National Cancer Institute

Office of Cancer Complementary and Alternative Medicine

ANNUAL REPORT ON

COMPLEMENTARY AND ALTERNATIVE MEDICINE

FISCAL YEAR

2010

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

DIRECTOR'S MESSAGE

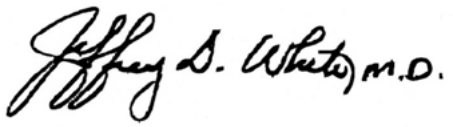
The research the National Cancer Institute (NCI) supports, both in our own laboratories and at institutions worldwide, is focused on the ultimate goal of helping cancer patients. That mission – achieved through rigorous science – extends to NCI's program on complementary and alternative medicine, also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

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

Among the highlights of NCI's CAM-related activities in fiscal year (FY) 2010, was the collaboration between NCI, the National Institutes of Health's Office of Dietary Supplements (ODS), and the National Center for Complementary and Alternative Medicine (NCCAM) to co-fund two Botanical Research Centers. The Botanical Research Centers Program aims to promote collaborative, integrated, interdisciplinary study of botanicals, particularly those found as ingredients in dietary supplements, and to conduct research with high potential for being translated into practical benefits for human health. The two centers co-funded by NCI are located at the University of Illinois at Urbana-Champaign and the University of Missouri. The NCI-funded centers will research botanical products used in the fight against cancer, specifically breast and prostate cancer.

NCI's commitment to CAM research and clinical practice has been steadily supported, coordinated, and expanded by the Office of Cancer Complementary and Alternative Medicine (OCCAM) over the years. OCCAM's goal is to increase NCI's ability to extend the search for effective therapies into areas that show promise, but which often are not thoroughly explored in 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 they are considering. It is our duty to conduct and support the science that makes wise and informed decisions possible.



Jeffrey D. White, M.D.
Director
Office of Cancer Complementary
and Alternative Medicine
Division of Cancer Treatment and Diagnosis
National Cancer Institute

The following acronyms are used throughout this report:

NCI	National Cancer Institute
FY	Fiscal Year
CAM	complementary and alternative medicine
OCCAM	Office of Cancer Complementary and Alternative Medicine
NIH	National Institutes of Health
DCB	Division of Cancer Biology
DCCPS	Division of Cancer Control and Population Sciences
DCP	Division of Cancer Prevention
DCTD	Division of Cancer Treatment and Diagnosis
CCR	Center for Cancer Research
DCEG	Division of Cancer Epidemiology and Genetics
BRC	Botanical Research Center
ODS	Office of Dietary Supplements
NCCAM	National Center for Complementary and Alternative Medicine
MOU	Memorandum of Understanding
ERP	Extramural Research Program
COP	Communications and Outreach Program
CRISP	Case Review and Intramural Science Program
ARRA	American Recovery and Reinvestment Act
FOA	funding opportunity announcement
CARRA	Consumer Advocates in Research and Related Activities
BCS	Best Case Series
PDQ®	Physician Data Query®
CIS	Cancer Information Service
CRTA	Cancer Research Training Award

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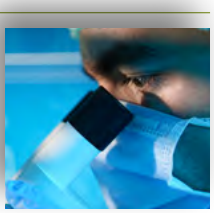
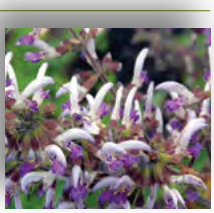
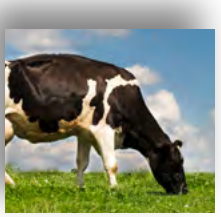






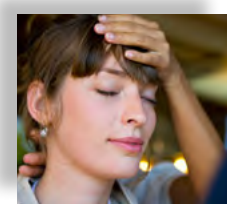


Figure 1. Major Categories of CAM Therapies

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** 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 certain prescription drugs, hormones, complex natural products, vaccines, and other biological interventions not yet accepted in mainstream medicine.

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

Sub-category: 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

This report highlights the National Cancer Institute's initiatives and annual expenditures in complementary and alternative medicine (CAM)* research. It is intended as a way for NCI to communicate its progress in this area of medical research to all interested stakeholders including cancer researchers, CAM practitioners, health care providers, advocacy organizations, cancer patients and the general public.

Similar to the previous reports, this publication provides an overview of the NCI-supported work in this field along with details on selected projects in the areas of cancer CAM relating to communication, training and conferences, and research. For more information on specific projects included in this report please visit the NIH Research Portfolio Online Reporting Tools (RePORTER) database (http://projectreporter.nih.gov/reporter.cfm) and search the grant or project number.

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 (DCCPS), Division of Cancer Prevention (DCP), and the Division of Cancer Treatment and Diagnosis (DCTD), along with projects from NCI's intramural laboratories in the 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. Also included in the report is a breakdown of NCI's CAM research portfolio. In FY 2010, NCI's research expenditures for CAM were an estimated $114,460,116 for the funding of 406 CAM research projects. In addition, during FY 2010, NCI used $6,646,594 in funds from the American Recovery and Reinvestment Act (ARRA) to award 27 CAM research grants.

As this report on cancer CAM indicates, we at the NCI are committed to an integrated approach to bring together all of the many resources and approaches necessary to decrease the frequency, destructiveness, and lethality of cancer. We believe that evidence-based CAM techniques, systems, and products can have an important role in reaching 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 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.)

NCI CAM Research Funding Portfolio Analysis:
FY 2010

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 OCCAM is responsible for gathering the data needed to report the total CAM expenditures budget figure each year.

It is a common misconception that OCCAM manages all of the CAM projects for NCI. The vast majority of CAM projects are managed by other programs and laboratories throughout the Institute. After the close of the fiscal year, NCI's Division of Extramural Activities (DEA) provides OCCAM with a list of funded grants and cooperative agreements coded as containing some component of CAM research. Similarly, NCI's two intramural components, the Center for Cancer Research (CCR) and the Division of Cancer Epidemiology and Genetics (DCEG), provide lists of their potentially relevant projects. Also, a list of contracts identified as potentially containing CAM research is provided. OCCAM staff review each project to confirm they are accurately classified as CAM research. Then aspects of each project are identified allowing their placement into sub-categories based on the type of research and CAM intervention investigated.

NCI's total CAM expenditure figure includes money awarded for intramural projects (projects conducted within NIH facilities and labs), extramural grants (projects conducted outside of NIH), cooperative agreements, contracts, and supplements. It is important to note the reported figure for total NCI CAM expenditures for a fiscal year only includes projects for which NCI is the primary funder.

Total Estimated Cancer CAM Research Expenditure

In FY 2010, NCI invested $114,460,116 for 406 intramural and extramural research projects relevant to CAM. For the purpose of the FY 2010 analysis, the following types of funding are included: intramural projects and extramural grants, cooperative agreements, contracts, and supplements (Figure 3).

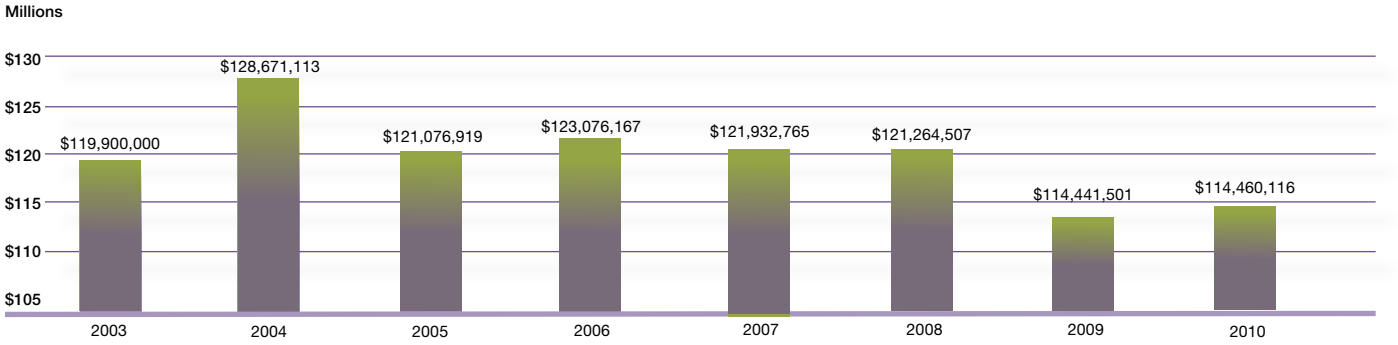
In addition, during FY 2010, NCI used $6,646,594 in funds from the American Recovery and Reinvestment Act (ARRA) to award 27 CAM research grants.

The above numbers do not include CAM training grants (T and F awards), K (research career) or R25 (cancer education) grants. These numbers are listed separately in Figure 4.

Grant Awards by Funding Opportunity Announcement

In FY 2010, there were 65 funding opportunity announcements (FOA) that yielded cancer CAM grants. The program announcement (PA) "Research Project Grants (Parent R01)" (PA-07-070) was the most productive mechanism for attracting new CAM grants to NCI. A total of 85 of the 238 CAM grants awarded through FOAs in FY 2010 came to NCI through this announcement (Figure 5).

Figure 3. NCI CAM Expenditures: FY 2003-2010*



* 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) and ARRA funds. Total projects include all active projects in FY 2010.

Figure 4. NCI CAM Training Projects 2010

Training Grant Mechanisms	Number of Grants	Total Funding
F (31, 32)	3	$ 48,892
K (01, 05, 07, 22, 23, 24)	19	$1,427,308
R25	4	$ 782,445
T32	1	$ 46,140
TOTAL	**27**	**$2,304,785**

Note: does not include ARRA funded projects.

Breakdown by Research Type

The accompanying pie-chart (Figure 6) shows the distribution of the projects by prevention, treatment, symptom/side effects management, epidemiology, and conferences. In FY 2010, 61.5% of cancer CAM-related research project funds went to various cancer prevention efforts, while treatment, symptom/side effects management, epidemiology, and conferences received 19.7%, 11.2%, 7.5%, and 0.004% respectively.

Breakdown by Major CAM Therapy Category

In FY 2010, NCI performed or supported research addressing a variety of CAM approaches (Figure 7). These CAM therapies fall into nine groups: alternative medicine systems, energy therapies, exercise therapies, manipulative and body-based methods, mind-body interventions, nutritional therapeutics, pharmacological and biologic treatments, spiritual therapies, and miscellaneous. (See page 4 for definitions of CAM categories.)

Figure 5. Number of Grant Awards by Funding Opportunity Announcement

AT03-002	2	PA04-046	1	PA06-351	4	PA07-100	2	PA07-362	8	PA08-220	2	PAR08-020	1
AT08-003	1	PA04-099	2	PA06-400	3	PA07-174	1	PA08-032	1	PA09-010	3	PAR08-055	14
CA04-004	1	PA05-027	1	PA06-412	3	PA07-175	4	PA08-051	1	PA09-149	1	PAR08-135	4
CA05-001	1	PA05-040	1	PA06-413	4	PA07-176	1	PA08-074	1	PA09-167	3	PAR08-237	3
CA05-013	2	PA05-125	2	PA06-414	1	PA07-177	1	PA08-121	1	PA10-067	1	PAR09-025	1
CA05-014	1	PA06-042	1	PA06-440	1	PA07-257	2	PA08-149	1	PAR05-156	4	Total Solicited	238
CA07-025	6	PA06-283	1	PA06-510	8	PA07-258	1	PA08-185	4	PAR06-294	2	Total Unsolicited	137
CA08-004	1	PA06-303	1	PA07-007	3	PA07-280	1	PA08-208	2	PAR06-313	13		
CA09-022	2	PA06-314	2	PA07-046	1	PA07-320	1	PA08-209	1	PAR06-458	1	**TOTAL GRANTS AWARDED**	**375**
HL08-013	1	PA06-315	5	PA07-070	85	PA07-356	1	PA08-210	1	PAR06-505	1		

Figure 6. NCI CAM Research Projects by Research Type*

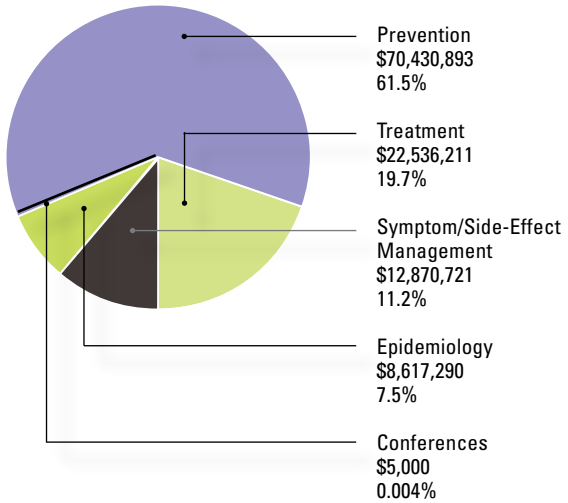


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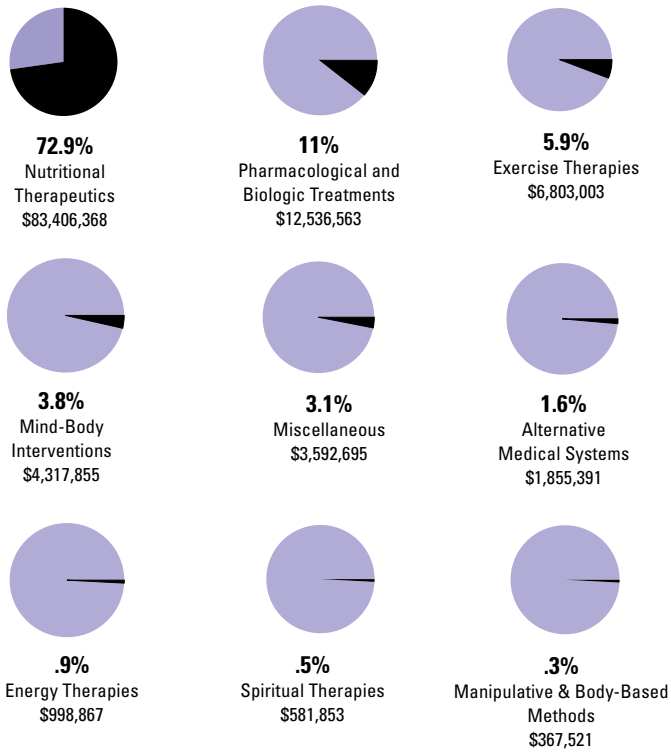
Figure 7. NCI CAM Research Projects by CAM Category*



The largest percentage (72.9%) 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).

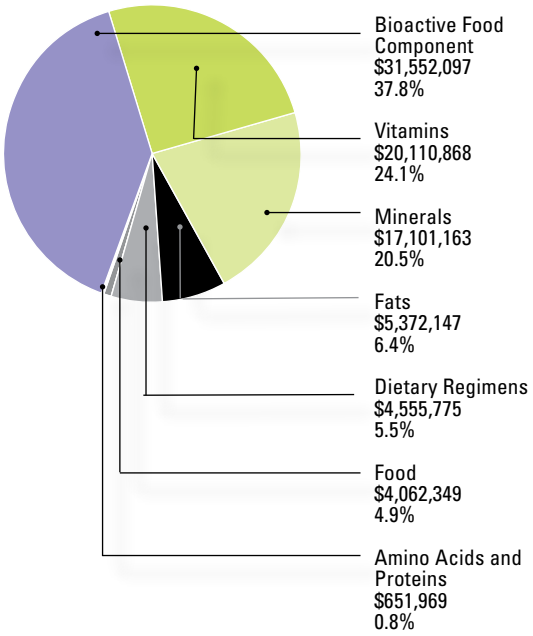
Figure 8 shows the distribution of projects by the subcategories of nutritional therapeutics.

Breakdown by Cancer Type

The research projects that make up NCI's FY 2010 CAM research portfolio address 17 categories of cancer types. Among the various categories, prostate, breast, colorectal, and lung cancers received the largest amounts of cancer CAM research funding. Nearly 28% of NCI's cancer CAM research funding supported projects addressing "multiple types" of cancer.

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) and ARRA funds. Total projects include all active projects in FY 2010.

Figure 9. NCI CAM Research Projects by Cancer Type*

Bladder	$1,257,201
Brain	$308,138
Breast	$16,092,015
Cervical	$1,124,471
Childhood Cancer	$544,632
Colorectal	$14,868,217
Esophageal	$1,535,074
Gastric	$1,714,307
Head and Neck	$2,989,885
Hematologic	$2,128,574
Liver	$1,114,248
Lung	$10,001,521
Multiple Types	$31,728,976
Pancreatic	$3,140,236
Prostate	$20,832,378
Skin: Melanoma and Non-Melanoma	$5,030,124
Small Intestine	$50,119
TOTAL:	**$114,460,116**

* 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) and ARRA funds. Total projects include all active projects in FY 2010.

NCI Collaborative Partnerships Supporting Complementary and Alternative Medicine

Botanicals Research

The Botanical Research Center (BRC) Program was established in 1999 by the Office of Dietary Supplements (ODS) to provide funding for United States research centers to investigate the safety, effectiveness, and biology of botanical products. The awards, worth approximately $1.5 million each year for 5 years, are jointly funded by ODS and the National Center for Complementary and Alternative Medicine (NCCAM). In FY10, the NCI co-supported two of the five centers selected. The NCI-supported centers are located at the University of Illinois at Urbana-Champaign and the University of Missouri.

As women approach menopause, estrogen levels in their bodies decrease. Many women look to botanical estrogens (such as wild yam, soy, and dong quai) as safe and natural replacements for the estrogen they are losing. However, estrogens have a variety of effects on cells and not much is known about the exact actions of botanical estrogens. At the Botanical Estrogens: Mechanisms, Dose, and Target Tissues Center (University of Illinois at Urbana-Champaign) researchers are investigating how

plant-derived estrogens affect molecular and cellular activity and see how similar (or how different) they are to estrogens naturally found in the body. In addition this BRC, which is headed by William Helferich, Ph.D., will determine how botanical estrogens affect breast cancer metastasis.

The Center for Botanical Interaction Studies at the University of Missouri also received support from the BRC program in FY10. The principal investigator of this center is Dennis Lubahn, Ph.D. One of the research projects at this center focuses on actions by commonly-used botanical dietary supplements on five signaling pathways, which may have chemopreventive effects. The botanicals that will be studied at this BRC include garlic, soy, sutherlandia (a medicinal plant from Africa), picrorhiza (a plant found in the Himalayan mountains), and elderberry. The researchers hope to gain a better understanding of exactly how these botanicals may act to help prevent prostate cancer.

Intramural Research Collaboration with Chinese Academy of Sciences

In March 2010, NCI signed a Memorandum of Understanding (MOU) with the Key Laboratory of Chemistry for Natural Products of Guizhou Province and Chinese Academy of Sciences, China. The MOU states that the Key Laboratory will provide compounds and extracts isolated from Traditional Chinese Medicine, folk/tribal medicine, and other Guizhou-area specific botanicals to NCI for anti-cancer activity screening and other cellular pathway functional assays.

