II
Phase II Randomized Study of Different Doses of Cholecalciferol (Vitamin D) in Patients with Prostate Cancer	RPCI-I-95406	Treatment	18 and over	NCI	Phase II
Phase II Randomized Study of Selenium in Patients with Adenocarcinoma of the Prostate	UARIZ-97-0395	Treatment; Biomarker/ Laboratory analysis	Under 85	NCI	Phase II
Phase II Randomized Study of Neoadjuvant Dietary Supplementation with Soy in Patients Undergoing Radical Prostatectomy for Localized Prostate Cancer	CCCWFU-98203	Treatment; Biomarker/ Laboratory analysis	Over 18	NCI	Phase II
Phase II Study of Calcitriol and Dexamethasone in Patients with Androgen-Independent Prostate Cancer	RPCI-I-65405	Treatment; Biomarker/ Laboratory analysis	Not specified	NCI	Phase II

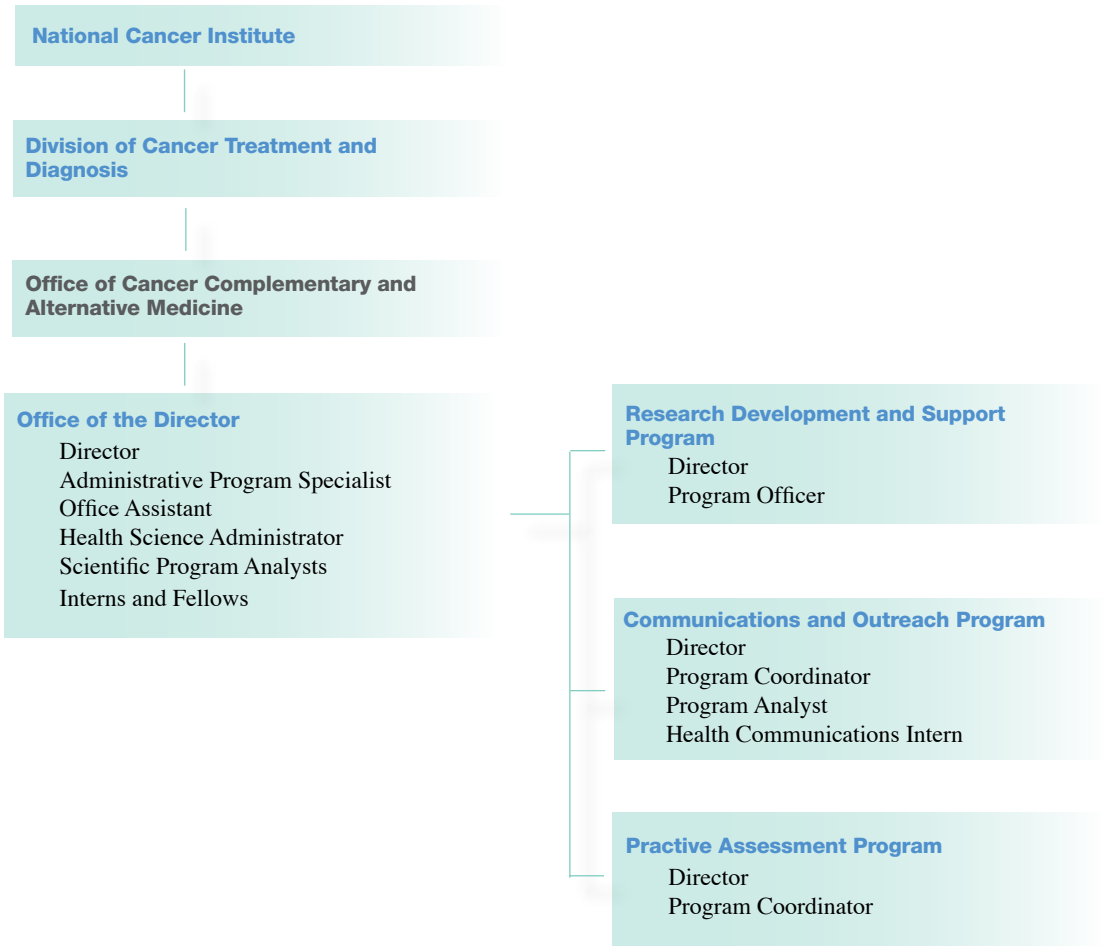
PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Phase II Randomized Study of Green Tea and Decaffeinated Black Tea Versus Water in Patients with Adenocarcinoma of the Prostate Scheduled to Undergo Prostatectomy	UCLA-061109702	Treatment; Biomarker/ Laboratory analysis	40 to 75	NCI	Phase II
Phase II Randomized Study of Neoadjuvant Lycopene Supplementation in Patients Undergoing Radical Prostatectomy for Prostate Cancer	MDA-04-3-01	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Phase II Randomized Study of Selenomethionine and Finasteride Prior to Prostatectomy or Bracytherapy in Patients with Stage I or II Prostate Cancer	RPCI-I-104607	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Phase II Randomized Study of Selenomethionine Supplementation in Patients Undergoing Prostatectomy or Brachytherapy for Stage I or II Prostate Cancer	RPCI-I-104307	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Phase I Study of Absorption-Enhanced Diindolylmethane (BioResponse-DIM) in Patients with Nonmetastatic, Hormone-Refractory Prostate Cancer and Rising Prostate-Specific Antigen Levels	WSU-D-2979	Treatment	18 and over	NCI	Phase I
Phase I Randomized Study of Neoadjuvant Diindolylmethane in Patients Undergoing Radical Prostatectomy for Stage I or II Adenocarcinoma of the Prostate	WCCC-CO05186	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase I
Phase I Study of Defined Green Tea Catechin Extract in Patients with Prostate Cancer Scheduled to Undergo Prostatectomy	UARIZ-UAZ05-6-01	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase I
Phase I Study of White Button Mushroom Extract at Six Different Dose Levels in Patients with Biochemically Recurrent, Hormone-Naive Prostate Cancer After Local Therapy	CHNMC-08012	Treatment; Biomarker/ Laboratory analysis	Not specified	NCI	Phase I
Randomized Study of the Molecular Effects of Lycopene Versus Omega-3 Fatty Acid Nutritional Supplements in Patients with Stage I or II Prostate Cancer	UCSF-03553	Biomarker/Laboratory analysis; Treatment	Not specified	NCI	No phase specified

