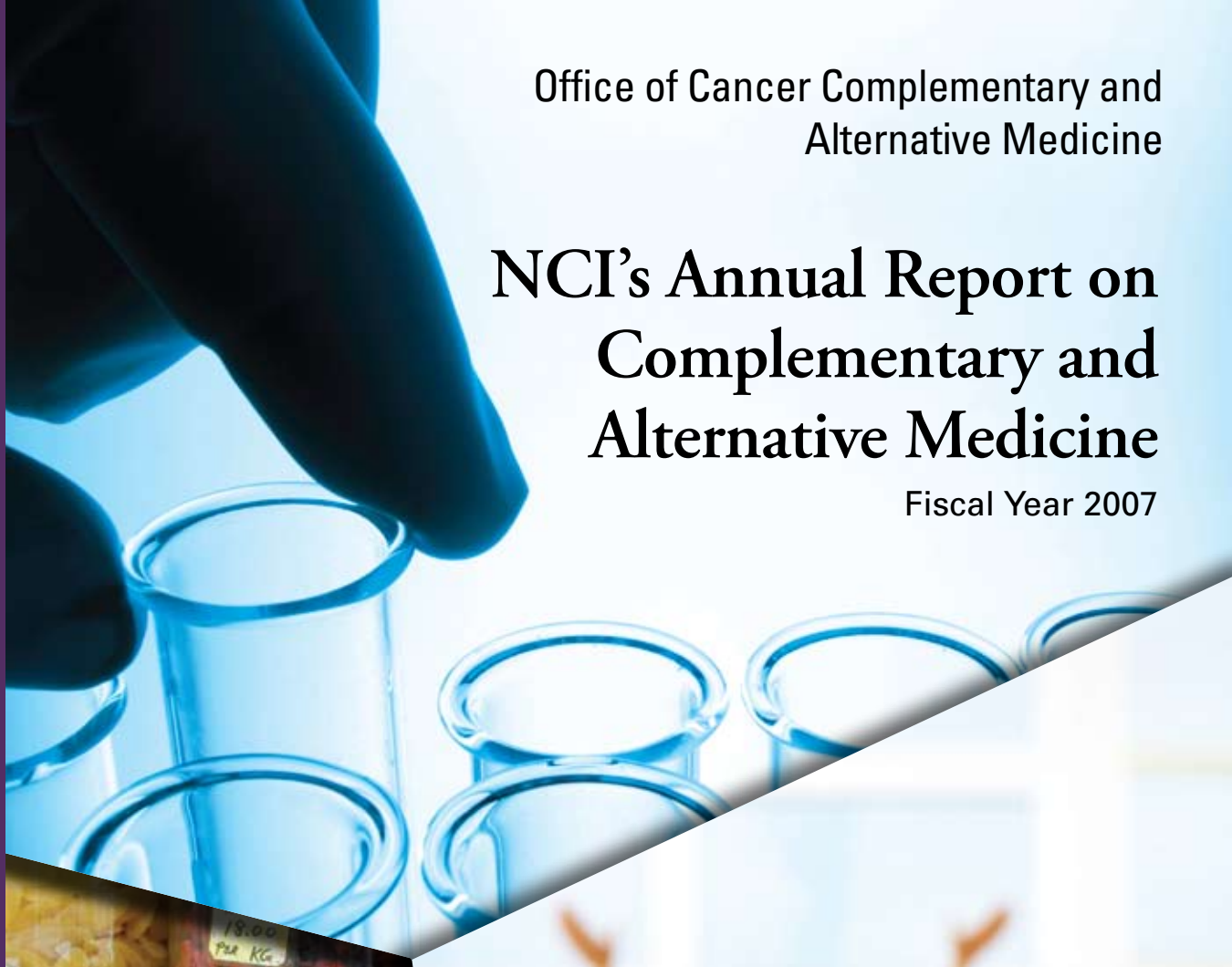
National Cancer Institute

Office of Cancer Complementary and Alternative Medicine

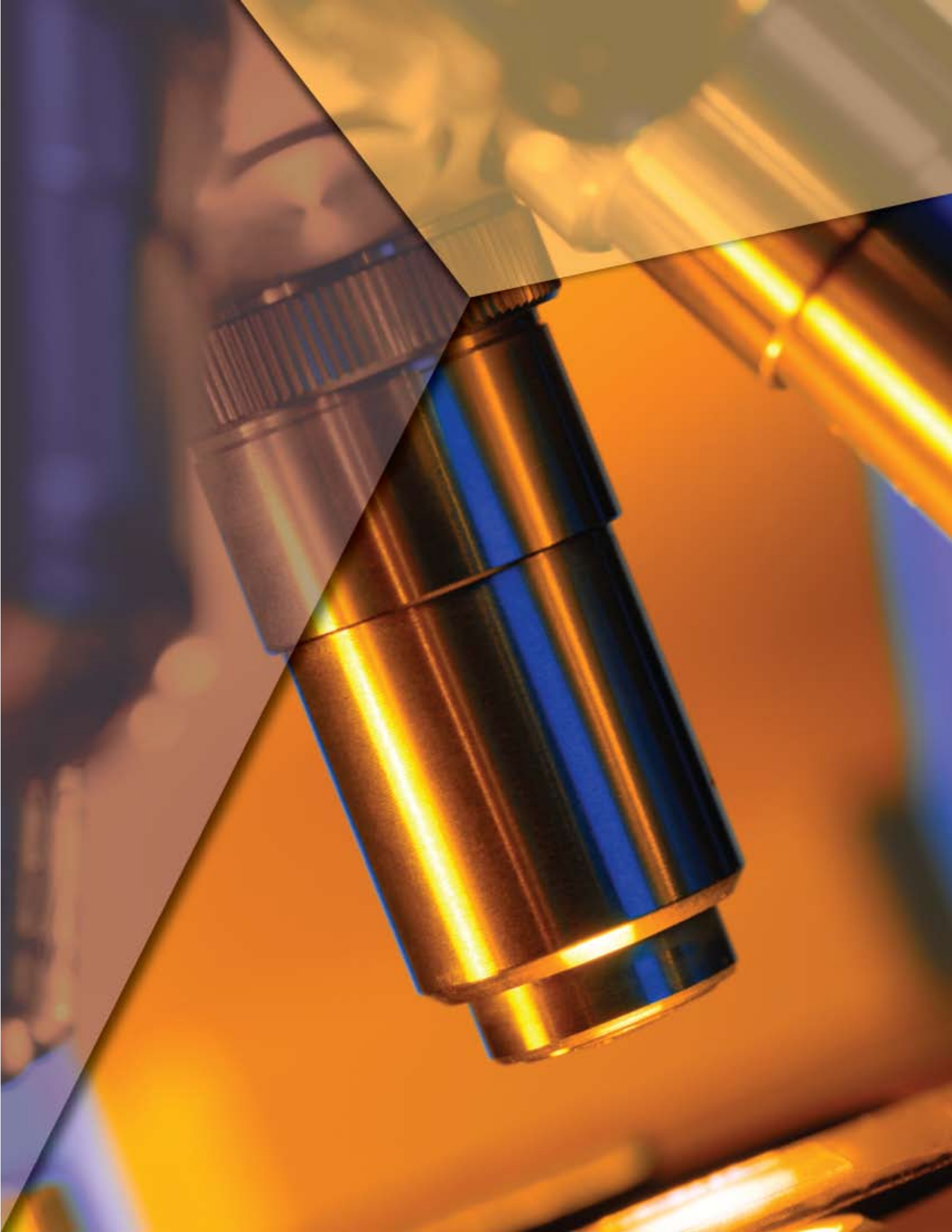
NCI's Annual Report on Complementary and Alternative Medicine

Fiscal Year 2007



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health



Director's Message

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

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

While the study of CAM is challenging, we are fortunate to have many partners in this endeavor, as demonstrated in the brief research profiles you'll find featured in this report. Many of the major cancer centers and academic biomedical research institutions in the United States have formal programs or centers in CAM, allowing for an optimal integrative medicine approach that combines conventional and alternative therapies. Much of the research discussed herein takes place at those centers, seeded by funding from NCI.

NCI's Office of Cancer Complementary and Alternative Medicine (OCCAM) does an excellent job of coordinating our CAM research portfolio and partnerships with extramural researchers as well as within NCI's intramural programs to expand our ability to extend the search for effective therapies into areas outside the mainstream of conventional biomedical research.