Currently, a group of 243 chemical compounds with determined structures isolated at the Guizhou Key Laboratory are being studied via the NCI 60 human cancer cell line screen for growth inhibitory activity, as well as in cellular pathway analysis studies targeting specific cellular signaling, and metabolic pathways involved in growth of cancers. Research for this partnership is ongoing.

Office of Cancer Complementary and Alternative Medicine (OCCAM)

NCI's Office of Cancer Complementary and Alternative Medicine (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 the NCI Division of Cancer Treatment and Diagnosis (DCTD); (http://dctd.cancer.gov). 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's research priorities include:

- Identifying novel therapeutics in the pharmacopeia of traditional medical systems as defined by the World Health Organization
- Research of complementary approaches to improve the therapeutic ratio of standard and investigational anti-cancer therapies
- Research on lifestyle modifications (e.g., diet, exercise, mind-body approaches) for their impact on cancer outcomes (e.g., response to conventional cancer therapy, survival)

OCCAM Programs

In April 2010 OCCAM changed the names of two of its programs. The Research Development and Support Program was changed to the Extramural Research Program or ERP, and the Practice Assessment Program was changed to the Case Review and Intramural Science Program or CRISP. Activities, staff, and organizational structure of each program remain the same. For more information about each program, visit: http://www.cancer.gov/cam/about_programs.html.

Extramural Research Program

OCCAM's Extramural Research Program (ERP) staff manages a portion of NCI's CAM research portfolio, works with other program staff throughout NCI on CAM research issues, assists investigators in identifying funding opportunities, and provides guidance to applicants in the pre- and post-review periods of grant applications. The 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.

ERP continues to support funding opportunity announcements (FOAs) for small grant mechanisms: R21 and R03. The R21 funding opportunities encourage and support the development of basic and clinical complementary and alternative cancer research projects (prevention, therapeutic, and palliative) through exploratory/developmental research grants. The R03 mechanism offers researchers a chance to generate data needed for conducting larger scientific studies of CAM. OCCAM continues to encourage new and young, as well as seasoned veteran investigators to pursue research in areas not typically explored in studies funded by larger grant mechanisms. R21 and R03 grants provide that opportunity.

More information about these FOAs is available online:

- Developmental Projects in Complementary Approaches to Cancer Care and Treatment (R21) PA-09-167
  http://grants.nih.gov/grants/guide/pa-files/PA-09-167.html

- Developmental Projects in Complementary Approaches to Cancer Care and Treatment (R03) PA-09-168
  http://grants.nih.gov/grants/guide/pa-files/PA-09-168.html

In FY10, NCI co-sponsored three new program announcements which specifically solicited CAM-related research:

- Biology of Manual Therapies (R01) PA-10-209
  http://grants.nih.gov/grants/guide/pa-files/PA-10-209.html

- Biology of Manual Therapies (R21) PA-10-210
  http://grants.nih.gov/grants/guide/pa-files/PA-10-210.html

- Limited Competition: Fogarty International Research Collaboration – Basic Biomedical (FIRCA-BB) Research Award (R03) PAR-11-037
  http://grants.nih.gov/grants/guide/pa-files/PAR-11-037.html

Highlights from OCCAM's grant portfolio

In FY 2010, OCCAM provided a competitive supplement to a cooperative agreement held by Dr. Lorenzo Cohen at M.D. Anderson Cancer Center (U19CA121503-04S1) in support of the International Center of Traditional Chinese Medicine for Cancer (ICTCMC), which is jointly coordinated by the M.D. Anderson Cancer Center in Houston, TX and the Cancer Hospital, Fudan University in Shanghai, China. The supplement supports ICTCMC's work on the use of Huachansu (a toad skin extract) in pancreatic cancer patients and is given with gemcitabine (a commonly used conventional chemotherapy) and radiotherapy. Huachansu was tested for efficacy via documentation of tumor response rate, 6 month survival, safety and toxicity, and changes in quality of life in patients.

More information about this project is available by searching the NIH Research Portfolio Online Reporting Tools database (http://projectreporter.nih.gov/reporter.cfm).

A competitive supplement was also awarded to Dr. Yung Chi-Cheng of Yale University (U01CA063477-14S2) for work on the project titled "Nucleoside Analogs as Anticancer Compounds" that aims to develop deoxynucleoside analogs for the treatment of cancer.

More information is available at the NCI Funded Research portfolio: http://fundedresearch.cancer.gov/search/details?action=abstract&grantNum=3U01CA063477-14S2&grantID=8047232&grtSCDC=FY%202010&absID=7917406&absSCDC=CURRENT

During FY10 a grant managed by OCCAM received supplemental funding from NIH's Office of Dietary Supplements (ODS). This collaborative effort marks the first time that ODS has co-funded an OCCAM-managed grant. The supplemental funding for the R21 grant (3R21CA138277-03s1) titled "Ginger Extract: Bioavailability Study and Lung Cancer Preventive Effect" will support detailed study on the bioavailability, biotransformation, and metabolic profile of ginger extract and its key constituents by fully utilizing the samples collected in the parent project. The parent project of this R21 supplement seeks to study the biological activities of ginger extract and its key constituents, [6]-gingerol and [6]-shogaol, and develop a ginger extract containing high levels of shogaols as a lung cancer preventive agent.

More information is available: http://fundedresearch.cancer.gov/search/details?action=abstract&grantNum=3R21CA138277-03S1&grantID=8148074&grtSCDC=FY%202010&absID=8148074&absSCDC=CURRENT

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 publications and Web site (http://www.cancer.gov/cam).

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

Major communication initiatives in FY 2010 included:

- Participation in Open Call usability testing with the NCI Office of Communication and Education for the new NCI CAM Portal website.

- Launch of an inventory project that assessed the research, education, and clinical practice of NCI-designated Cancer Centers and their affiliated or stand alone Integrative Medicine Centers throughout the United States. Information gathered from this inventory will be used to understand the unique research and educational issues that surround NCI-designated Cancer Centers and Integrative Medicine Centers and how the Centers can best serve patients interested in complementary and alternative medicine.

- COP assisted in the development of a complementary and alternative medicine YouTube video featuring OCCAM Director Dr. Jeffrey D. White. This video is part of the NCI LifeLines video series and is available on YouTube: http://www.youtube.com/watch?v=zPgUiBPp9mY and the OCCAM website (http://www.cancer.gov/cam).

COP exhibit program

In addition to sending staff and publications to professional meetings of interest to the field of cancer complementary and alternative medicine, COP also exhibits at key conferences. The exhibit program increases awareness of OCCAM and NCI funding opportunities in cancer CAM to the research, CAM practitioner, and academic communities. Goals of the program include soliciting new grant applications, engaging with patient communication professionals, and connecting members of OCCAM with relevant researchers, practitioners, and patients in the community.

Conferences in which OCCAM exhibited and/or sent representatives or materials:

- 6th International Conference of the Society for Integrative Oncology, November 2009, New York, NY
- Annual Meeting of the American Public Health Association, November 2009, Philadelphia, PA
- Evidence-Based Complementary and Alternative Cancer Therapies Conference, January 2010, West Palm Beach, FL
- Integrative Health Care Symposium, February 2010, New York, NY
- International Congress for Complementary Medicine Research, May 2010, Tromsø, Norway
- Association of Naturopathic Physicians Annual Conference, August 2010, Portland, OR

COP organized publication support at the following meetings:

- Oncology Nursing Society, May 2010, San Diego, CA
- American Society for Clinical Oncology, June 2010, Chicago, IL
- American Association of Cancer Research, April 2010, Washington, DC
- Institute for Functional Medicine, May 2010, Carlsbad, CA

In FY 2010, cancer patient advocates were involved in the review of NCI's CAM Annual Report. OCCAM solicited feedback from four Consumer Advocates in Research and Related Activities (CARRA) members who agreed to review a draft of the FY 2009 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. The feedback from these CARRA members improved the quality of the *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2009* (http://www.cancer.gov/cam/attachments/nci_cam_annual_report_fy09.pdf).

Case Review and Intramural Science Program

The mission of the Case Review and Intramural Science Program (CRISP) is to identify and develop novel complementary and alternative (CAM) therapies for the treatment of cancer. This aim is implemented through various program activities, such as the rigorous scientific evaluation of retrospective case reports (NCI Best Case Series Program) and round table discussions, with the ultimate goal of identifying those CAM interventions that have enough evidence to support NCI-initiated prospective research.

NCI Best Case Series new protocol

During FY10, in response to a request from the NIH Office of Human Subjects Research (OHSR) and Office for Human Research Protection (OHRP), the long-standing NCI Best Case Series (BCS) Program was converted to a research protocol. Under the new protocol, the OCCAM investigators (Drs. Zia and Olaku) will provide the CAM practitioner with a "mini-consent" form to document that a patient, whose medical case history is being considered for submission, agrees to the release of their basic contact information (such as name and telephone number) to OCCAM. Once OCCAM receives this "mini-consent," one of the BCS investigators will contact the patient to review and complete the protocol consent. In essence, this is a written consent allowing the patient's identified medical records to be reviewed as part of this retrospective case study. This step is an important requirement for the new protocol – it ensures that all of the patients receive accurate and consistent information regarding the Program and it makes clear that their medical records will be viewed by different people associated with the program (including the BCS investigators, pathologists, radiologists, and external reviewers). Overall, the NCI Best Case Series Submission Criteria remain the same with the only other change being that practitioners must submit from 3 to 20 cases (prior to the new protocol, there were no restrictions on the number of cases submitted by a practitioner). The protocol received final approval by the Special Studies Institutional Review Board (IRB) and by the NIH Clinical Center Director in early FY11.

In FY 2010, 13 cases of cancer patients treated with an alternative approach were submitted to the NCI Best Case Series Program and reviewed for eligibility.

CRISP highlights

In June 2010, CRISP facilitated a meeting of researchers and clinicians to discuss cases of cancer patients treated with a metal-based Ayurvedic treatment submitted to the NCI Best Case Series Program. Cases were submitted by Vaidya Balendu Prakash, an Ayurvedic practitioner from Mumbai, India. The meeting provided an opportunity for NCI staff and outside experts to review and discuss the case reports and possible future collaborations as a result of the evidence gained from the cases. Follow-up information was requested and discussions are on-going to gather more cases for submission, as well as ideas for future research collaboration.

In July 2010, Dr. Zia organized and presented the CAM section of the Division of Cancer Prevention's *Summer Curriculum in Cancer Prevention*. This was a 4 week summer course that provided specialized instruction in the principles and practice of cancer prevention and control. The target audiences were physicians, research fellows, scientists, and other health care professionals from the United States as well as abroad, with an interest in the field. The CAM section was received well and overall highly rated by the participants.

CRISP is involved in an on-going collaboration with NCI's Community Oncology and Prevention Trials Research Group of the Division of Cancer Prevention, which plays a role in all aspects of the design and implementation of NCI's large cancer prevention and symptom management clinical trials. Dr. Zia participates in concept and protocol reviews of trials utilizing CAM approaches, providing medical oncology and CAM research expertise and guidance.

OCCAM Staff Publications in FY2010

In FY 2010 OCCAM Director Dr. Jeffrey D. White was published in the *Journal of the National Cancer Institute* for his solo-authored editorial titled: "The challenge of rational development of complex natural products as cancer therapeutics."

The article is available in the National Library of Medicine's PubMed medical literature database: http://www.ncbi.nlm.nih.gov/pubmed/20505150

OCCAM's Participation at Major Professional Conferences (OCCAM staff attending)

- 2009 International Cancer Education Conference, October 15-17, 2009, Houston, TX (Shea Buckman)
- American Public Health Association Annual Meeting, November 7-11, 2009, Philadelphia, PA (Elizabeth Austin, Shea Buckman, Dr. Isis Mikhail participated in a Meet-the-Expert Session)
- 6th International Conference of the Society for Integrative Oncology, November 12-13, 2009, New York City, NY (Shea Buckman, Dr. Isis Mikhail, Dr. Dan Xi)
- Evidence-Based Complementary and Alternative Cancer Therapies Conference, January 7-9, 2010, West Palm Beach, FL (Shea Buckman, Dr. Farah Zia, Dr. Oluwadamilola Olaku)
- 9th Annual Oxford International Conference on the Science of Botanicals, April 12-15, 2010, Oxford, MS (Dr. Jeffrey D. White gave a presentation titled "Botanicals Research and Cancer: What is needed for high-impact US clinical trials?")
- 101st American Association for Cancer Research Annual Meeting, April 17-21, 2010, Washington, DC (Drs. Jeffrey D. White, Libin Jia, Dan Xi, and Farah Zia)
- National Cancer Registrars Association 36th Annual Education Conference, April 20-23, 2010, Palm Springs, CA (Dr. Isis Mikhail gave an oral presentation titled "Use of Complementary and Alternative Medicines Among Cancer Patients in SEER")
- Oncology Nursing Society 35th Annual Congress, May 13-16, 2010, San Diego, CA (CDR Colleen Lee presented a poster titled "Oncology Nursing Society, Special Interest Group, Complementary and Integrative Therapies")

- 5th International Congress on Complementary and Alternative Medicine, May 19-21, 2010, Tromsø, Norway (Shea Buckman led a workshop titled "What are the Best Practices in the Development of Patient Education Materials" and gave an oral presentation titled "Cures, Conspiracy, and CAM: Common Myths of Cancer Patients;" Dr. Isis Mikhail presented a poster titled "NCI Cancer Centers Program and Integrative Medicine Programs in the United States")

- The 17th International Symposium on Functional Medicine, May 20-23, 2010, Carlsbad, CA (Dr. Jeffrey D. White gave a presentation titled "The National Cancer Institute and Complementary and Alternative Medicine Research")

- Medical Library Association Conference, May 21-16, 2010, Washington, DC (Dr. Jeffrey D. White gave a presentation titled "Providing Quality Complementary and Alternative Medicine Information to Cancer Patients")

- American Society of Clinical Oncology Annual Meeting 2010, June 4-8, 2010, Chicago, IL (Dr. Farah Zia participated in a Meet-the-Expert Session)

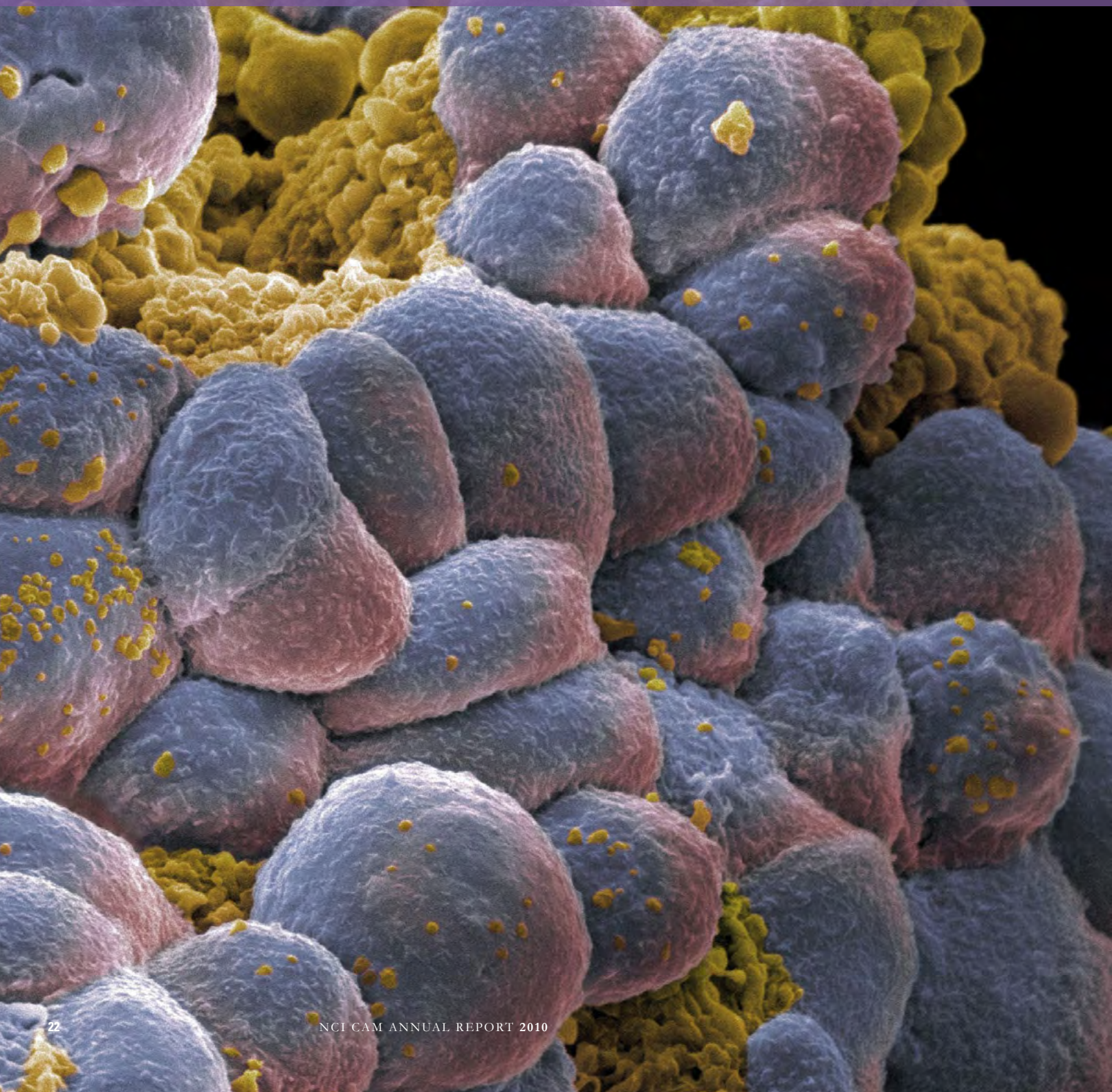
- Drug Information Association, 46th Annual Conference, June 15, 2010, Washington, D.C. (Dr. White gave a talk titled "The National Cancer Institute and Herbal and Dietary Supplement Research" and chaired a session titled "NIH Research and Development in Botanicals Including Dietary Supplements")

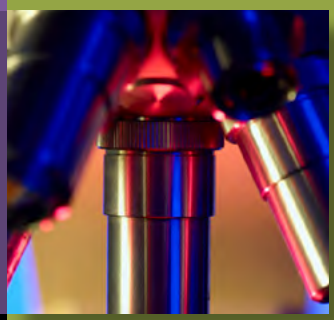
- Meeting of the President's Cancer Panel: America's Demographic and Cultural Transformation – Implications for the Cancer Enterprise, Feb. 2, 2010 Miami, FL (Dr. White gave a presentation titled "Complementary and Alternative Medicine and Cancer: Cultural and Demographic Perspectives")

OCCAM Staff List: FY 2010

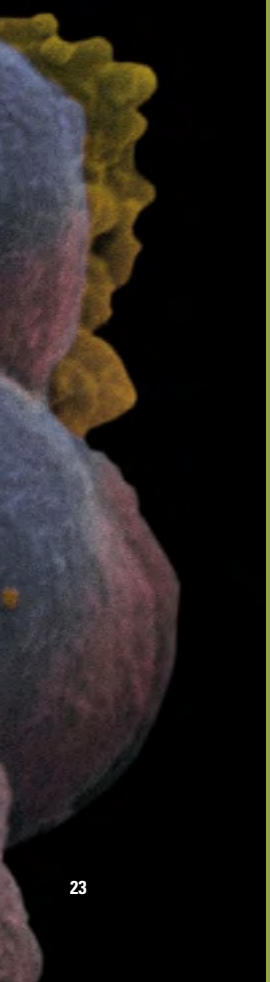
Jeffrey D. White, M.D.	Director, OCCAM
Christina Armstrong	Administrative Program Specialist
Akia Samuda	Administrative Assistant
Isis Mikhail, M.D., Dr.P.H., M.P.H.	Director, Extramural Research Program
Dan Xi, Ph.D.	Program Officer, Extramural Research Program
Oluwadamilola Olaku, M.D., M.P.H.	Scientific Program Analyst
Libin Jia, M.D.	Health Scientist Administrator
Akiko Nakayama, M.S.	Scientific Program Analyst
Farah Zeba Zia, M.D.	Director, Case Review and Intramural Science Program
CDR (U.S. PHS) Colleen Lee, M.S., AOCN®	Coordinator, Case Review and Intramural Science Program
Shea Buckman, M.A.	Coordinator, Communications and Outreach Program
Elizabeth Austin, M.S.	Communication Analyst, Communications and Outreach Program
Miriam Al-Keliddar, M.P.H.	Cancer Research Training Award Fellow
Jeans Santana, B.A.	Cancer Research Training Award Fellow

NCI CAM Communications Programs





NCI directs communications programs 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®), which is NCI's comprehensive cancer database. PDQ® produces summaries covering topics such as cancer treatment, prevention, screening, and CAM.