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Randomized Study of Fish Oil Supplements and Green Tea Extract in Preventing Prostate Cancer in Patients Who Are at Risk for Developing Prostate Cancer	OHSU-CI-CPC-04131-LX	Prevention	18 and over	NCI	No phase specified
Randomized Study of Lycopene in Preventing Prostate Cancer in Healthy Participants	UIC-2004-0217	Prevention; Biomarker/ Laboratory analysis	18 and over	NCI	No phase specified
Study of Acupuncture in Treating Hot Flashes in Patients with Prostate Cancer Undergoing Androgen Deprivation	OHSU-7235	Supportive care	Over 18	NCI	No phase specified
Randomized Study of Polyunsaturated Fatty Acids in Patients with Prostate Cancer Undergoing Prostate Biopsy and/or Surgery	DFCI-03116	Treatment; Biomarker/ Laboratory analysis	Adult	NCI	No phase specified
Ovarian					
Randomized Study of Hypnosis, Massage Therapy, and Healing Touch in Patients Undergoing Chemotherapy for Ovarian Epithelial or Primary Peritoneal Cavity Cancer	UMN-2000NT790	Supportive care	Any age	NCI	No phase specified
Non-Specified					
Phase III Randomized Study of (Valerian) for Improving Sleep in Patients with Cancer Receiving Adjuvant Therapy	NCCTG-N01C5	Supportive care	18 and over	NCI	Phase III
Phase III Randomized Study of Levocarnitine (L-carnitine) for the Management of Fatigue in Cancer Patients	ECOG-E4Z02	Supportive care	18 and over	NCI	Phase III
Phase III Randomized Study of Alpha-Lipoic Acid in Preventing Platinum-Induced Peripheral Neuropathy in Cancer Patients Receiving a Cisplatin- or Oxaliplatin-Containing Chemotherapy Regimen	MDA-CCC-0327	Supportive care	Not specified	NCI	Phase III
Phase III Randomized Study of Vitamin E in Preventing Chemotherapy-Induced Peripheral Neuropathy in Patients Undergoing Curative Neurotoxic Chemotherapy for Cancer	NCCTG-N05C3	Supportive care	18 and over	NCI	Phase III