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

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

The following acronyms are used throughout this report:

NCI	National Cancer Institute
CAM	complementary and alternative medicine
OCCAM	Office of Cancer Complementary and Alternative Medicine
DCTD	Division of Cancer Treatment and Diagnosis
CCR	Center for Cancer Research
FY	fiscal year
RDSP	Research Development and Support Program
NIH	National Institutes of Health
COP	Communications and Outreach Program
PAP	Practice Assessment Program
BCS	Best Case Series
CARRA	Consumer Advocates in Research and Related Activities
CRTA	Cancer Research Training Award
PDQ	Physicians Data Query
CIS	Cancer Information Service
TCM	Traditional Chinese Medicine
S1P	sphingosine-1-phosphate
SPL	S1P lyase
HGPIN	high-grade prostatic intraepithelial neoplasia
MRI	magnetic resonance imaging
PET	positron emission tomography
PFAs	polyunsaturated fatty acids
PanINs	pancreatic intraepithelial neoplasias
SPORE	Specialized Program of Research Excellence
EGCG	epigallocatechin-3-gallate
EGFR	epidermal growth factor receptor
UCI	University of California, Irvine
IGF-IR	insulin-like growth factor-I receptor
OD	*Oldenlandia diffusa*
SQF	Sheng Qi Formula
MIC	myeloid immunosuppressive cell
NSCLC	non-small cell lung cancer
$1,25D_3$	1□, 25-dihydroxyvitamin D_3
AML	acute myeloid leukemia
ALL	acute lymphoblastic leukemia
QOL	quality of life
Th2	T helper type 2

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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*** involve the unconventional use of electromagnetic fields, such as pulsed fields, magnetic fields, or alternating current or direct current fields.
  Examples: Pulsed electromagnetic fields, Magnet therapy

Exercise Therapies

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

Examples: T'ai chi, Yoga asanas

Manipulative and Body-Based Methods

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

Examples: Chiropractic, Therapeutic massage, Osteopathy, Reflexology

Mind-Body Interventions

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

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

Nutritional Therapeutics

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

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

Pharmacological and Biologic Treatments

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

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

- *Complex Natural Products*
  Definition: Complex natural products are an assortment of plant samples (botanicals), extracts of crude natural substances, and un-fractionated extracts from marine organisms used for healing and treatment of disease.
  Examples: Herbs and herbal extracts, Mistletoe, Mixtures of tea polyphenols, Shark cartilage

Spiritual Therapies

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

Examples: Intercessory prayer, Spiritual healing

Introduction

Each year, Congress requests a report of the National Cancer Institute's (NCI) annual expenditures in complementary and alternative medicine* (CAM) research. To give more meaning to the numbers provided to Congress, a more detailed account of the Institute's investment in CAM has been produced for the last few years. The reports (including last year's *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2006*) are intended as a way for NCI to communicate its progress in this area of medical research, not only to Congress but also to other interested stakeholders including cancer researchers, CAM practitioners, health care providers, advocacy organizations, cancer patients, and the general public.

This year, NCI's Office of Cancer Complementary and Alternative Medicine (OCCAM) is proud to present the latest such report, *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2007*. 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.

This report highlights projects, grants, and cooperative agreements supported by each of the Institute's extramural grant funding divisions – Division of Cancer Biology, Division of Cancer Control and Population Sciences, Division of Cancer Prevention, and Division of Cancer Treatment and Diagnosis (DCTD) – along with projects from NCI's intramural laboratories – Center for Cancer Research (CCR) and Division of Cancer Epidemiology and Genetics. 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 fiscal year (FY) 2007, NCI's research expenditures for CAM are an estimated $121,932,765 for the funding of 456 CAM research projects.

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

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

Office of Cancer Complementary and Alternative Medicine

NCI's OCCAM is a coordinating office responsible for: identifying gaps in the science of cancer CAM and creating corresponding funding opportunities; partnering with NCI program staff and other governmental and nongovernmental organizations to increase the testing of CAM approaches with regard to 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.