Most Frequently Accessed PDQ® CAM Summaries

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

In FY 2010, the patient version summary with the highest number of page views was Coenzyme Q10, with 44,792 page views. The next most frequently accessed patient summary was for Essiac/Flor Essence with 41,624. Third in the rankings was the Gerson Therapy summary with 33,791.

During FY 2010, the highest number of page views received for a health professional version of a PDQ® CAM summary was 18,062 for Aromatherapy and Essential Oils. The second most frequently accessed health professional version was the Mistletoe Extracts summary with 14,015. The Essiac/Flor Essence professional summary received the third most page views, with 13,417.

Figure 10 shows the total number of page views during FY 2010 for all of the PDQ® CAM summaries in both the patient and health professional versions. The complete list of PDQ® Complementary and Alternative Medicine Summaries can be viewed at http://www.cancer.gov/cancertopics/pdq/cam.

NCI CAM Clinical Trials

The NCI Clinical Trials Registry, including CAM-related and non CAM-related trials, is available on the NCI Web site at http://www.cancer.gov/clinicaltrials/search/. This database includes approximately 11,000 abstracts of protocols that are open and approved to accept patients.

Many CAM approaches are being studied via clinical trials in cancer patients. The OCCAM Web site hosts a database which organizes CAM clinical trials by cancer types and types of symptoms (http://www.cancer.gov/cam/clinicaltrials_table.html). Clicking on an entry in the table triggers a search of the NCI's Cancer Clinical Trials Registry. The table also archives trials that are currently closed.

In FY 2010, there were 90 NCI-supported cancer CAM clinical trials. (See Appendix for the complete list.)

Note: NCI 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 10. PDQ® CAM Summaries FY10

Patient summary page views

	714X	Acupuncture	Antineoplastons	Aromatherapy and Essentail Oils	Cancell/Cantron/Protocel	Cartilage (Bovine and Shark)	Coenzyme Q10	Essiac/Flor-Essence	Gerson Therapy
Totals	**7283**	**17656**	**13811**	**19194**	**6616**	**10325**	**44792**	**41624**	**33791**

Health professional summary page views

	714X	Acupuncture	Antineoplastons	Aromatherapy and Essentail Oils	Cancell/Cantron/Protocel	Cartilage (Bovine and Shark)	Coenzyme Q10	Essiac/Flor-Essence	Gerson Therapy
Totals	**2481**	**12874**	**4444**	**18062**	**9872**	**6340**	**9946**	**13417**	**9457**

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 by cancer, and the general public.

NCI's Annual Report on CAM

OCCAM published *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2009*, 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/nci_cam_annual_report_fy09.pdf

Newsletter on NCI's CAM Activities

OCCAM's twice-yearly 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. *NCI CAM News* also includes features on cancer CAM projects representing the full range of NCI's activities as well as OCCAM program updates.

The following issues of *NCI CAM News* were made available online in FY 2010:

- Spring 2010 http://www.cancer.gov/cam/newsletter/2010-spring/spring2010_OCCAM_newsletter_home.html
- Fall 2010 http://www.cancer.gov/cam/newsletter/2010-fall/fall2010_OCCAM_newsletter_home.html

NCI CAM News is available via email by subscribing online at https://list.nih.gov/cgi-bin/wa.exe?SUBED1=NCI_CAM_NEWS&A=1

Gonzalez Regimen	Hydrazine Sulfate	Laetrile/Amygdalin	Milk Thistle	Mistletoe Extracts	Newcastle Disease Virus	PC-SPES	Selected Vegetables/ Sun's Soup	Spirituality in Cancer Care
5757	**9584**	**29104**	**25706**	**22502**	**4955**	**5080**	**8090**	**12987**

Gonzalez Regimen	Hydrazine Sulfate	Laetrile/Amygdalin	Milk Thistle	Mistletoe Extracts	Newcastle Disease Virus	PC-SPES	Selected Vegetables/ Sun's Soup	Spirituality in Cancer Care
3585	**1686**	**6793**	**8881**	**14015**	**3195**	**4022**	**4749**	**8519**

CAM in NCI Newsletters and Publications

The *NCI Cancer Bulletin* (http://www.cancer.gov/ncicancerbulletin) is a biweekly online newsletter designed to provide useful, timely information about cancer research to the cancer research community. During FY 2010, several cancer CAM studies were featured in the *NCI Cancer Bulletin:*

- ***Antioxidant Supplement May Prevent Return of Precancerous Colorectal Growths*** (http://www.cancer.gov/aboutnci/ncicancerbulletin/archive/2009/121509/page3#e), December 15, 2009
- ***Adapting the Science of Supplements and Cancer Prevention*** (http://www.cancer.gov/aboutnci/ncicancerbulletin/archive/2009/121509/page6), December 15, 2009
- ***Acupuncture Reduces Joint Pain in Some Women with Breast Cancer*** (http://www.cancer.gov/aboutnci/ncicancerbulletin/archive/2010/012610/page3#d), January 26, 2010
- ***Fatigue: Is it Normal or Pathological? And How Can We Best Treat It?*** (http://www.cancer.gov/ncicancerbulletin/032310/page5), March 23, 2010
- ***Complementary and Alternative Medicine Commonly Used by Pediatric Patients*** (http://www.cancer.gov/ncicancerbulletin/040610/page3#c), April 6, 2010
- ***Shark Cartilage Extract Ineffective Against Lung Cancer*** (http://www.cancer.gov/ncicancerbulletin/060110/page3#d), June 1, 2010
- ***Vitamin D Concentrations in Blood Not Linked to Risk of Less Common Cancers*** (http://www.cancer.gov/ncicancerbulletin/062910/page3#d), June 29, 2010
- ***Guidelines Urge Exercise for Cancer Patients, Survivors*** (http://www.cancer.gov/ncicancerbulletin/062910/page5), June 29, 2010
- ***Consuming High Levels of Red Meat and Fat May Increase Liver Cancer Risk*** (http://www.cancer.gov/ncicancerbulletin/090710/page3#e), September 7, 2010

NCI Fact Sheets on CAM

The NCI fact sheet collection addresses a variety of cancer topics, including cancer CAM. The fact sheets are frequently updated and revised based on the latest cancer research.

See the table on the next page for the list of the current nine NCI CAM fact sheets and the number of page views each fact sheet received during FY 2010. The NCI fact sheets collection can be found at http://www.cancer.gov/cancertopics/factsheet.

The NCI Fact Sheet "Thinking About Complementary and Alternative Medicine: A Guide for People with Cancer" was viewed 22,462 times in FY 2010. To view this publication, please visit http://www.cancer.gov/cancertopics/factsheet/therapy/cam.

Table 1: NCI CAM FACT SHEETS PAGE VIEWS STATISTICS FY 2010

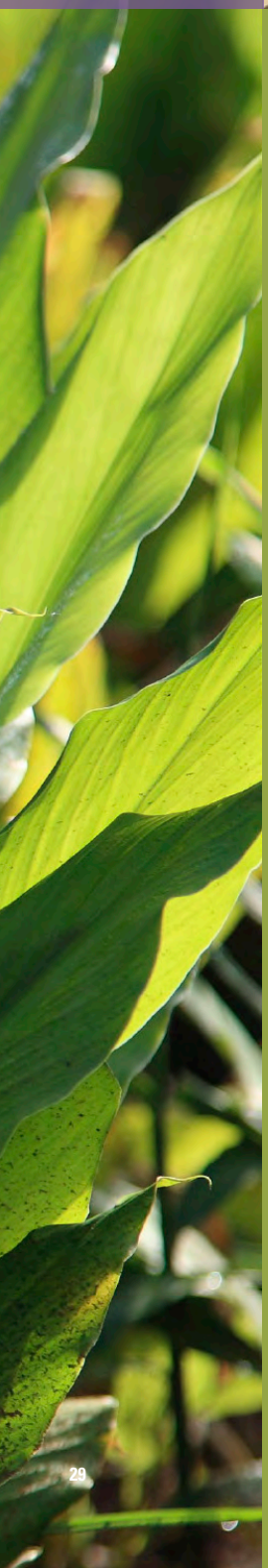
Fact Sheet Title	Total Views
Antioxidants and Cancer Prevention: Fact Sheet	83,669
Calcium and Cancer Prevention: Strengths and Limits of the Evidence	9,503
Garlic and Cancer Prevention: Questions and Answers	20,268
Physical Activity and Cancer: Fact Sheet	17,017
Questions and Answers About Beta Carotene Chemoprevention Trials	373
Red Wine and Cancer Prevention: Fact Sheet	13,985
Tea and Cancer Prevention: Fact Sheet	20,217
Vitamin D and Cancer Prevention: Strengths and Limits of the Evidence (New)	39,769
Thinking About Complementary and Alternative Medicine: A Guide for People with Cancer	22,462

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 to answer questions via phone, live online chat, mail, and e-mail about cancer treatment and clinical trials, including CAM therapies. During FY 2010, CIS responded to 1,135 inquiries regarding CAM approaches for cancer.

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 a variety of training-support programs on different aspects of CAM research including grant writing workshops and scientific conference sponsorships.

Training Opportunities at OCCAM

During FY 2010, OCCAM hosted two Cancer Research Award Training (CRTA) Fellows, Jeans Santana and Miriam Al-Keliddar who worked with the Case Review and Intramural Science Program and the Extramural Research Program, respectively. Mr. Santana's work included writing a manuscript analyzing cancer CAM use among Hispanics in the United States and reviewing case reports for the NCI Best Case Series Protocol. Ms. Al-Keliddar worked on two manuscripts about prostate cancer and herbs, and canine cancer models.

NCI Lectures and Workshops on CAM

NCI provides educational opportunities for its staff, fellows, and the public on topics related to cancer. In FY 2010, the following seminars and lectures relevant to CAM research were held at NCI:

- 3rd Congress of the International Society of Nutrigenetics/Nutrigenomics
  (Division of Cancer Prevention, NCI)
  October 21-23, 2009

- Soliciting Nature's Help for Prevention of Cancer
  (Frederick Cancer Research Facility, NCI)
  November 4, 2009

- Dietary Chemopreventive Agents – Findings from Shanghai and Singapore Cohort Studies
  (Epidemiology and Genetics Research Program, NCI)
  March 15, 2010

- Natural Products: Keys to Treating Cancer and Infection
  (Office of the Director, NIH)
  March 16, 2010

- Can we Prevent Breast Cancer Using Natural Compounds?
  (Division of Cancer Prevention, NCI)
  June 4, 2010

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 50 minute presentation on a cancer CAM topic and allow 10 minutes for questions. The lectures are open to the public and are archived as videocasts on the OCCAM Web site at http://www.cancer.gov/cam/news_lectures.html

In FY 2010 the following lectures were presented as part of the OCCAM Monthly Lecture Series:

- Inhibition of the Anti-apoptotic Activity of Galectin-3 with GCS-100, a Citrus Pectin Derivative in B-cell Lymphoma

- Melatonin via the MT1 Receptor and the Circadian Clock Suppresses the Initiation, Promotion, and Progression of Breast Cancer

- Solubility and Permeability Enhancement by New Nano-micellar Natural Compounds

- Prostate Cancer Prevention by Soy: Pitfalls and Opportunities

- Clinical and Biologic Effects of Curcumin in Multiple Myeloma

- Head and Neck Cancer Chemoprevention: Intervention Using Local Delivery Strategies

- MR Visible Changes in Prostate Cancer Choline Metabolism: Response to Soy-based Dietary Interventions that Inhibit Tumor Growth

- Therapeutic Effects of Boswellia Extracts and Pure Components in Prostate Cancer and Leukemia

- Curcumin/TRAIL Combination Therapy for Prostate Cancer

- Acupuncture and Cancer Pain

SUPPORTING SCIENTIFIC CONFERENCES

In FY 2010, NCI supported the following conferences that included CAM content:

- American Psychosocial Oncology Society Annual Conference: Integrating Psychosocial Research and Practice in Quality Cancer Care
  February 18-21, 2010
  New Orleans, LA
  Grant number: 5R13CA138133-02

- 2010 Marine Natural Products: Gordon Research Conferences
  February 28-March 5, 2010
  Ventura, CA
  Grant number: 1R13CA144320-01

- Society of Behavioral Medicine 50th Annual Meeting
  April 27-30, 2010
  Washington, DC
  Grant number: 5R13CA091918-10

- 2010 Federation of American Societies Experimental Biology Conference on Retinoids
  June 13-18, 2010
  Carefree, AZ
  Grant number: 1R13DK088433-01

- 2010 Metals in Medicine: Gordon Research Conferences
  June 27-July 2, 2010
  Andover, NH
  Grant number: 1R13GM093354-01

- 11th International Congress of Behavioral Medicine (ICBM2010)
  August 4-7, 2010
  Washington, DC
  Grant number: 1R13CA144430-01

- International Symposium on Breast Cancer Prevention: Nutrition, Communication, and Public Policy
  October 18-19, 2010
  West Lafayette, IN
  Grant number: 1R13CA153904-01

- American Society of Pharmacognosy 51st Annual Meeting
  July 30-August 3, 2011
  San Diego, CA
  Grant number: 5R13CA139768-02

HIGHLIGHTS FROM
NCI's CAM Training Projects

The highlights on the following pages are selected from the 27 CAM training projects that NCI supported during FY2010 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 control research into CAM therapies and interventions.

Abstracts of projects featured in this report can be found by searching the grant or project number the NIH RePORTer research trials database at http://projectreporter.nih.gov/reporter.cfm.

Center for
Cancer Training

Exercise Researcher Refocuses Career on Cancer Prevention and Control Studies

Lynette Craft, Ph.D., is a kinesiologist who began her scientific career studying the use of exercise to improve symptoms in patients with clinical depression. However, while pursuing her post-doctoral work at Boston University she had the opportunity to work on an NCI-funded research study "in which we were primarily looking at physical health outcomes related to exercise involvement with breast cancer patients," she recalled. "I became very interested in the mental health outcomes that might also result from breast cancer survivors participating in exercise programs."

Now an Assistant Professor of Preventive Medicine at Northwestern University School of Medicine, Dr. Craft is using an NCI Mentored Career Development Award* to shift gears and refocus her research into the growing field of exercise and cancer prevention and care. "It will allow me the time I need to initiate this new line of research and to develop collaborative relationships with other investigators who are doing similar types of work and move forward in my career," she noted.

Dr. Craft is currently using the career award to conduct a pilot randomized controlled trial to explore the feasibility and effectiveness of an intermittent exercise intervention in women with early stage breast cancer who are at least 6 months post adjuvant treatment. This intermittent-exercise group will be compared to a standard exercise intervention and a usual care control group, to determine which intervention can most effectively alleviate cancer-related symptoms (depression, pain, and fatigue) and positively impact biomarkers of metabolic function.

"We know that, physiologically, the accumulation of exercise through shorter bouts (15 minutes each) generates the same kind of physical health outcomes as does one longer bout of 30 minutes," Dr. Craft said. "However, we don't really know whether the effects of two small bouts of exercise will be the same as one longer session on relieving pain, depression, and fatigue. That's one thing we're looking at: Will we find equivalent effects on those outcomes?"

The study will also examine exercise adherence rates because if breast cancer patients "are experiencing pain, fatigue, and depression, they may find it easier to do shorter bouts of exercise than to do 30 minutes all at once," she added.

Dr. Craft has assembled an "A-team" of co-mentors at Northwestern University and its NCI-designated Cancer Center and elsewhere who are helping her with this cancer exercise study. "When I came to Northwestern University, the Cancer Center here was very excited about having someone who could do exercise-related research," she recalled. Her team includes a cancer epidemiologist, a clinical psychologist and behavioral medicine expert, an expert in quality of life measurement in cancer patients, a breast surgeon, and an expert in developing exercise interventions with cancer survivors. These experienced researchers will guide Dr. Craft's progress, provide supervision, and support the activities outlined in her career development plan.

Dr. Craft said, "I hope to continue my career along this path of cancer survivor research. I see exercise and mental health as an important area that can benefit all types of cancer survivors, not just breast cancer patients. There are several other types of cancer, like head and neck cancer or prostate cancer, whose survivors experience high rates of depression but have not been extensively studied with respect to exercise interventions."

Another group of people who have not received much attention in the exercise literature are adolescent and young adult cancer survivors. "Often they have higher levels of distress, for some of the same, but also for different, reasons than older patients," Dr. Craft commented. "We know that lifestyle issues like being overweight and obesity are starting younger and younger, so that might be an interesting group to look at with respect to how exercise affects their mental health, as well as how exercise affects physical health outcomes."