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Phase II/III Randomized Study of Ginger for Chemotherapy-Related Nausea in Patients with Cancer	URCC-U1902	Supportive care	18 and over	NCI	Phase II; Phase III
Phase II Randomized Study of a Multimedia Program About Massage Therapy for Cancer Patients and Their Care Partners	COLLINGE-06-200	Educational/Counseling/ Training; Supportive care	21 and over	NCI	Phase II
Phase II Randomized Pilot Study of Massage Therapy in Patients with Cancer Pain	MSKCC-03046A	Supportive care	18 and over	NCI	Phase II
Phase II Randomized Study of Ginger in Patients with Cancer and Chemotherapy-Induced Nausea and Vomiting	CCUM-0201	Supportive care	18 and over	NCI; NCCAM	Phase II
Phase II Randomized Study of Hatha Yoga for Persistent Sleep Disturbance in Cancer Survivors	URCC-U3905	Supportive care	21 and over	NCI	Phase II
Pilot Study of Psilocybin in Patients with Clinically Significant Depression or Anxiety Secondary to Cancer	JHOC-J0647	Supportive care; Biomarker/ Laboratory analysis	21 to 70	NCI	Phase II
Phase II Randomized Chemoprevention Study of Bowman-Birk Inhibitor Concentrate in Patients with Oral Leukoplakia	UCIRVINE-UCI-98-34	Treatment; Prevention; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Phase I/II Pilot Study of Genistein in Patients Undergoing Palliative External Beam Radiotherapy for Osseous Metastases	UMN-2008LS035	Treatment	18 and over	NCI	Phase I; Phase II
Phase I Study of High-Selenium Brassica Juncea in Combination with Irinotecan Hydrochloride and Capecitabine in Patients with Advanced Malignancies	CHNMC-05122	Treatment	18 and over	NCI	Phase I
Pilot, Randomized Study of Mindfulness Relaxation Versus Relaxing Music Versus Standard Symptom Management Education in Patients with Newly Diagnosed Solid Tumors Undergoing Chemotherapy	MDA-CCC-0106	Educational/ Counseling/Training	18 and over	NCI	No phase specified
Randomized Study of Stress Management Therapy in Patients Undergoing Chemotherapy for Cancer	MCC-0501	Educational/ Counseling/Training; Supportive care	18 and over	NCI	No phase specified

PDQ Cancer CAM Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Adult Trials					
Randomized Study of Magnetic Acupressure in Reducing Pain in Cancer Patients Undergoing Bone Marrow Aspiration and Biopsy	JHOC-J07103	Supportive care; Diagnostic	18 and over	NCI	No phase specified
Randomized Pilot Study of Glutamine Supplementation for the Prevention of Paclitaxel-Induced Myalgia and/or Arthralgia in Patients with Cancer	OHSU-ONC-99037-L	Supportive care	18 and over	NCI	No phase specified
Pilot Study of Art Therapy Intervention for Caregivers of Pediatric Patients Undergoing Bone Marrow Transplantation for Cancer	CHNMC-08028	Supportive care	18 and over	NCI	No phase specified
Randomized Study of Resistance Exercise via Negative-Eccentric Work (RENEW) in Improving Mobility and Reducing Fatigue and/or Weakness in Elderly Cancer Survivors	UUMC-R21CA114523	Supportive care	60 and over	NCI	No phase specified
Randomized Study of an L-Arginine-Based Nutritional Supplement (ArginMax®) in Female Cancer Survivors	CCCWFU-05-04-01	Supportive care	Adult	NCI	No phase specified
Randomized Study of the Effect of Animal-Assisted Therapy and Recreational Therapy on Distress in Cancer Patients Undergoing Treatment for Pain	NCI-05-CC-0093	Supportive care; Biomarker/ Laboratory analysis	18 and over	NCI	No phase specified

OCCAM Organizational Chart



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