*Grant number:
5K07CA134936-02

Center to Reduce Cancer Health Disparities

Curcumin Investigated to Prevent Prostate Cancer Metastasis

Prostate cancer claims the lives of about 30,000 men each year in the United States. Those deaths are due almost entirely to metastasis, or spread of the cancer to other organs. Approximately 75% of men with early-stage prostate cancer can be successfully treated with surgery and will not have a recurrence of their disease. Oncologists, however, currently lack the ability to accurately distinguish the remaining 25% of patients at high risk for recurrence who would benefit from adjuvant, or additional, therapy after surgery."

A recent study* identified a trio of substances known as chemokines (small proteins secreted by cells) found in prostate tissue that accurately predicted whether prostate cancer would recur within five years of surgery. When prostate tissue contained abnormally high amounts of two of these substances, known as CX3CL1 and IL-15, the cancer was highly unlikely to recur within that period. By contrast, when tissue contained abnormally high amounts of the third identified chemokine, CCL4, recurrence was likely.

Magaly Martinez-Ferrer, Ph.D., of the University of Puerto Rico Comprehensive Cancer Center (UPRCCC) – one of the researchers who participated in the study – is now trying to extend these findings by determining whether this trio of chemokines can affect prostate cancer metastasis. In addition, with NCI funding in the form of a Continuing Umbrella of Research Experience (CURE) K01 diversity training grant**, she is examining whether treatment with curcumin, a chemical component of the spice turmeric, can promote or inhibit metastasis by modifying the levels of these chemokines in prostate tissue.

Curcumin has previously been shown to inhibit colon tumors and, in some studies, has been associated with a reduction in the size of prostate tumors, according to Dr. Martinez-Ferrer. Other studies have found that curcumin has anti-inflammatory properties, although the mechanism for this is unclear. Previous research also suggests that chronic inflammation may promote prostate cancer metastasis. A randomized, double-blind, placebo-controlled clinical trial is currently under way at UPRCCC to determine whether curcumin can shrink precancerous growths in patients with a genetic disorder that puts them at an extremely high risk for colorectal cancer.

At the 2011 American Association for Cancer Research annual scientific meeting, Dr. Martinez-Ferrer reported the initial results of experiments in which CX3CL1 and IL-15 chemokines were added to a highly metastatic prostate cancer cell line.*** The addition of the chemokines significantly decreased proliferation and migration of the cells, suggesting that they may suppress metastasis.

Dr. Martinez-Ferrer plans to investigate whether treatment with curcumin modifies metastasis, tumor size, or inflammation in both cell lines to which CX3CL1 and IL-15, or CCL4 have been added, or in laboratory mice implanted with prostate tumors.

She hopes this work will ultimately show that these three chemokines can either promote or inhibit prostate cancer metastasis and, further, that treatment with curcumin can modify these effects by altering levels of these chemokines in prostate cancer cells or in laboratory mice. If that proves to be the case, the next step, according to Dr. Martinez-Ferrer, would be to conduct a clinical trial in which patients at risk for prostate cancer recurrence would be treated with curcumin to determine whether this intervention reduces the risk of disease metastasis.

*Blum DL, Koyuama T, M'Koma AE, et al. Chemokine markers predict biochemical recurrence of prostate cancer following prostatectomy. *Clinical Cancer Research,* 2008; 14(23): 7790-7

***Martinez-Ferrer M, Qi Y, Sanchez MM, Bhowmick NA. Inflammatory mediators of prostate cancer metastasis. Abstract #391, presented at American Association for Cancer Research 102nd Annual Meeting; April 3, 2011; Orlando, FL.

**Grant number:
7K01CA140711-02

HIGHLIGHTS FROM
NCI's CAM Research

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.

Compound in Red Sage Plant May Help Control Blood Vessels that Feed Tumors

Division of Cancer Treatment and Diagnosis

Among the most widely used plants in traditional Chinese medicine (TCM) is red sage, known in China as Danshen (*Salvia miltiorrhiza*). It stimulates blood flow and is used to treat inflammation, cardiovascular disease, and cerebrovascular disease. According to TCM principles, cancer is a form of tissue swelling, and thus using substances that stimulate blood flow may help treat many types of cancer.

But there is a paradox at work here, said Bin Chen, Ph.D., who was trained in TCM and pharmacology at Nanjing University of Chinese Medicine in China. "Cancers also make use of the circulatory system by growing blood vessels into a pipeline that delivers oxygen and nutrients to nourish and extend tumors."

It is therefore common in the West to treat some tumors with antiangiogenic therapy, using drugs that prevent new blood vessels from growing. Dr. Chen's research focuses on vascular-disrupting therapy, because he is not only interested in preventing new blood vessels from forming but is also seeking to destroy the existing blood vessels within the cancerous tissue.

With NCI funding*, his laboratory at the University of the Sciences in Philadelphia is conducting a pilot study of how tanshinone IIA (Tan IIA), one of Danshen's active ingredients, might become a key piece in vascular-disrupting therapy. In previous laboratory studies on cancerous endothelial cells that line blood vessels, Tan IIA was able to attack and kill cells in several different ways. What hasn't been studied is exactly how these effects might be marshaled to target the blood pipelines that can feed tumors throughout the body.

Dr. Chen and his colleagues will try to fill in the important details about how Tan IIA works against prostate cancer by experimenting on mice that have been implanted with human tumor cells. "We give the Tan IIA compound to the mice, and with a special imaging system we can watch to see if blood vessels grow or not," he said. "If the impact is evident shortly after treatment begins, the Tan IIA is probably disrupting the blood vessels that are already in place."

However, if new blood vessels do not develop in the mice, then the Tan IIA is behaving more like an antiangiogenic drug by denying the tumor the new blood supply that it needs to grow, Dr. Chen added. This effect on the tumor growth is evident only over time, because it targets the endothelial cells that are necessary for new blood vessels to grow.

"Our longstanding interest in how the vascular system affects cancer encouraged us to look at whether Tan IIA might be used to control blood flow in ways that we could exploit," Dr. Chen explained. Because most cancer cell-killing chemotherapeutic drugs used in the West travel in the bloodstream, this work will also focus on whether Tan IIA can help deliver such drugs more effectively to the site of the tumor, Dr. Chen added.

He is also testing whether Tan IIA could be used to improve the delivery of other anticancer agents. "Tumors in the prostate and elsewhere survive in part by developing defenses against our drug therapies," he explained. "For example, the tumors' blood vessels are not efficient for the delivery of chemotherapy drugs circulating in the bloodstream."

"Because Tan IIA is so safe and essentially has no side effects, we can deliver it chronically and in large amounts," Dr. Chen said. The goal would be to change the permeability of tumor vessels to allow more of the accompanying chemotherapy drug to reach the tumors. The basic challenge with chemotherapy drugs is how toxic they can be to other parts of the body beside the tumor, he noted. If the Tan IIA allows more of the cancer drug to reach the tumor, then less of the drug overall would be needed, and thus other side effects could be reduced.

*Grant number: 5R21CA150277-02

Scientists Study Biomarkers of High-Fiber Diets to Lower Risk of Colorectal Cancer

Center for Cancer Research

Colorectal cancer (CRC) is the third leading cause of cancer death among both men and women in the United States. Screening for CRC can both reduce the death rate from this disease and prevent it by detecting and removing precancerous growths known as adenomatous polyps. Yet despite its demonstrated effectiveness, most Americans over age 50 – the group most at risk for CRC – do not undergo screening.

NCI's Polyp Prevention Trial (PPT) was a 4-year randomized trial designed to determine the effect of a low-fat, high-fiber diet high in fruit and vegetables on polyp recurrence. Study participants included more than 2,000 people at high risk for CRC because of a history of polyps. Participants were randomly assigned to follow either their usual diet or the diet high in fruits and vegetables. Although the trial results showed no overall difference in adenoma recurrence between the two groups, closer analysis found a substantial decrease in recurrence among the 25% of participants who most consistently adhered to the diet high in fruits and vegetables*.

For example, the 25% of PPT participants who consumed the largest quantities of beans had a three-fold reduced risk of adenoma recurrence compared with the 25% of participants who consumed the lowest quantities. Beans, or legumes, are rich in fiber and soluble substances with anti-inflammatory and anticancer effects. And the 25% of PPT participants who consumed the most flavonols – substances abundant in foods such as beans, onions, apples, and tea – had a 76% decreased risk of adenoma recurrence.

Other studies have suggested that insulin resistance and low-level chronic inflammation may act together to promote CRC and that a high-fiber diet may influence blood levels of both C-peptide, an established biomarker for insulin resistance, and C-reactive protein (CRP), an established biomarker for inflammation.

Building on these findings, researchers from NCI's Center for Cancer Research, Pennsylvania State University (PSU), and Texas A & M University designed a study to compare the effects of a high-bean diet or a healthy, low-fat control diet on these biomarkers in men at risk for CRC**. Half of the 64 men in the study – known as the Legume Inflammation Feeding Experiment (LIFE) – had a history of polyp removal and half did not***.

"We have learned from the PPT and other studies that not everybody is going to benefit from a particular dietary intervention," said Nancy H. Colburn, Ph.D., chief of NCI's Laboratory of Cancer Prevention, who has played a leadership role in both the PPT follow-up studies and the LIFE study, along with Elaine Lanza, Ph.D., who led the PPT while at NCI, and Terryl Hartman, Ph.D., of PSU. "But we have also learned that subgroups of people can benefit."

The men in LIFE were randomly assigned to spend 4 weeks on one of the two study diets, followed by a 3-week break, followed by 4 weeks on the other study diet. The diets were designed to maintain the men's existing weight. Blood concentrations of CRP declined by 20% while the men were on the high-bean diet and by about 18% while they were on the control diet. A trend was seen toward reduced blood concentrations of C-peptide on the high-bean diet. In preliminary results using a novel method that isolates RNA from patients' fecal stools, researchers identified sets of gene expression changes after 4 weeks on the high-bean diet that may predict a reduced risk for polyp recurrence.

**Project number:
ZIA BC 011159

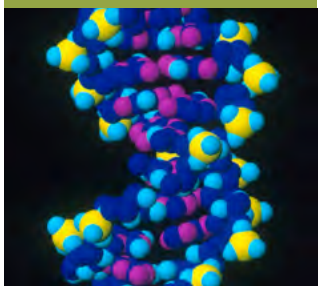
Meanwhile, further analyses of the PPT have identified two potential biomarkers for adenoma recurrence. PPT participants with elevated blood levels of homocysteine – an amino acid that can promote inflammation, tissue damage, cardiovascular disease, and cancer – had a two-fold increased risk of adenoma recurrence. And the greatest reduction in risk for recurrence of high-risk and advanced adenomas (those most likely to become cancerous) was seen in participants who consumed the most flavonols and had decreased blood concentrations of IL-6, a substance that promotes inflammation and may promote growth of colorectal tumors.

Dr. Colburn noted that the goal of the post-PPT studies "is to personalize dietary interventions to prevent CRC by matching them with the groups of people most likely to benefit. To achieve that goal, we need biomarkers that accurately identify those most likely to benefit from an intervention and that can be measured noninvasively by means of a simple blood or stool test."

* Lanza E, Hartman TJ, Albert PS, Shields R, Slattery M, Caan B, Paskett E, Iber F, Kikendall JW, Lance P, Daston C, Schatzkin A. High dry bean intake and reduced risk of advanced colorectal adenoma recurrence among participants in the polyp prevention trial. *The Journal of Nutrition*. 2006 Jul;136(7):1896-903.

*** Hartman TJ, Albert PS, Zhang Z, Bagshaw D, Kris-Etherton PM, Ulbrecht J, Miller CK, Bobe G, Colburn NH, Lanza E. Consumption of a legume-enriched, low-glycemic index diet is associated with biomarkers of insulin resistance and inflammation among men at risk for colorectal cancer. *The Journal of Nutrition,* 2010 Jan;140(1):60-7.

Researchers Study Whether Altering Cellular Fats Raises Cancer Risk



Division of Cancer Biology

Oxygen, while necessary for life, can also damage molecules inside our bodies due to its highly reactive nature. Oxygen can "pull" electrons from many other molecules in the body through a process called oxidation, causing them to be reactive and unstable. If these reactive molecules interact with DNA, the result can be DNA damage, which is an early step in carcinogenesis (cancer formation). The fatty acids widespread in the body, including those found on the membranes of cells, are vulnerable to a type of oxidative damage called lipid peroxidation. Fung-Lung Chung, Ph.D., professor of oncology at Georgetown University Medical Center, is interested in how DNA damage, driven by lipid peroxidation, may contribute to cancer formation.

Previous research from his laboratory has shown* that the oxidation of polyunsaturated fatty acids found on cellular membranes can cause a type of DNA damage called a "cyclic adduct," where a reactive compound formed by lipid peroxidation attaches itself to the double-helix structure of DNA. These cyclic adducts have been found in animals, in humans, and even in cultured cells. However, whether cyclic adducts contribute to cancer formation – and if so, how – remains unclear.

"There's a lot of talk in the literature about cancer risk related to fat intake—for example, a fatty liver is a risk factor for liver cancer," explained Dr. Chung. "And a high-fat diet is associated with colon cancer. So we thought there might be some sort of mechanistic role for this type of DNA modification caused by fatty acid peroxidation in those cancers." In his current research funded by NCI**, Dr. Chung and his colleagues are using two animal models with spontaneous liver cancer to better understand this process. One model, the Long Evans Cinnamon rat, accumulates abnormal levels of copper in the liver and subsequently shows an increase in lipid peroxidation and liver cancer.

The second model is a mouse strain that lacks the DNA-repair mechanism, called nucleotide excision repair, that the body normally uses to repair cyclic adducts caused by lipid peroxidation. These mice also have a high incidence of spontaneous liver cancer.

The researchers will look at the relationships between accumulation of cyclic adducts in the liver and progressive stages of liver carcinogenesis. Researchers will also closely examine cyclic adduct binding to the p53 gene and the relationship between adduct binding and other p53 mutations found in liver tumors from these animals. The p53 gene is a known tumor-suppressor gene that is inactivated ("turned off") by mutations in many types of cancer that contributes to runaway tumor-cell growth.

In addition, Dr. Chung plans to test several antioxidants, including a mixture of green tea polyphenols (Polyphenon E) and dihydrolipoic acid (DHLA), to see if adding these compounds to the animals' diets slows or prevents cyclic adduct formation. In a study published in 2010***, Dr. Chung and his colleagues found that epigallocatechin gallate E, a green tea polyphenol, and DHLA inhibited the formation of cyclic DNA adducts in laboratory model systems.

* Chung FL, Chen HJ, Nath RG. Lipid peroxidation as a potential endogenous source for the formation of exocyclic DNA adducts. *Carcinogenesis,* October 1996;17(10):2105-11.

*** Nath RG, Wu MY, Emami A, Chung FL. Effects of epigallocatechin gallate, L-ascorbic acid, alpha-tocopherol, and dihydrolipoic acid on the formation of deoxyguanosine adducts derived from lipid peroxidation. *Nutrition and Cancer,* 2010;62(5):622-9.

**Grant number: 5R01CA134892-02

Milk Thistle Extract Evaluated Against Cancer-Causing Liver Disease

Division of Cancer Epidemiology and Genetics

Chronic hepatitis C is a devastating disease that can lead to a variety of other illnesses including liver cancer. Available therapies don't work for everyone and can have many adverse side effects. As a result, many people with chronic hepatitis C turn to CAM remedies, such as herbal products, noted Neal Freedman, Ph.D., M.P.H., of NCI's Division of Cancer Epidemiology and Genetics (DCEG).

One of the herbal products used most commonly by people with chronic liver disease is silymarin, which is an extract of the milk thistle plant *Silybum marianum*. Silymarin has been used to treat liver disease since the time of the ancient Greeks. However, few studies have rigorously tested the effectiveness of this herbal ingredient for chronic liver disease, and results from previous studies are inconsistent, Dr. Freedman added.

As part of a large, NIH-supported clinical trial known as the Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C) study*, NIH investigators asked patients about their use of CAM treatments, including silymarin. The HALT-C trial was designed primarily to test the effectiveness of long-term treatment of hepatitis C with low doses of the drug peginterferon-alpha for patients who had not responded to previous standard-of-care therapy. At the outset of the study, investigators found that approximately one-third (34 percent) of patients in the trial reported that they had used silymarin, and half of those patients were current users of this herbal remedy, Dr. Freedman reported.

"When we learned that silymarin use was part of the information collected in HALT-C, we thought we should examine the possible effects of silymarin use on liver disease progression, as these results could contribute to the larger scientific understanding of the role of silymarin in liver disease," Dr. Freedman commented.

Dr. Freedman and his colleagues in DCEG studied 1,049 patients in the HALT-C trial and compared clinical outcomes for current users of silymarin, against outcomes for patients who reported former silymarin use, and patients who said they had never used silymarin. The researchers looked at two outcomes for the three groups of patients: 1) progression of liver fibrosis, which was assessed by examining liver biopsies over the course of the study; and 2) liver-related clinical outcomes, which included liver cancer (hepatocellular carcinoma), ascites (accumulation of fluid in the abdominal cavity), variceal hemorrhage (rupturing of the veins in the esophagus), or liver disease-related death.

"Fibrosis is the term used when some of the liver tissue has been destroyed and replaced by scar tissue, and cirrhosis is where most of the liver has been destroyed," explained Dr. Freedman. "As liver disease gets worse, patients progress from fibrosis to cirrhosis, and at each step their risk of liver cancer and other adverse clinical outcomes is much higher."

Dr. Freedman reported that patients in the HALT-C trial who were currently taking silymarin were less likely to progress from fibrosis to cirrhosis**. "However, there was no association between silymarin use and clinical outcomes, and we're not clear why that's the case," he added. It could be that the follow-up period for the current study was too short to see an effect of silymarin on clinical outcomes or to determine whether silymarin affects the progression of fibrosis but not other aspects of chronic liver disease, he suggested.

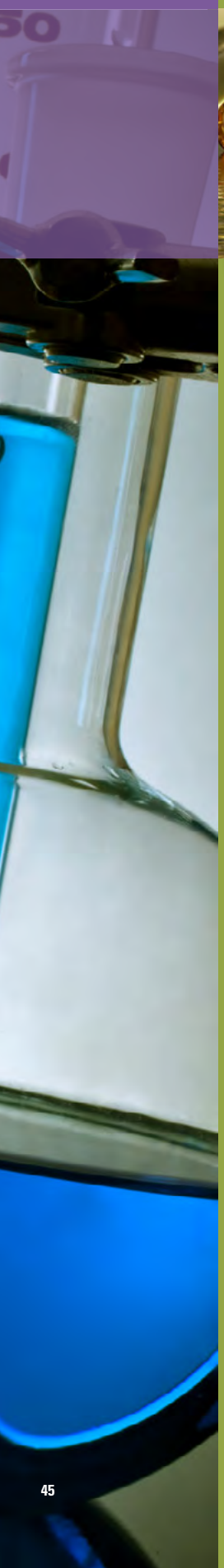
Dr. Freedman noted that the main limitation of the study was that investigators lacked information on how much silymarin each patient used. "Also, as an observational study, patients using silymarin may be different from patients who are not users of the herbal remedy. For example, they may have a different stage of disease, or silymarin use may be a proxy for another 'habit' that has an effect," Dr. Freedman said.

"Our results suggest that there might be an association between silymarin use and progression of liver disease, and future studies should look at this further," he continued. "But, by itself, our study isn't definitive and I think many more studies need to be done." Future studies should assess exactly how much silymarin each patient is using, Dr. Freedman said, and ideally should compare patients who are randomly assigned to take a specific dose of silymarin with patients not receiving any silymarin.

*Grant number:
Z01 CP005782

**Freedman ND, Curto TM, Morishima C, Seeff LB, Goodman ZD, Wright EC, Sinha R, Everhart JE, HALT-C Trial Group. Silymarin use and liver disease progression in the Hepatitis C Antiviral Long-Term Treatment against Cirrhosis trial. *Alimentary Pharmacology and Therapeutics,* January 2011;33(1):127-37. Epub 2010 Nov 2

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.

Exercise May Stop Cancer from Spreading to the Brain

Division of Cancer Prevention

Michal Toborek, M.D., Ph.D., has devoted much of his research to the blood-brain barrier, which appears to have an important role in some metastatic cancers. Metastases are the cause of most cancer deaths, said Dr. Toborek, "and the number of people who develop cancer in the brain (primary or metastatic) each year is enormous, probably around 200,000 in the United States alone." Only about 1 in 9 of these people have primary brain tumors, he added, while the rest develop metastatic brain cancer that originated in other organs.

For years, researchers have been trying to learn about and prevent the process of metastasis. Because metastatic cancer cells travel through the bloodstream, if they are turned away by the blood-brain barrier, you will prevent cancer metastasis to the brain, explained Dr. Toborek, who is a professor in the Department of Neurosurgery at the University of Kentucky. The capillaries feed the brain with nutrients from the bloodstream such as glucose and amino acids, he said. There are certain protein structures known as transporter systems that recognize and send these vital nutrients across the blood-brain barrier, he continued, but other foreign substances and other cells that arrive via the capillaries – from cancer and other diseases – are recognized as intruders and cannot get into the brain.

What stops them are the endothelial cells that make up the barrier and stick together like bricks. The metaphor extends to the "mortar" that holds them together, which are various types of adhesion molecules, Dr. Toborek said. What is new about his research is the recognition that exercise helps to keep these joints tightly bound together; they are referred to as "tight junctions." It has been found that these junctions can be compromised by oxidative stress, which often occurs when any of a number of foreign substances – tumor cells or cells from the body's hormone and immune systems – arrive at the blood-brain barrier, he commented.

With NCI support,* Dr. Toborek's lab is studying how certain proteins that fortify these tight junctions against oxidative stress are enhanced by exercise. They have developed a mouse model to explore this phenomenon. The mice are trained as runners on a wheel in their cage, and are genetically engineered to be especially vulnerable to brain metastases. After some animals are rigorously trained for 5 weeks, and others remain sedentary, the researchers inject lung cancer cells into their carotid arteries, which is the access route that metastatic cancer cells would naturally travel in the circulatory system if they were headed for the brain. The results showed that the fit animals had dramatically fewer cases of brain metastases.

If the promising findings in the mouse studies can be confirmed in clinical trials of human patients, the public health impact of this line of research could be significant, Dr. Toborek commented. "This work follows a lot of compelling evidence that show that exercise reduces cancer risk by up to 50 percent in breast and colon cancer," he noted. The challenge is that currently 3 in 5 Americans don't exercise regularly and 1 in 4 Americans are limited to a sedentary lifestyle, he added.

*Grant number: 1R01CA133257-01A2

Compound in Cruciferous Vegetables Studied Against Pancreatic Cancer

Division of Cancer Prevention

"Eat your broccoli – it's good for you" is a common refrain of many parents. Subrata Haldar, Ph.D., a pharmacology researcher at Case Western Reserve University, would agree. Dr. Haldar and his colleague Aruna Basu, Ph.D., are interested in the possible anti-cancer effects of a compound that is produced when our digestive system breaks down certain substances found in abundance in broccoli and other cruciferous vegetables, including cabbage and cauliflower.

With support from NCI*, Drs. Basu and Haldar are exploring whether the compound benzyl isothiocyanate, or BITC, that is produced when consuming these vegetables could be used to help prevent or even treat pancreatic cancer. "Pancreatic cancer is one of the most aggressive malignancies in the world," and few effective treatments are available, noted Dr. Haldar. Several epidemiological studies have shown that frequent consumption of cruciferous vegetables is linked with a reduced risk of some types of cancer, including pancreatic cancer. Moreover, preliminary studies by Drs. Haldar and Basu showed that BITC impairs the ability of pancreatic cancer cells grown in the laboratory to proliferate, or multiply.

BITC is produced when microbes that live in the human gut break down substances called glucosinolates, which are plentiful in cruciferous vegetables. "BITC readily accumulates in the cell at high concentrations, and it is a multi-target compound that can attack multiple signaling pathways [in the cell] simultaneously," making it appealing as an anti-cancer agent, Dr. Haldar noted. One key goal of Drs. Basu and Haldar's current study is to determine the molecular mechanism by which BITC inhibits the growth of pancreatic cancer cells. In a series of recent experiments, they found that BITC alters the levels of microRNAs in pancreatic cancer cells.

MicroRNAs are small RNA molecules that regulate gene expression, the process by which a gene gets turned on in a cell to make proteins. These small RNA molecules help regulate gene expression by preventing the translation of target genes. In translation, the information in genes is converted, or "translated," into proteins. There are many types of microRNAs and a single microRNA can block the translation of hundreds of genes.

Studies in patients with pancreatic cancer have revealed that levels of a select set of microRNAs are altered in pancreatic ductal adenocarcinoma (PDAC), the most common type of pancreatic cancer, as compared to levels in normal pancreas or benign pancreatic tissue. Researchers discovered that the levels of one microRNA, miR-221, commonly go up in PDAC patients, whereas the levels of another microRNA, miR-375, go down in these patients. Drs. Haldar and Basu found that in laboratory-grown pancreatic cancer cells treated with BITC, miR-221 levels went down, while miR-375 levels went up – in other words, the effects of BITC on these microRNAs were the opposite of what was seen in people with pancreatic cancer.

These findings suggest that BITC may target the levels of certain microRNAs "to switch hyperproliferative (rapidly dividing) cancer cells to a hypoproliferative (slower dividing) state," said Dr. Haldar – that is, to stop cancer cells from growing out of control. "These microRNAs have been shown to have important roles in other cancers too," he added.

Drs. Haldar and Basu are now working to see whether BITC has similar effects on microRNA in a mouse model of pancreatic cancer and, if so, whether those effects can prevent the development of pancreatic cancer or even help treat the disease in mice. If the findings in mice are promising, the researchers hope that eventually BITC could be tested in humans.

"Our investigation is now focused on whether we can reprogram microRNA networks in pancreatic cancer which would hold the potential of an important therapeutic and preventive target" if such findings can be extended to humans, Dr. Haldar added.

*Grant number: 5R03CA137476-02

Vitamin A Studied as Possible Preventive Agent Against Cancer

Division of Cancer Prevention

Vitamin A is an essential nutrient that plays a crucial role in a wide range of biological processes, from bone growth and vision to immune function and cellular maturation. Compounds derived from vitamin A have been used to treat cancer with mixed results. The vitamin's role in cancer appears to be complex: recent evidence suggests that, in certain circumstances, it may inhibit cancer in some, but promote cancer in others. Nevertheless, a large body of scientific literature supports the role of vitamin A in blocking the proliferation and maturation of breast cancer cells. Unfortunately, the doses required to achieve these effects produce adverse side effects and therefore cannot be used for cancer prevention.

An alternative and potentially less toxic approach might be to find a way to deliver immature forms (or precursors) of vitamin A to breast cells and make use of the cells' own machinery to turn the precursors into retinoic acid (the active form of vitamin A), explains Matthew J. Rowling, Ph.D., of Iowa State University, who is being funded by NCI* to determine how to optimally use vitamin A for breast cancer prevention.

Because the mechanisms by which vitamin A enters breast cells are poorly understood, it has not been clear how to deliver the vitamin A precursors into the cells. Dr. Rowling's research initially focused on a group of cell-membrane proteins that are found in breast cells and had previously been shown to be essential in enabling both vitamin D and retinol (the main circulating form of vitamin A) to gain entry into kidney cells. A series of experiments, however, failed to show that these proteins were actively involved in helping retinol gain entry to breast cells. Then scientists at the University of California Los Angeles (UCLA) published a paper** in which they identified a receptor, dubbed STRA6, that separates retinol from its binding protein and ushers it inside cells, where it is then broken down. These experiments were conducted in cells from the retina (the membrane at the rear of the eyeball that is important for vision), raising the question as to whether STRA6 also facilitates retinol uptake in other types of cells.

Dr. Rowling turned his attention to trying to elucidate whether STRA6 is the mechanism by which vitamin A enters cancer cells or cells susceptible to cancer. His experiments to date seem to confirm that the mechanism described by the UCLA scientists is at work not only in breast cells but also in colon and prostate cells.

"Our thinking now is that STRA6 is essential for the uptake and anti-proliferative effects of vitamin A in breast, colon, and prostate cells," he said. "A corollary to this is that if STRA6 is missing or disabled, vitamin A–mediated control of cell proliferation might be lost, creating the conditions for a cancer to develop. A deficiency of STRA6 could be a marker for increased risk for breast, colon, or prostate cancer."

If follow-up studies confirm this hypothesis, Dr. Rowling's research could lead to novel approaches to cancer prevention by boosting vitamin A uptake in these organs.

*Grant number: 5R03CA128091-03

**Kawaguchi R, Yu J, Honda J, et al. A membrane receptor for retinol binding protein mediates cellular uptake of vitamin A. *Science,* 2007;315(5813):820-5.

Vitamin D Tested for Preventing Lung Cancer in High-Risk Patients

Division of Cancer Prevention

At the Roswell Park Cancer Institute (RPCI) in Buffalo, New York, more than a decade's worth of work developing vitamin D-based approaches to cancer therapy has produced some possible options and hope for the millions of current and former smokers at high risk for lung cancer. "The burden of lung cancer is not shouldered exclusively by people who continue to smoke cigarettes," explained Mary E. Reid, Ph.D., associate professor of oncology and Director of Collaborative Research at RPCI. "While 40-50 million Americans have stopped smoking, their risk of developing lung cancer remains high for as many as 30 years after smoking cessation." And there are still many people who have been unable to stop smoking, despite the known risks, she added.

This is where calcitriol (1,25-dihydroxycholecalciferol) – the primary active form of vitamin D – comes in. Normally, the body takes in vitamin D through foods like fish and milk, dietary supplements, and produces its own vitamin D with the aid of sunlight. Vitamin D exerts its effect on the body via the vitamin D receptor (VDR) which is found in the cells of many types of tissues, including the lungs and prostate gland. Calcitriol has shown promise in preventing lung, prostate, and other cancers, Dr. Reid explained. She was the senior author on a study* that was the first to demonstrate that VDR is expressed in many different types of human lung tissue, from normal cells through the spectrum of precancerous changes, to full-blown tumors.

With NCI funding**, RPCI will soon begin a Phase II clinical trial testing calcitriol as a preventive agent in people at high risk for lung cancer, Dr. Reid reported. But first, the U.S. Food and Drug Administration (FDA) has asked RPCI scientists to conduct a small pilot study on 40 current and former smokers between ages 40-80 from their High Risk Lung Cancer Cohort. It will determine the safety of the proposed dose of calcitriol they are planning to use for the larger Phase II prevention study.

The patients in the pilot study will receive 45 micrograms of calcitriol every other week for 3 months, Dr. Reid explained. A common daily dose of calcitriol for patients with low calcium levels is 0.25 micrograms per day. Clinicians have found at least some form of precancerous tissue in the lungs of these patients – all of whom suffer from chronic obstructive pulmonary disease (COPD) – by passing a bronchoscope through the mouth or nose into the lungs to examine and collect samples. Dosing toxicities (or side effects) in the pilot study are graded from 1 through 4, with grades 1 and 2 being less serious. The pilot study will not only look for any grade 3 or 4 toxicities in the calcitriol dose but will also report any other adverse effects to the FDA. Since 1999, RPCI researchers have conducted 6 clinical trials studying calcitriol and this dosage level has never produced any high-grade toxicities, and only a handful of low-grade toxicities, Dr. Reid said.

"I feel it's important to be able to offer these high-risk patients some real options," Dr. Reid commented. "They are fully aware that lung cancer can amount to a death sentence, and even so some are unable to quit smoking. Generally they are very happy to faithfully take a pill that reduces their risk, as long as there are no serious side effects. We see so many people at the clinic with COPD and damage to their airways, usually from smoking or other environmental exposures." The current standard of care in the United States is simply to screen such patients routinely to detect changes in their lung and airway tissue indicating early cancer. "Understandably people want, and deserve more," she said.

The Phase II trial that will follow the pilot safety study will provide calcitriol for 6 months to about half of the patients. The remaining patients, serving as a control group, will get a placebo for only the first 6 months and will then receive calcitriol for another 6 months, Dr. Reid said. "All study participants will be getting at least some of the treatment that we believe may be effective in preventing progression of any disease they may be harboring," she concluded.

**Grant number: 5R01CA112238-04

*Menezes RJ, Cheney RT, Husain A, Tretiakova M, Loewen G, Johnson CS, Jayaprakash V, Moysich KB, Salgia R, Reid, ME. Vitamin D receptor expression in normal, premalignant, and malignant human tissue. *Cancer Epidemiology, Biomarkers and Prevention,* May 2008;17(5):1104-10.

Black Raspberries Studied To Prevent Oral Cancer

Division of Cancer Prevention

The Ohio State University (OSU) Comprehensive Cancer Center and College of Public Health have a long and successful tradition of studying food for its health and anticancer properties. One of the well-studied components found in ripe black raspberries is anthocyanins, which give the berries their deep purple color. A number of studies in different animals (such as rats and hamsters) have shown that a liquid mixture of these fruits taken orally interferes with the growth of tumors in the oral cavity, esophagus, and colon.

"We think the primary reason that the berry mixture inhibits cancer is because it makes physical and biological contact with the precancerous tissue all along the digestive route of the animals," noted Christopher Weghorst, Ph.D., a professor of Environmental Health Sciences and Otolaryngology at OSU. He said that many of the compounds found in black raspberries are not well absorbed through the digestive system into the bloodstream. "This certainly includes some of the components we think might be responsible for the protective effect we are finding," he added. "We and others have also designed some novel delivery methods aimed at extending the period of time the berry components remain in contact with the target tissue."

Many CAM researchers face a dilemma when trying to determine which ingredient in a food plant is responsible for the health effects they find in their studies, said Dr. Weghorst. While it is often possible to isolate just a single compound from the plant, test it for activity against a particular health problem, and then produce (and market) it as a supplement, "this may not be the best approach," he commented. "In fact, there is a lot of evidence to the contrary."

The study that NCI is funding* in Dr. Weghorst's lab is not intended to isolate and test the anthocyanins in black raspberries that many believe are the "active ingredient." Instead, he is testing the relative importance of anthocyanins by using green berries before they fully ripen into black raspberries. Anthocyanins are not developed in green berries because the fruit has not yet ripened. In hamsters, when the green berries were compared to the ripe raspberries, their inhibiting impact on oral cancer in the test animals was about the same, he reported.

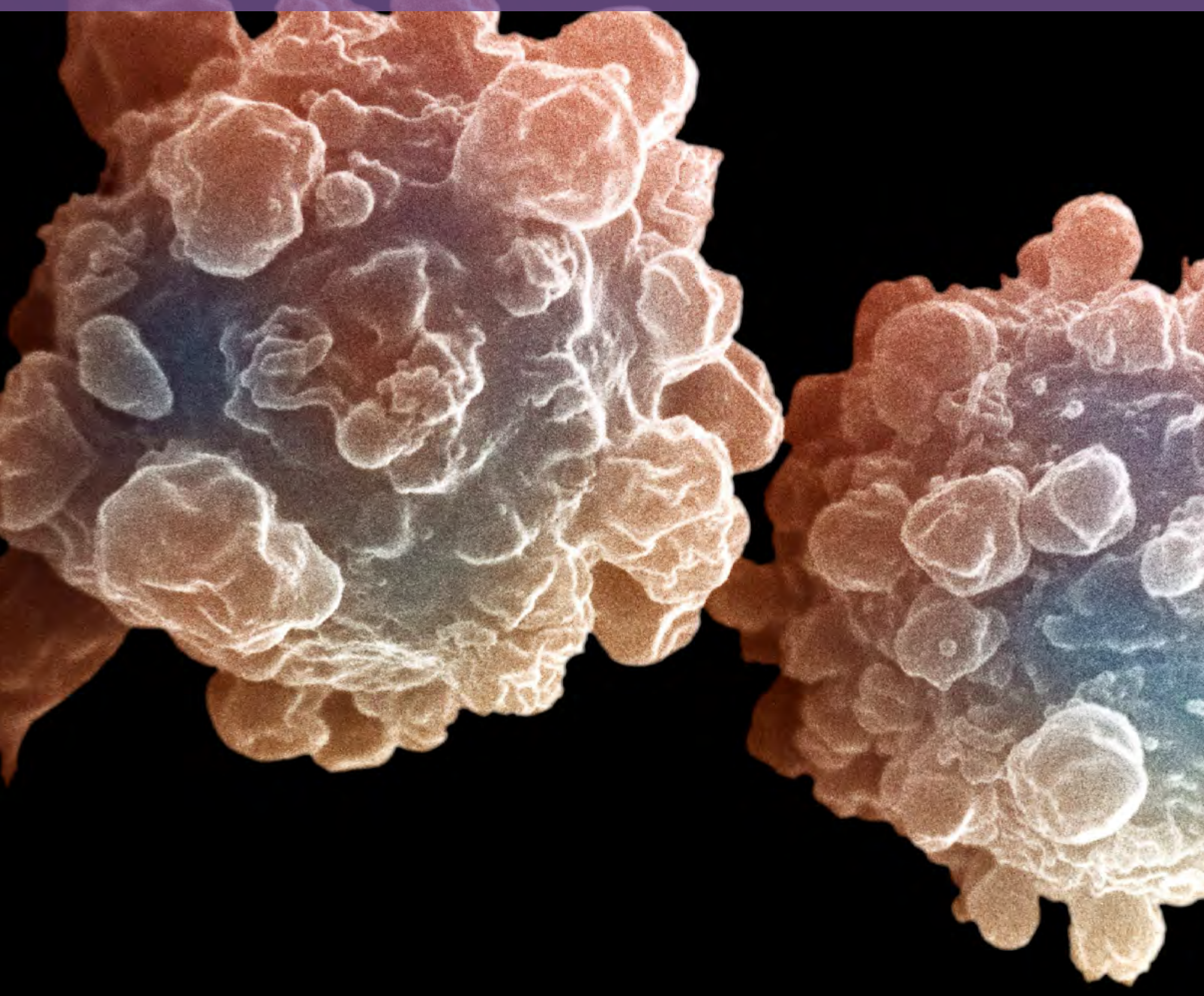
One possible mode of action for the berries' beneficial impact on cancer cells may involve gankyrin, a cancer-causing gene (or oncogene) "that produces a cell growth stimulus and is over-expressed in head and neck cancers," said Dr. Weghorst. "Both the green and the ripe black raspberries reduced the expression of this oncogene to a more normal level. Thus, the anthocyanins cannot logically be the sole cause." On the other hand, the researchers found that the P16 tumor suppressor gene, which is often inactivated in oral cancers, was found in abundance in animals given the ripe black raspberries but not in those given the green berries. Thus, there are numerous helpful ingredients in the berries which can change gene expression patterns in a manner that might favor cancer prevention, Dr. Weghorst explained.

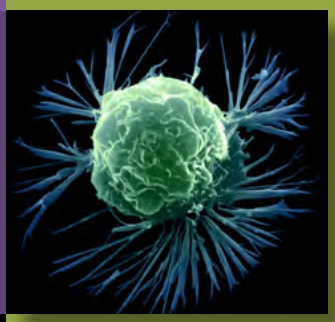
"All of this demonstrates there are multiple pathways involved in this type of cancer development and cancer prevention," Dr. Weghorst said. "We now know that that there are also bioactive components of the green forms of these plants that are effective against oral cancer." This helps confirm the food-based approach to cancer prevention, even using food at various stages of ripeness, he believes, and emphasizes the capability of the complex mixtures of chemicals found in "whole" foods to inhibit multiple processes of cancer development.

These types of animal studies have set the stage for larger studies in humans, Dr. Weghorst stated. One such study already underway is evaluating the molecular effects of ripe black raspberries on "at risk" normal oral cells in post-surgical oral cancer patients. "Oral cancer has a strong connection with alcohol consumption and smoking," he noted, "and reducing these behaviors would have a really dramatic impact." But proving the preventive value of berries could enhance the options available to people, despite the consequences of their past behaviors or their personal risk of cancer recurrence, he commented.

*Grant number: 5R03CA137798-02

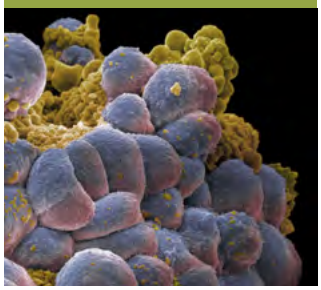
Developing Effective and Efficient Treatments





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.

Special Electric Signals Attack Cancer Cells with Lethal Force and Accuracy



Division of Cancer Treatment and Diagnosis

Directing X-ray energy into the body has been a mainstay of cancer therapy since early in the 20th century, but an entirely different approach using electric pulses now shows great promise. The first research center in the United States devoted to this burgeoning field of electroporation (EP) was established about a decade ago at Old Dominion University in Norfolk, Virginia, where Andrei G. Pakhomov, Ph.D., currently works as a research associate professor in cell biology and biophysics.

"The idea is to deliver electric pulses of extremely short duration through an electrode directly to a tumor," Dr. Pakhomov explained. If the pulses last only a matter of nanoseconds (a few billionths of a second), they create an electric field that blows open pores in the cellular membrane and disrupts the internal workings of the cell.

Nanosecond electrical pulses (nsEP) are bad news for the cancer cell in a many ways, Dr. Pakhomov noted. For example, the cellular membrane normally balances electrically charged molecules inside and outside the cell, but when the pores open up, the cell loses control of what's going in and out. This change in the permeability of the membrane leads to osmotic imbalance, where "ions pour into the cell, followed by water, you get swelling, and more swelling until they eventually explode," he added. "This is a form of necrotic cell death."

The good news for cancer researchers is that killing cells by high-power electric pulses is virtually without side effects, because the intervention is carefully delivered directly to the tumor site and has little effect on nearby tissue, Dr. Pakhomov said. Other researchers have shown that a single treatment using nsEPs has killed melanoma cells in mice. The exciting results from such early work has made many researchers eager to further test nsEPs in animals and eventually in people.

However, researchers still need to figure out many of the details about how nsEP works and how the electric pulses might be modified to match their targets. "I think that we're going to find different mechanisms for different kinds of cancer," he explained, "because nsEPs have the power to cause both apoptotic and necrotic damage."

Apoptosis – also known as programmed cell death – is a housekeeping process that cleans out unwanted cells by interfering with various cell survival functions. Many cancer cells are resistant to this process, leading researchers to develop drugs and therapies that induce apoptosis in various ways. "Apoptotic death is very clean," Dr. Pakhomov continued, "with less pain and inflammation [to the patient] and no scarring. We can control nsEPs very precisely to induce apoptosis when we want, but some researchers maintain that the immune reaction is actually an important part of the fight against cancer."

Dr. Pakhomov's NCI-funded work* is laying the groundwork for a therapy that clinicians will be able to adapt according to the type of cancer they are targeting. By altering the characteristics of the electrical pulse (such as pulse width, voltage, and duration of the pulse train), the signal can be tailored to the target tissue. This is important, he said, because preliminary studies have shown that, while most cancers are vulnerable to nsEPs, they differ in how resistant they are, and at what point in their basic cell cycle they are most vulnerable. He foresees a time when the pulse delivery system will be sophisticated enough to allow doctors to create a mix of pulses that will target different types of tumor tissue at different times and with a combination of certain drugs.

*Grant number: 5R01CA125482-03

Soy Bread Studied in Men with Prostate Cancer

Division of Cancer Prevention

Compared with men in the United States, men living in many Asian nations have a lower risk of prostate cancer. "If you look at what factors may contribute to the differences in risk, one of the many variables that jumps out is the much greater consumption of soy in Asia," said Steven Clinton, M.D., Ph.D., a professor of Medical Oncology at Ohio State University (OSU), who studies the role of dietary factors in prostate and other cancers.

Research in Dr. Clinton's laboratory and elsewhere – including studies in mouse models of prostate cancer – have shown that certain phytochemicals (chemicals that are found in plants) in soy have potential anti-prostate-cancer properties. However, the ability of soy to help prevent or treat prostate cancer in men remains unproven.

One of the challenges researchers face in studying this question is coming up with a convenient – and tasty – way to incorporate adequate, well-defined amounts of soy phytochemicals into the typical Western diet. With support from NCI*, Yael Vodovotz, Ph.D., an associate professor in OSU's Department of Food Science and Technology, is collaborating with Dr. Clinton to compare two types of soy bread that the researchers developed for that purpose. The soy bread "provides in two slices a dose of soy phytochemicals that would be similar to that consumed daily by many Asian populations," said Dr. Clinton.

The researchers are focusing on soy bread as a so-called functional food (foods that have potential health benefits, beyond just basic nutrition), rather than giving people individual soy phytochemicals, and in particular, soy compounds known as isoflavones. "The idea is that not only the isoflavones, but also the other components of soy may be very critical" for the biological effects in humans, Dr. Vodovotz said. She said that using soy bread as a "phytochemical delivery system" allows researchers to create a consistent product, yet provide a complex variety of soy components.

The OSU researchers are conducting a small clinical study to compare two types of soy bread as a source of phytochemicals in the diet. Both varieties contain isoflavones, but one of the breads includes an enzyme that yields twice as much of an altered form of isoflavone, known as the aglycone form, Dr. Vodovotz explained. The aglycone form is believed to be more biologically active and more readily absorbed from the digestion into the bloodstream than unaltered forms of isoflavones.

The 40 men in the study all had active prostate cancer and rising prostate specific antigen (PSA) -a biological marker of prostate cancer- levels but were not undergoing active therapy during the 20-week study period. For the first 8 weeks, half of the men ate three slices per day of the regular soy bread, while the other half ate three slices daily of the aglycone-enriched bread. After a 2-week, soy-free period, each study participant ate the other form of soy bread for another 8 weeks.

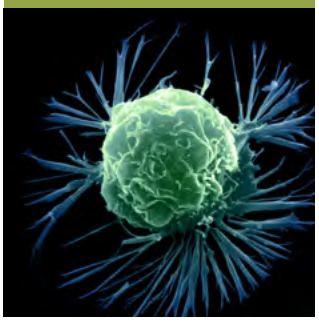
The researchers found that about 90% of the men could eat the soy breads on a daily basis without any difficulties, while about 5% experienced very minor gastrointestinal distress. No other serious problems were observed, Dr. Clinton said. "Overall, the majority of men found the food easily incorporated into the diet, and some men are even purchasing soy bread that is now on the market, while others are making their own soy bread at home," he noted. "At least a third of the men suggested that we need to improve the product to make it competitive with breads available on the market."

The researchers are analyzing blood samples from the men and running a range of tests to find out whether the aglycone form of isoflavones is in fact better absorbed and has a greater effect on various biomarkers that have been linked with anti-cancer activity.

Once the final results are in, the researchers hope to use an optimized form of soy bread in clinical trials that will rigorously test the ability of soy phytochemicals to improve the treatment of prostate cancer or to prevent the disease in men who are considered at high risk. Dr. Vodovotz commented, "We hope to eventually have the bread in a commercially available form, because if you're going to recommend something for prostate cancer, it better be available in the marketplace."

*Grant number: R21CA125909-02

Clinical Trial Inspired by Breast Cancer Cells, Cows, and Collaboration



Division of Cancer Treatment and Diagnosis

With more than 13 years of experience running early phase clinical trials, Raymond Perez, M.D., currently the Medical Director of the Clinical Research Center at the University of Kansas, knows that in early drug development "you can't sustain a clinical program with just one line of research. You have to look all over for opportunities for treatments that are ready to test in people, and help investigators make that happen."

Dr. Perez and his former colleague William Kinlaw, M.D., Professor of Medicine at Dartmouth Medical School (where Dr. Perez led the Phase I clinical trials program at the Norris Cotton Cancer Center from 1998 until 2011 before heading to Kansas) have pursued one such opportunity down a winding path from basic lipid metabolism studies to testing in dairy cows, and now to an early phase, NCI-funded clinical trial* testing conjugated linoleic acid (CLA) as a targeted anti-cancer agent.

About 10 years ago, Dr. Perez heard Dr. Kinlaw give a presentation on a protein called Spot 14, which helps cells produce necessary fatty acids from glucose. When the researchers blocked Spot 14 with an antisense nucleotide (a single strand of DNA or RNA, produced in the lab, which will bind to a corresponding section of DNA or RNA in the cell and interfere with production of proteins), they saw breast cancer cells die in laboratory cell cultures. "After Dr. Kinlaw's presentation, I approached him and started talking about Spot 14 and he'd never really thought about it therapeutically," recounted Dr. Perez.

Over the next several years, Dr. Kinlaw, an endocrinologist by training, moved his laboratory over to the Norris Cancer Center and his team engaged in a frustrating search for a drug to potentially target Spot 14 in people. No pharmaceutical company would commit to producing antisense against Spot 14, he said. Some drugs that he and Dr. Kinlaw tested in animals – such as Cerulenin (an antifungal agent) – were too toxic. Other drugs – such as Orlistat (a weight-loss drug) – were not absorbed into the bloodstream after oral administration.

The researchers put the idea of an anti-Spot 14 therapy aside for a while and concentrated on understanding its biology, showing that the protein is a marker for aggressive primary breast cancers.** Then, serendipitously, Dr. Kinlaw received a call from Dale Bauman, Ph.D., a professor of animal science at Cornell University. Dr. Bauman had been looking at a condition in dairy cows called milk-fat depression. The condition happens when cows eat plants in the wild that contain linoleic acid. Bacteria in their stomachs convert linoleic acid into another compound called conjugated linoleic acid (CLA), which is absorbed into the blood stream and suppresses milk-fat production.

In an experiment, he had fed some cows linoleic acid-containing plants and gave other cows injections of pure CLA, and then performed microarray analysis to analyze gene expression changes. "The biggest hit he got from both was that Spot 14 was turned off," Dr. Kinlaw recalled. "Dr Bauman had never heard of Spot 14 before so he called me out of the blue." Interestingly, CLA also interfered with an enzyme called lipoprotein lipase, which cancer cells can use to extract fatty acids from the local circulatory bed, Dr. Kinlaw added.

"We had a series of discussions about this and the obvious thing that came up was that if CLA could shut down lipid synthesis in the cows' mammary epithelial cells, maybe it could do the same thing in malignant human epithelial cells," Dr. Kinlaw commented. "We got some CLA and tested it in breast cancer and liposarcoma cells, and it inhibited their growth quite promptly." ***

CLA is used as a dietary supplement and had shown no severe side effects in a clinical trial testing it for weight loss, Dr. Kinlaw continued. He and other investigators performed a

*Grant number: 5R21CA131820-02

small proof-of-concept pharmacology trial in 23 women diagnosed with breast cancer. Between the 10 to 12 days from diagnosis to mastectomy, the women received 7.5 grams of CLA per day and then tissue taken during their surgeries was examined for Spot 14. "CLA significantly turned down Spot 14 in the tumors, so it did seem to actually work in humans," Dr. Kinlaw noted.

"We realized that CLA might be the compound that could hit this target; now we have to prove it," Dr. Perez said. In the ongoing Phase I trial, they will first determine the recommended therapeutic dose of CLA. The study dose will be escalated in patients until side effects are observed or the larger doses no longer increase the effect of CLA on Spot 14, he added. In this first part of the trial, samples of fat tissue from patients will be used to measure the activity of CLA.

Once the recommended dose has been determined, a second group of patients will be given CLA and tumor biopsies will be taken to make sure CLA is hitting its target in the tumors, Dr. Perez continued. The researchers will also look at the effect of CLA on proteins involved in the Spot 14 signaling pathway that also play a role in fat metabolism and examine the compound's effects on cell proliferation, apoptosis (programmed cell death), and other measurements of tumor growth.

Dr. Kinlaw is currently writing a grant application to study the mechanisms behind CLA's effects on Spot 14 in more detail, and also to explore how the compound might be most effectively delivered to tumors, using mice genetically engineered to lack either Spot 14 or lipoprotein lipase. "These are pretty good models to help us figure out how CLA might be working in humans," he said.

**Wells WA, Schwartz GN, Morganelli PM, Cole BF, Gibson JJ, Kinlaw WB. Expression of Spot 14 (THRSP) predicts disease free survival in invasive breast cancer: immunohistochemical analysis of a new molecular marker. *Breast Cancer Research and Treatment,* July 2006;98(2):231-40. Epub March 22, 2006.

***Donnelly C, Olsen AM, Lewis LD, Eisenberg BL, Eastman A, Kinlaw WB. Conjugated linoleic acid (CLA) inhibits expression of the Spot 14 (THRSP) and fatty acid synthase genes and impairs the growth of human breast cancer and liposarcoma cells. *Nutrition and Cancer,* 2009;61(1):114-22.

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.

Yoga Studied to Relieve Fatigue and Stress in Breast Cancer Patients

Division of Cancer Control and Population Sciences

Breast cancer survivors confront a number of post-treatment problems. Persistent fatigue, the most common and distressing problem, appears to be related in part to patients' inflammatory responses to various stressors from their disease and its aftermath.

"The best treatment that we know about to remedy this problem is exercise," noted Janice Kiecolt-Glaser, Ph.D., who holds the S. Robert Davis Chair of Medicine in The Ohio State University College of Medicine. "But the problem is, of course, that if you're pretty tired and feeling that you don't have a lot of energy, one of the last things you want to do is exercise." With NCI funding*, she is conducting a clinical trial of a gentle regimen of hatha yoga (which is physically less demanding than other forms of yoga) "that we thought could be quite useful in terms of reducing fatigue, and potentially inflammation at the same time."

Dr. Kiecolt-Glaser and her colleagues have enrolled approximately 200 women, ages 40 and older, who have been diagnosed with stage I, II, or IIIA breast cancer. The women have all completed cancer treatment within the past year (except for tamoxifen/aromatase inhibitors), and will not start in the study until at least two months after their surgery and completion of adjuvant chemotherapy or radiation (if any). They will be assigned to either a 12-week, twice-weekly hatha yoga intervention or to a delayed "wait list" group who will receive the yoga intervention after a 6-month observation period.

The researchers will measure differences between the two groups at the start (baseline) of the study, at 3 months (at the conclusion of the 12-week yoga intervention), and at 6 months.

Also at baseline and 3 months, responses of inflammation-related molecules to a laboratory stressor will be assessed. The primary aim is to determine if the yoga intervention will decrease inflammation, fatigue, and depressive symptoms relative to the wait-listed group.

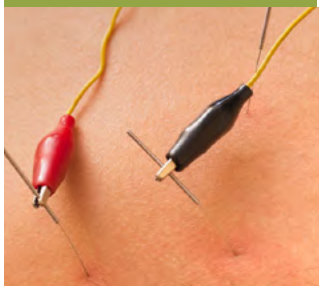
They will also determine the extent to which the intervention affects psychological, behavioral, and physical functioning; evaluate the relationship between depressive symptoms and the magnitude of the physiological responses elicited by a laboratory stressor, as well as the relationship of both to fatigue; and assess the extent to which the yoga intervention decreases physiological stress responses.

Although they have not yet analyzed data on the two comparison groups of breast cancer patients because the trial is still in progress, "the women in the yoga group have been incredibly enthusiastic about it once they actually get into the program," Dr. Kiecolt-Glaser noted. "We have small groups that we schedule around the women's availability. The yoga groups meet twice a week and they're encouraged strongly to practice at home and we're getting pretty good compliance in terms of actual home practicing as well."

If the study results prove positive, yoga could be a good addition to standard medical care for these types of patients, she added. "We believe yoga should be able to offer a lot of other physical benefits in the way that modest exercise does, such as increased flexibility. Yoga could also serve as a 'gateway' exercise to other, perhaps more strenuous, kinds of exercise programs for these patients."

*Grant number: 5R01CA126857-05

Electroacupuncture May Counter Patients' Nausea After Chemotherapy



Division of Cancer Prevention

Many cancers are treated with chemotherapy agents that circulate throughout the body. When the drugs reach organs and tissues not affected by cancer, they can cause adverse side effects. Among the most prevalent and troublesome side effects are nausea and vomiting, though recently a new class of molecules – known as 5HT3 agonists, and used in combination with corticosteroid dexamethasone pills – have been found to help reduce or even prevent these symptoms.

"But those drugs [5HT3 agonists] work effectively only against what we call acute-onset nausea and vomiting," said Dr. Jiande Chen, Ph.D., professor of Medicine at the University of Texas Medical Branch. "Once you get past the first day, many patients suffer from delayed nausea and vomiting, which is really a different problem altogether, can last for many hours or several days, and is much more difficult to treat." Patients with advanced cancer can also develop chronic nausea symptoms.

Older patients and others can wear down from the rigors of chemotherapy and many are reluctant to add yet another medication to their treatment regimen, especially if it is supposed to counter symptoms that were caused by medication in the first place. For example, with a drug like cisplatin, "it is not uncommon to find patients choosing to discontinue chemotherapy altogether – even when it is effectively treating their cancer – in order to avoid these debilitating side effects," explained Dr. Chen.

In China, there is widespread use and acceptance of acupuncture to treat nausea. "It is encouraging to find more and more practitioners and patients in the United States willing to accept this therapy," he said. Acupuncture relies on the stimulation of very precise points on the body located beneath the skin. Each of these "acupoints" is associated with pain or other symptoms at a specific, usually distant, site in the body. After several thousand years of use, acupuncture practitioners have been able to develop detailed "body maps" for these points. Two of the acupoints that inhibit nausea and vomiting have been found to be PC6 – a few inches above the inside of the wrist – and ST36 – slightly below and behind the knee, Dr. Chen explained. In previous studies, needles inserted at these points and then manually manipulated have produced some results, but they were only partial responses, and worked only against acute vomiting after chemotherapy.

Dr. Chen believes those mixed results were due, not to any limits in acupuncture per se, but rather to how it has been applied. With NCI funding*, Dr. Chen and his colleagues have been testing electroacupuncture (EA), to see if it is even more effective than traditional acupuncture against chemotherapy-induced nausea. Electroacupuncture is a procedure in which pulses of weak electrical current are sent through acupuncture needles into acupuncture points in the skin. Using rats and dogs, their current study is testing the precise location and depth the acupuncture stimulation should be applied; whether to use EA before or after chemotherapy, or both; whether the regimens should be continuous; and also the frequency and intervals of the electric pulses themselves.

The researchers are working on several aspects of EA that would be important in delivering therapy to patients for whom current antiemetics (drugs to counter nausea and vomiting) are not working. That group potentially includes the majority of patients with delayed or chronic nausea and vomiting.

Dr. Chen believes that a successful series of experiments with the EA approach could have a major impact on treating symptoms that threaten the quality of life of cancer patients. "This EA therapy has no discernible side effects on the patient, and therefore we can give it chronically, as necessary, to respond to symptoms," he added. Dr. Chen and his colleagues are also testing a system where a small power stimulator is implanted in the abdomen of the experimental animals, with conducting wires leading under the skin to electrodes that have been carefully inserted at the acupoints. The researchers will be able to trigger the EA stimulation by an external transmitter, but ultimately Dr. Chen foresees a time when patients will be able to control a similar system themselves.

*Grant number: 1R21CA149956-01

Division of Cancer Control and Population Sciences

Behavioral Stress Management Program, Even in Small Doses, May Help Breast Cancer Patients

Over the past 20 years, Professor Michael Antoni, Ph.D. and his colleagues at the University of Miami have received NCI support to research and develop the Cognitive Behavioral Stress Management (CBSM) intervention for women recovering from breast cancer. CBSM – a 10-week program that combines cognitive behavioral therapy techniques, relaxation training, and learning interpersonal skills – has proven successful in helping many patients achieve improvements in multiple indicators of psychosocial adaptation after treatment, including better social and psychological functioning and less intrusive thoughts and social disruption.*

These successes have led to the adoption of the CBSM program by the University of Miami Sylvester Comprehensive Cancer Center and by numerous other cancer centers in the United States. However, Dr. Antoni cautions that the full 10-week program – which includes 2-hour sessions each week – can be difficult for some breast cancer patients to participate in, either due to debilitating symptoms from their illness and treatments, scheduling, transportation problems, or other concerns. This has led him and his colleagues to explore whether condensed or alternative formats for delivering CBSM will make the intervention a realistic option for more patients.

With NCI funding**, Dr. Antoni is currently studying two 5-week, partial versions of CBSM. Dr. Antoni reported that "previous research has shown that women who had attended on average 5 of the 10 CBSM sessions did just about as well as did women who attended 8-10 sessions, and did much better than women who only attended 1-2 sessions."

The investigators also discovered that two components of CBSM provided most of the beneficial effects for breast cancer patients. "One thing from the intervention that seemed to be accounting for most of the positive effects was relaxation training and the patients' confidence in using relaxation skills," Dr. Antoni recalled. "One other variable that seemed to drive most of the effects was the amount of time the women were spending each week in expressing their emotions" with cognitive behavioral therapy.

"This suggests that shorter forms of the CBSM intervention – focusing on elements of the full intervention such as cognitive behavioral therapy techniques or on relaxation training skills – might be a cost-effective way to facilitate adaptation among a larger portion of the population of women receiving treatment for breast cancer," Dr. Antoni said.

As a result, the current study is randomizing women, newly diagnosed with Stages I to III breast cancer, into three groups: 1) cognitive behavioral therapy; 2) relaxation training intervention; or 3) an attention-social support control. Groups of 80 individuals each will run for 5 weeks.

While that study is running, Dr. Antoni is also planning research into new delivery formats – including teleconferencing, videophone, and Internet Skype technologies – to bring CBSM directly to patients' homes. "A lot of breast cancer patients are suffering side effects during treatment, like fatigue, that might make it hard for them to attend even a 5-week group," he noted. "We want to be able to reach those patients."

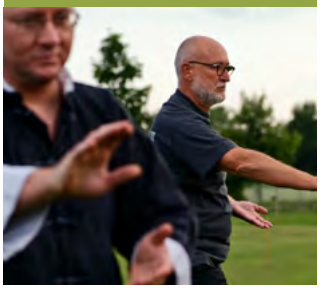
Dr. Antoni and his colleagues are studying bringing CBSM "to the community for the lower-income minority patients." They're currently testing whether CBSM works in women from one lower income African- American community, he said. "We're running groups in the churches and community health centers that serve these women."

In addition, Dr. Antoni added, they will delve further into their earlier research findings on the biological impact of CBSM on breast cancer patients. In previous CBSM studies, they collected blood samples from study participants and "found reductions in serum cortisol (a marker of stress) and changes in immune system activity such as increases in lymphocyte proliferative responses and increased Th-1 cytokine production (interferon-gamma and interleukin-2)," he noted. Dr. Antoni and his colleagues are now examining other molecules involved in stress response and seeing how they change following participation in the CBSM program.

**Grant number: 5R01CA064710-14

*Antoni M, Wimberly S, Lechner S, Kazi A, Sifre T, Urcuyo K, Phillips K, Smith R, Petronis V, Guellati S, Wells K, Blomberg B, Carver C. Reduction of cancer-specific thought intrusions and anxiety symptoms with a stress management intervention among women undergoing treatment for breast cancer. *American Journal of Psychiatry,* October 2006;163:1791-1797.

Tai Chi Exercise Studied to Improve Quality of Life for Senior Cancer Survivors



Division of Cancer Control and Population Sciences

There are over 28 million cancer survivors worldwide and the majority of these survivors are over age 60. Compared to elderly individuals who have never had cancer, both short-term and long-term elderly cancer survivors are more likely to report worse quality of life (QOL), high rates of psychological distress, poorer general health status, and more functional limitations. Mind-body exercise interventions have been suggested as a way to improve both mental and physical aspects of QOL in cancer patients who are undergoing or who have completed treatment. However, few studies have been conducted among older cancer survivors.

Anita Kinney, Ph.D., Jon & Karen Huntsman Presidential Professor in Cancer Research at Huntsman Cancer Institute and the Department of Internal Medicine, University of Utah, explained that Tai Chi Chih (TCC), a westernized version of Tai Chi Chuan, is a mind-body program designed for use in the elderly and medically compromised populations. TCC is considered to be a moderate-intensity aerobic exercise that consists of a combination of slow, deliberate movements and meditation.

With NCI funding*, Dr. Kinney is conducting a randomized controlled clinical trial to determine the feasibility and preliminary efficacy of TCC for improving physical performance, mental and physical health-related QOL, and biomarkers associated with stress, inflammation, and healthy aging among senior, female cancer survivors. "We have enrolled 64 women, ages 55 and older," she noted. "About 84% of our enrollees are breast cancer survivors. Initially, the study was focusing solely on breast cancer survivors but there was a large community interest for enrolling women who had other types of cancer. We felt that it was important to be responsive to the community's interest and address the needs of other female sedentary cancer survivors."

The women are randomized to the TCC or a health education control (HEC) group. They all receive 12 weeks of TCC or HEC, for 60 minutes, 3 times a week, for a total of 36 sessions. "We evaluate them for physical performance," Dr. Kinney noted. "They come into our Cancer Institute's Wellness Center and receive exams by physical fitness professionals. Then we collect their survey data to assess their QOL. We also collect blood samples to test for some biomarkers. We're measuring the TCC intervention's effects on inflammatory cytokines, as well as on cortisol which is a stress biomarker and also oxytocin which has been coined the 'happy' hormone."

The trial is ongoing, but Dr. Kinney is hopeful the study's data will provide support for the feasibility and the potential health benefits of a TCC program for senior, female cancer survivors. If so, she plans to seek NCI funding for a larger, multi-site randomized clinical trial. "We hope that if our findings are borne out in a larger trial, this may pave the way for mind-body exercise interventions to become a routine part of cancer wellness care," Dr. Kinney explained. "We hope the studies will provide evidence to policy-makers for the inclusion of TCC and similar types of interventions into survivorship care plans and for third-party payers reimbursing cancer survivors for TCC."

*Grant number: 5R21CA135250-02

SCIENTIFIC PUBLICATIONS

This is a selected list of some of the most important peer-reviewed scientific articles about the finding and analyses of NCI-supported CAM research studies published during FY 2010. The articles are classified and grouped according to research type: cancer prevention, cancer treatment, cancer side effect/symptom management and quality of life/survivorship.

Article citations marked with an asterisk (*) are studies which were featured in the *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2009,* which can be read and downloaded from http://www.cancer.gov/cam/attachments/nci_cam_annual_report_fy09.pdf.

Abstracts of all the articles are available online through the National Library of Medicine's "PubMed" database at http://www.pubmed.com.

Prevention

*Adhami VM, Khan N, Mukhtar H. Cancer chemoprevention by pomegranate: laboratory and clinical evidence. *Nutrition and Cancer,* 2009;61(6):811-5.

*Aslam MN, Kreider JM, Paruchuri T, Bhagavathula N, DaSilva M, Zernicke RF, Goldstein SA, Varani J. A mineral-rich extract from the red marine algae Lithothamnion calcareum preserves bone structure and function in female mice on a Western-style diet. *Calcified Tissue International,* 2010 Apr;86(4):313-24. Epub 2010 Feb 24.

*Aslam MN, Paruchuri T, Bhagavathula N, Varani J. A mineral-rich red algae extract inhibits polyp formation and inflammation in the gastrointestinal tract of mice on a high-fat diet. *Integrative Cancer Therapies,* 2010 Mar;9(1):93-9.

Nath RG, Wu MY, Emami A, Chung FL.Effects of epigallocatechin gallate, L-ascorbic acid, alpha-tocopherol, and dihydrolipoic acid on the formation of deoxyguanosine adducts derived from lipid peroxidation. *Nutrition and Cancer,* 2010;62(5):622-9.

Sarkar FH, Li Y, Wang Z, Kong D. Novel targets for prostate cancer chemoprevention. *Endocrine-Related Cancer,* 2010 Aug 16;17(3):R195-212. Print 2010 Sep.

Zick SM, Ruffin MT, Djuric Z, Normolle D, Brenner DE. Quantitation of 6-, 8- and 10-Gingerols and 6-Shogaol in Human Plasma by High-Performance Liquid Chromatography with Electrochemical Detection. *International Journal of Biomedical Science,* 2010 Sep;6(3):233-240.

Treatment

Ansenberger K, Richards C, Zhuge Y, Barua A, Bahr JM, Luborsky JL, Hales DB. Decreased severity of ovarian cancer and increased survival in hens fed a flaxseed-enriched diet for 1 year. *Gynecologic Oncology,* 2010 May;117(2):341-7.

*Luo W, Karpf AR, Deeb KK, Muindi JR, Morrison CD, Johnson CS, Trump DL. Epigenetic regulation of vitamin D 24-hydroxylase/CYP24A1 in human prostate cancer. *Cancer Research,* 2010 Jul 15;70(14):5953-62.

*Muindi JR, Yu WD, Ma Y, Engler KL, Kong RX, Trump DL, Johnson CS. CYP24A1 inhibition enhances the antitumor activity of calcitriol. *Endocrinology,* 2010 Sep;151(9):4301-12.

Sarkar FH, Li Y, Wang Z, Kong D. The role of nutraceuticals in the regulation of Wnt and Hedgehog signaling in cancer. *Cancer Metastasis Reviews,* 2010 Sep;29(3):383-94.

*Shoulars K, Rodriguez MA, Thompson T, Markaverich BM. Regulation of cell cycle and RNA transcription genes identified by microarray analysis of PC-3 human prostate cancer cells treated with luteolin. *Journal of Steroid Biochemistry Molecular Biology,* 2010 Jan;118(1-2):41-50.

Volate SR, Kawasaki BT, Hurt EM, Milner JA, Kim YS, White J, Farrar WL. Gossypol induces apoptosis by activating p53 in prostate cancer cells and prostate tumor-initiating cells. *Molecular Cancer Therapeutics,* 2010 Feb;9(2):461-70.

Wang Z, Ahmad A, Banerjee S, Azmi A, Kong D, Li Y, Sarkar FH. FoxM1 is a novel target of a natural agent in pancreatic cancer. *Pharmaceutical Research,* 2010 Jun;27(6):1159-68. Epub 2010 Mar 31.

Wang Z, Li Y, Sarkar FH. Notch signaling proteins: legitimate targets for cancer therapy. *Current Protein & Peptide Science,* 2010 Sep 1;11(6):398-408.

*Wei G, Wang M, Carr BI. Sorafenib combined vitamin K induces apoptosis in human pancreatic cancer cell lines through RAF/MEK/ERK and c-Jun NH2-terminal kinase pathways. *Journal of Cellular Physiology,* 2010 Jul;224(1):112-9.

*Wei G, Wang M, Hyslop T, Wang Z, Carr BI. Vitamin K enhancement of sorafenib-mediated HCC cell growth inhibition in vitro and in vivo. *International Journal of Cancer,* 2010 Dec 15;127(12):2949-58

Side Effect/Symptom Management

Kwan ML, Darbinian J, Schmitz KH, Citron R, Partee P, Kutner SE, Kushi LH. Risk factors for lymphedema in a prospective breast cancer survivorship study: the Pathways Study. *Archives of Surgery,* 2010 Nov;145(11):1055-63.

Kiecolt-Glaser, J. Stress, Food, and Inflammation: Psychoneuroimmunology and Nutrition at the Cutting Edge. *Psychosomatic Medicine,* 2010 May;72(4):365–369.

*Lyon DE, Schubert C, Taylor AG. Pilot study of cranial stimulation for symptom management in breast cancer. *Oncology Nursing Forum,* 2010 Jul;37(4):476-83.

Vargas S, Wohlgemuth WK, Antoni MH, Lechner SC, Holley HA, Carver CS. Sleep dysfunction and psychosocial adaptation among women undergoing treatment for non-metastatic breast cancer. *Psychooncology,* 2010 Jun;19(6):669-73.

Quality of Life/Survivorship

Kwan ML, Ergas IJ, Somkin CP, Quesenberry CP Jr, Neugut AI, Hershman DL, Mandelblatt J, Pelayo MP, Timperi AW, Miles SQ, Kushi LH. Quality of life among women recently diagnosed with invasive breast cancer: the Pathways Study. *Breast Cancer Research and Treatment,* 2010 Sep;123(2):507-24.

APPENDIX

An NCI-supported 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 Clinical Trials	Protocol ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Pediatric Trials						
Phase III Randomized Study of Acupressure to Control Chemotherapy-Induced Nausea in Children With Central Nervous System or Solid Tumors Receiving Cisplatin-Containing Chemotherapy	COG-ACCL1032	Active	Supportive care	4 to 18	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	SCUSF-0402	Active	Supportive care, Treatment	3 to 20	NCI	Phase III
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	Active	Supportive care	5 to 35	NCI	Phase I
Adult Trials						
Bladder						
Green Tea Extract in Treating Patients With Nonmetastatic Bladder Cancer	CDR0000594276	Active	Biomarker/Laboratory analysis, Treatment	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	Active	Treatment	18 and over	NCI	Phase II
Breast						
Diindolylmethane in Treating Patients With Breast Cancer	10-0366-04	Active	Biomarker/Laboratory analysis, Diagnostic, Treatment	19 and over	NCI	Phase III, Phase II
Phase II/III Study of Curcumin in Patients With Breast Cancer With Radiation-Induced Dermatitis	URCC-10054	Active	Biomarker/Laboratory analysis, Supportive care, Treatment	21 and over	NCI	Phase III, Phase II
Acupressure for Persistent Cancer Related Fatigue	CA151445	Active	Supportive care	18 to 75	NCI	Phase III, Phase II
Phase III Randomized Study of Cranial Microcurrent Electrical Stimulation in Reducing Chemotherapy-Related Symptoms in Women With Stage I-IIIA Breast Cancer Receiving Adjuvant Chemotherapy	MCV-MCC-11995	Active	Biomarker/Laboratory analysis, Supportive care	Adult	NCI	Phase III

PDQ Clinical Trials	Protocol ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Phase III Randomized Study of Omega-3-Fatty Acid in Treating Aromatase Inhibitor-Induced Musculoskeletal Pain and Stiffness in Patients With Stage I, II, or IIIA Breast Cancer	SWOG-S0927	Approved-not yet active	Biomarker/Laboratory analysis, Prevention	Not specified	NCI	Phase III
Menopause and Meditation for Breast Cancer Survivors	1R21CA106336-01A1	Active	Supportive care	30 to 70	NCI	Phase II, Phase I
Phase II Randomized Study of High-Dose Cholecalciferol in Premenopausal Women at High-Risk for Breast Cancer	SWOG-S0812	Approved-not yet active	Biomarker/Laboratory analysis, Supportive care	18 to 50	NCI	Phase II
IH636 Grape Seed Extract in Preventing Breast Cancer in Postmenopausal Women at Risk of Developing Breast Cancer	03178	Active	Prevention	40 to 75	NCI	Phase II
Acupuncture in Reducing Muscle and Bone Symptoms in Women Receiving Letrozole, Exemestane, or Anastrozole for Stage 0, Stage I, Stage II, or Stage III Breast Cancer	JHOC-J07110, CDR0000589108	Active	Biomarker/Laboratory analysis, Supportive care, Treatment	18 and over	NCI	Phase II
Broccoli Sprout Extract in Treating Women Who Have Had a Mammogram and Breast Biopsy	CDR0000634111	Active	Biomarker/Laboratory analysis, Treatment	21 and over	NCI	Phase II
Phase II Randomized Pilot Study of a Community-Based Yoga Intervention Versus an Educational Wellness Intervention in Women With Stage I-III Breast Cancer Undergoing Chemotherapy	CCCWFU-97309	Active	Educational/Counseling/Training, Supportive care	18 and over	NCI	Phase II
Soy Isoflavones and Breast Cancer Risk Reduction	03-260	Active	Prevention	30 to 42	NCI	Phase II
The Effect of Soy Protein on Post- Breast Cancer Surgery Pain	A02-M102-07A	Active	Supportive care	21 and over	NCI	Phase II
Study of CoQ10 During One Cycle of Doxorubicin Treatment for Breast Cancer	AAAD8521	Active	Supportive care, Treatment	21 and over	NCI	Phase I
Cook for Your Life	AAAE9701	Active	Behavioral study, Biomarker/ Laboratory analysis, Educational/ Counseling/Training	21 and over	NCI	No phase specified
Randomized Study of Vitamin D and Breast Cancer Biomarkers in Female Patients	CALGB-70806	Active	Biomarker/Laboratory analysis, Prevention	55 and under	NCI	No phase specified
Randomized Study of Hatha Yoga in Improving Physical Activity, Inflammation, Fatigue, and Distress in Female Breast Cancer Survivors	OSU-2007C0004	Active	Biomarker/Laboratory analysis, Supportive care	21 and over	NCI	No phase specified
Effects of Tibetan Yoga on Fatigue and Sleep in Cancer	2005-0035	Active	Supportive care	18 and over	NCI	No phase specified

PDQ Clinical Trials	Protocol ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Venlafaxine and Hypnosis or Focused Attention In Treating Patients With Hot Flashes	MC09C7	Active	Supportive care	18 and over	NCI	No phase specified
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	Active	Supportive care, Treatment	18 and over	NCI	No phase specified
Cervix						
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	Active	Biomarker/Laboratory analysis, Prevention	19 and over	NCI	Phase II
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	Active	Behavioral study, Biomarker/ Laboratory analysis, Educational/ Counseling/Training	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	Active	Natural history/Epidemiology, Prevention	50 and over	NCI	Phase III
Selenium for Prevention of Adenomatous Colorectal Polyps	CDR0000353185	Active	Prevention	40 to 80	NCI	Phase III
Cholecalciferol(25-[OH]-Vitamin D) in Treating Patients With Colorectal Cancer	CASE2210	Approved-not yet active	Biomarker/Laboratory analysis, Treatment	18 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	Active	Supportive care	Over 18	NCI	Phase II
Vitamin E Supplements in Treating Patients Undergoing Surgery for Colorectal Cancer	CDR0000642446	Active	Biomarker/Laboratory analysis, Treatment	18 and over	NCI	Phase I
Phase I/II Randomized Study of Inositol for the Prevention of Colorectal Cancer in Patients With Colitis-Associated Dysplasia	NU-NWU09-13-02	Active	Biomarker/Laboratory analysis, Prevention	18 and over	NCI	Phase I
Randomized Pilot Study of Oncologist Recommended Home-Based Exercise Program Versus Relaxation Training for Physical Functioning and Symptom Control in Patients With Unresectable Stage IV or Recurrent Colon Cancer	MDA-2009-0288	Active	Behavioral study, Supportive care	18 and over	NCI	No phase specified
Head/Neck						
Phase III Randomized Study of Acupuncture for Radiation-Induced Xerostomia in Patients With Head and Neck Cancer	MDA-04-01	Approved-not yet active	Supportive care	Not specified	NCI	Phase III
Xerostomia Acupuncture Trial	2010-0584	Approved-not yet active	Supportive care	18 and over	NCI	Phase III
Phase II Randomized Chemoprevention Study of Bowman-Birk Inhibitor Concentrate in Patients With Oral Leukoplakia	UCIRVINE-UCI-98-34	Active	Biomarker/Laboratory analysis, Prevention, Treatment	18 and over	NCI	Phase II

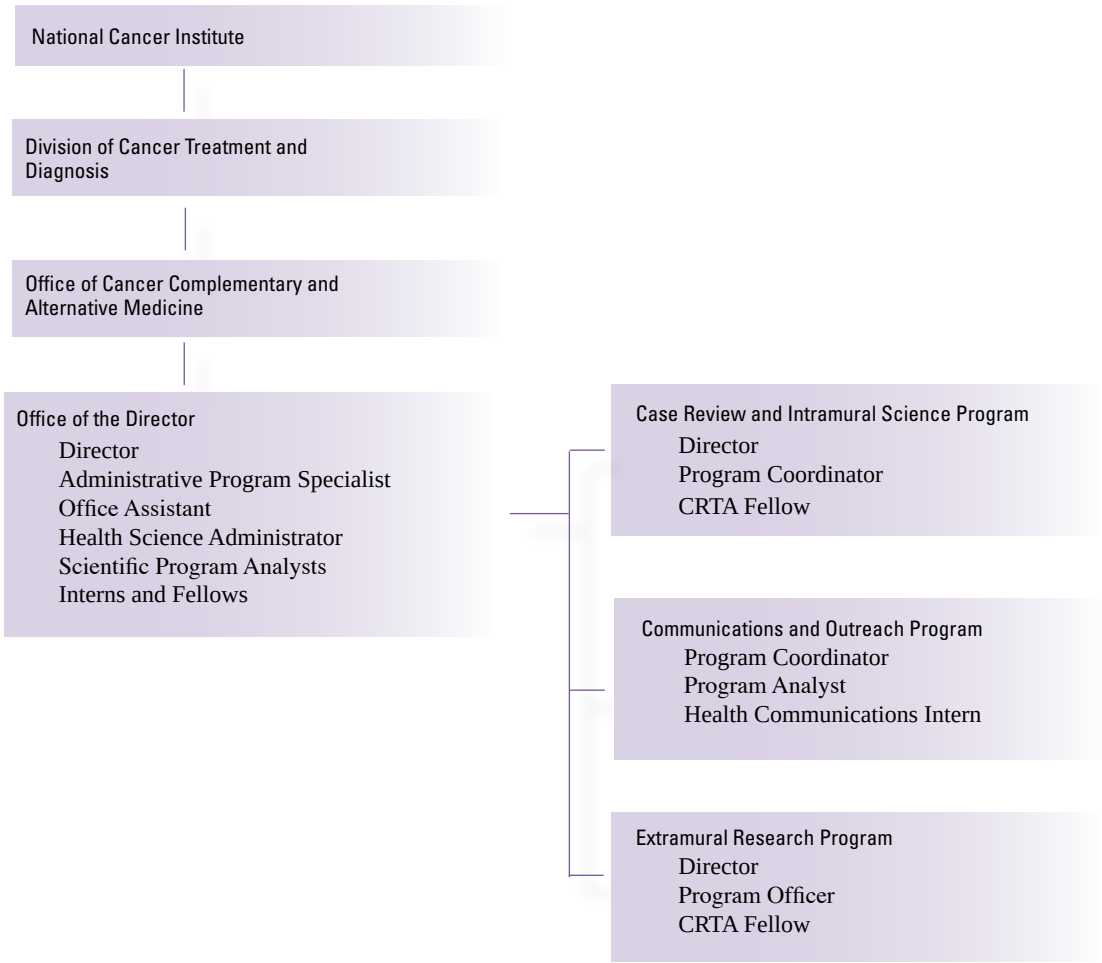
PDQ Clinical Trials	Protocol ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Curcumin Biomarker Trial in Head and Neck Cancer	H08-081	Active	Biomarker/Laboratory analysis, Treatment	18 to 90	NCI	No phase specified
Hematologic						
Green Tea Extract in Treating Patients With Monoclonal Gammopathy of Undetermined Significance and/or Smoldering Multiple Myeloma	CDR0000646899	Active	Biomarker/Laboratory analysis, Treatment	18 and over	NCI	Phase II
Efficacy of NF-kB Inhibition for Reducing Symptoms During Maintenance Therapy in Multiple Myeloma Patients	2010-0457	Approved-not yet active	Supportive care, Treatment	18 and over	NCI	Phase II
Lactobacillus in Preventing Infection in Patients Undergoing a Donor Stem Cell Transplant for Hematologic Cancer or Myelodysplastic Syndrome	CDR0000649274	Active	Supportive care	18 and over	NCI	No phase specified
Lung						
Exercise and Lung Cancer Trial	00018255	Active	Behavioral study	21 to 80	NCI	Phase III
Phase II Randomized Study of Manuka Honey for the Reduction of Chemoradiation Therapy-Induced Esophagitis-Related Pain During Treatment in Patients With Lung Cancer	RTOG-1012	Approved-not yet active	Supportive care, Treatment	18 and over	NCI	Phase II
Green Tea Extract in Treating Current or Former Smokers With Bronchial Dysplasia	CDR0000578224	Active	Biomarker/Laboratory analysis, Prevention	45 to 74	NCI	Phase II
Phase II Randomized Study of Inositol for the Prevention of Lung Cancer in Current or Former Smokers With Bronchial Dysplasia	MAYO-MAY06-8-01	Active	Biomarker/Laboratory analysis, Prevention	45 to 79	NCI	Phase II
Calcitriol in Preventing Lung Cancer in Smokers and Former Smokers at High Risk of Lung Cancer	CDR0000596506	Active	Biomarker/Laboratory analysis, Prevention	40 to 79	NCI	Phase I
Phase I Randomized Pilot Study of Dietary Flaxseed Supplementation in Patients With Locally Advanced or Metastatic Non-Small Cell Lung Cancer Undergoing Definitive Chemoradiotherapy	UPCC-03309	Active	Biomarker/Laboratory analysis, Treatment	18 and over	NCI	Phase I
Multiple						
Phase II Pilot Study of Magnesium Oxide in Treating Menopausal Hot Flashes in Women With Cancer	MCV-MCC-12062	Active	Supportive care	18 and over	NCI	Phase II
A Molecular Pharmacodynamic Dose-titration Trial of Conjugated Linoleic Acid (CLA; Clarinol®) in Patients With Advanced Solid Tumors	D0914	Active	Biomarker/Laboratory analysis, Treatment	18 and over	NCI	Phase I
Yoga-Based Cancer Rehabilitation Program	#2000-007	Active	Behavioral study, Supportive care	18 and over	NCI	No phase specified
Randomized Study of Magnetic Acupressure in Reducing Pain in Cancer Patients Undergoing Bone Marrow Aspiration and Biopsy	JHOC-J07103	Active	Diagnostic, Supportive care	18 and over	NCI	No phase specified
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	Active	Educational/Counseling/Training, Supportive care	Over 18	NCI	No phase specified

PDQ Clinical Trials	Protocol ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Pilot Randomized Study of Cognitive-Behavioral Therapy Versus Standard Care in Patients With Advanced Gastrointestinal Cancer or Lung Cancer	MGH-2007-P-000368	Active	Educational/Counseling/Training, Supportive care	Over 18	NCI	No phase specified
White Wine or Nutritional Supplement in Improving Appetite in Patients With Cancer	RC08C6	Active	Supportive care	21 and over	NCI	No phase specified
No Specific Cancer Type/Healthy Volunteer						
Clinical Trial of Vitamin D3 to Reduce Cancer Risk in Postmenopausal Women	CAPS08-15024	Active	Prevention	55 and over	NCI	Phase III
Phase III Randomized Study of a Psychoeducation, Paced Respiration, and Relaxation Intervention for Caregivers of Patients Undergoing Bone Marrow Transplantation	UCHSC-080303	Active	Biomarker/Laboratory analysis, Educational/Counseling/Training, Supportive care	18 and over	NCI	Phase II
Phase I Pilot Study of Resveratrol in Postmenopausal Women With High Body Mass Index	UARIZ-UAZ08-12-01	Active	Biomarker/Laboratory analysis, Prevention	35 and over	NCI	Phase I
Exercise or Relaxation for Smoking Cessation	09-097-2	Active	Behavioral study	50 and over	NCI	No phase specified
Patient-Directed Lifestyle Change and Health Promotion Program or Usual Care in Low-Income, Uninsured Participants in Los Angeles County, California	CDR0000561559	Active	Behavioral study, Educational/Counseling/Training, Health services research	18 and over	NCI	No phase specified
Studying the Effect of Freeze-Dried Table Grape Powder on Blood Estrogen Levels in Postmenopausal Women	CDR0000581219	Active	Biomarker/Laboratory analysis, Prevention	18 and over	NCI	No phase specified
Cruciferous Vegetable Intake and Histone Status in Screening Colonoscopy Patients	P01 CA090890	Active	Biomarker/Laboratory analysis, Prevention, Screening	50 to 75	NCI	No phase specified
Soy Isoflavones Supplementation in Treating Women at High Risk For or With Breast Cancer	1B-10-6	Active	Diagnostic, Prevention, Treatment	30 to 75	NCI	No phase specified
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	Active	Educational/Counseling/Training, Prevention	11 to 14	NCI	No phase specified
Vitamin D and Omega-3 Trial (VITAL)	2009P-001217	Active	Prevention	60 and over	NCI	No phase specified
Phase II Pilot Study of Electrical Stimulation Therapy Using the MC5-A Scrambler for the Management of Chronic Chemotherapy-Induced Peripheral Neuropathy	MCV-MCC-12110	Approved-not yet active	Supportive care	18 and over	NCI	Phase II
Pancreas						
Vitamin E d-Tocotrienol Administered to Subjects With Resectable Pancreatic Exocrine Neoplasia	MCC-15630	Active	Treatment	18 and over	NCI	Phase I
Prostate						
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	Active	Biomarker/Laboratory analysis, Treatment	40 to 75	NCI	Phase III, Phase II

PDQ Clinical Trials	Protocol ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Selenium in Preventing Prostate Cancer	CDR0000654651	Approved-not yet active	Biomarker/Laboratory analysis, Prevention	Under 80	NCI/Other	Phase III
Improving Continence and Quality of Life in Prostate Cancer Patients	1R01CA127493-01A2	Active	Health services research, Supportive care	21 and over	NCI	Phase III
Phase I/II Study of the Effects of Tomato-Soy Juice on Biomarkers of Prostate and Cardiovascular Health in Patients With Prostate Cancer Undergoing Prostatectomy	OSU-2007C0026	Active	Biomarker/Laboratory analysis, Treatment	Any age	NCI	Phase II, Phase I
Vitamin D and Soy Supplements in Treating Patients With Recurrent Prostate Cancer	CDR0000554969	Active	Biomarker/Laboratory analysis, Treatment	Over 18	NCI	Phase II
Green Tea, Decaffeinated Black Tea, or Water in Treating Patients With Prostate Cancer Undergoing Surgery	CDR0000596162	Active	Biomarker/Laboratory analysis, Treatment	40 to 75	NCI	Phase II
Study of Polyphenon E in Men With High-grade Prostatic Intraepithelial Neoplasia	MCC-15008	Active	Biomarker/Laboratory analysis, Treatment	30 to 80	NCI	Phase II
Selenium in Treating Patients With Prostate Cancer	CDR0000614471	Active	Biomarker/Laboratory analysis, Treatment	Under 85	NCI	Phase II
Diindolylmethane in Treating Patients With Stage I or Stage II Prostate Cancer Undergoing Radical Prostatectomy	CDR0000641168	Active	Biomarker/Laboratory analysis, Treatment	18 and over	NCI	Phase II
Genistein in Treating Patients With Prostate Cancer	NCI 09U2	Active	Biomarker/Laboratory analysis, Treatment	18 and over	NCI	Phase II
Defined Green Tea Catechin Extract in Treating Patients With Localized Prostate Cancer Undergoing Surgery	CASE13805	Active	Biomarker/Laboratory analysis, Treatment	45 to 75	NCI	Phase II
Phase II Randomized Study of the Effect of an L-Arginine/Korean Ginseng/ Gingko Biloba/ Damiana-Based Supplement With or Without Phosphodiesterase-5 Inhibitors on Erectile Function and Quality of Life in Prostate Cancer Survivors Previously Treated With Radiotherapy	CCCWFU-98110	Approved-not yet active	Supportive care	18 and over	NCI	Phase II
Vitamin E Supplements in Preventing Cancer in Patients at Risk of Prostate Cancer or Who Have Prostate Cancer	CDR0000639070	Active	Biomarker/Laboratory analysis, Prevention	18 and over	NCI	Phase I
White Button Mushroom Extract in Treating Patients With Recurrent Prostate Cancer After Local Therapy	08012	Active	Biomarker/Laboratory analysis, Treatment	Any age	NCI	Phase I
Polyunsaturated Fatty Acids in Treating Patients With Prostate Cancer Undergoing Prostate Biopsy and/or Surgery	CDR0000538993	Active	Biomarker/Laboratory analysis, Treatment	18 and over	NCI	No phase specified
Chemoprevention of Prostate Cancer, HDAC Inhibition and DNA Methylation	Portland VA-09-0607	Active	Biomarker/Laboratory analysis, Prevention	21 and over	NCI	No phase specified
Randomized Study of Lycopene in Preventing Prostate Cancer in Healthy Participants	UIC-2004-0217	Active	Biomarker/Laboratory analysis, Prevention	18 and over	NCI	No phase specified
Omega-3 Fatty Acids in Treating Patients With Advanced Prostate Cancer	CCCWFU 85108	Active	Diagnostic, Treatment	18 and over	NCI	No phase specified

PDQ Clinical Trials	Protocol ID	Current Status	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Cancer Survivors						
Phase II Randomized Study of Two Home-Based Interventions for Sleep-Wake Disturbances in Cancer Survivors	NCCTG-N07C4	Active	Supportive care	18 and over	NCI	Phase II
The HEALS Project - Health Education and Active Living for Surviving Seniors	34851	Active	Supportive care	55 to 90	NCI	Phase I
Randomized Pilot Study of Hypnosis in Controlling Hot Flashes in Women Who are Breast Cancer Survivors	UIC-2004-0217	Active	Biomarker/Laboratory analysis, Prevention	18 and over	NCI	No phase specified
Randomized Study of an L-Arginine-Based Nutritional Supplement (ArginMax®) in Female Cancer Survivors	CCCWFU-05-04-01	Active	Supportive care	Adult	NCI	No phase specified
Acupuncture for Sleep Disruption in Cancer Survivors	SU-04082010-5642	Active	Supportive care	18 and over	NCI	No phase specified

OCCAM ORGANIZATIONAL CHART



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