As of March 2007, OCCAM officially transitioned organizationally from the NCI Office of the Director to reside within DCTD. Under the leadership of DCTD Director Dr. James H. Doroshow, the division's goals are to identify promising research areas and to translate them into improved diagnostic and therapeutic interventions for patients with cancer. OCCAM's programs and activities complement these goals and enhance the other major programs and branches within DCTD, while continuing the cross division activities described above.

OCCAM PROGRAMS

Research Development and Support Program

As previously noted, NCI sponsors more than 450 cancer CAM research projects, each of which is managed within the various Divisions and Centers of the Institute. OCCAM's Research Development and Support Program (RDSP) staff manages a portion of this portfolio and works with other program staff throughout NCI. They assist investigators in identifying funding opportunities and provide guidance in the pre- and post-review periods of grant application. 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.

In FY 2007, RDSP's program announcement series "Developmental Projects in Complementary Approaches to Cancer Care" (includes PAR-02-040, PA-04-053, and PA-06-400) was one of the most productive mechanisms for attracting new CAM grants to NCI. A total of 30 of the 181 solicited CAM grants active in FY 2007 came to NCI through these announcements. **(See Figure 2)** RDSP staff also worked with staff from other NCI programs to fund new grants and supplements to existing grants.

On November 8, 2006, OCCAM hosted a workshop *Strategies for Success: How to Write a Grant in Cancer CAM* during the *3rd International Conference of the Society for Integrative Oncology* in Boston, Massachusetts. This 1-day workshop was attended by 70 researchers with an interest in cancer CAM and addressed many of the issues raised by review committees that are specific to cancer CAM grant applications. In addition to a mock review session, the agenda also included presentations from the National Institutes of Health (NIH) program staff interested in supporting research in cancer CAM. The workshop was helpful for those preparing grant proposals to NCI as well as other peer-review funders providing support for scientific cancer CAM research.

Communications and Outreach Program

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

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

COP developed the following publications in FY 2007:

- *NCI CAM News* – Winter 2007
- *NCI CAM News* – Fall 2007
- *OCCAM Invited Speakers Series*: 2002-2005

Figure 2. Cancer CAM-related Grants Awarded in FY07 by Program Announcement (PA) and Request for Applications* (RFA)

RFA and PA

*AT03-002	2	*CA04-002	1	PA02-001	1	PA05-027	1	PA06-315	1	PAR03-009	2	PAR06-313	15
*CA01-020	1	*CA04-004	6	PA02-124	2	PA05-040	1	PA06-400	4	PAR03-010	4	PAR06-451	1
*CA02-007	3	*CA04-008	2	PA02-169	1	PA05-059	1	PA06-412	3	PAR03-153	6	PAR06-458	1
*CA02-009	1	*CA05w-013	2	PA04-034	1	PA05-125	2	PA06-413	1	PAR04-011	1	PAS02-009	2
*CA03-001	3	*CA05-014	2	PA04-046	1	PA05-141	2	PA06-440	1	PAR04-147	17	PAR99-167	1
*CA03-003	8	*CA07-025	6	PA04-053	18	PA06-041	2	PA07-070	3	PAR04-155	1	Total solicited	181
*CA03-006	1	*ES02-009	1	PA04-068	1	PA06-042	1	PAR01-110	1	PAR04-159	3		
*CA03-016	1	*ES05-007	1	PA04-099	4	PA06-120	2	PAR02-037	1	PAR05-156	4	Total unsolicited	206
*CA03-018	1	*OD03-008	1	PA04-108	3	PA06-283	1	PAR02-040	8	PAR06-073	2	Total number of	
*CA04-001	1	PA01-015	1	PA04-146	1	PA06-303	2	PAR02-176	1	PAR06-294	4	grant awards	387

OCCAM Public Comment Forum

Striving to stay connected to the ever-growing field of cancer CAM, OCCAM polled the opinions of its stakeholders through an online public comment forum. The forum allowed responders to provide open-ended feedback to statements posted by OCCAM, who used the forum to gather input on two different topics. One public comment session sought input on the necessity and utility of collecting nationally representative data on CAM usage by U.S. cancer patients. The other sought assistance in identifying specific factors associated with both successful and unsuccessful collaborations between cancer researchers and CAM practitioners.

The two public comment sessions ran concurrently for 60 days, from May 1, 2007, through June 30, 2007. During this timeframe, dozens of unique responders provided OCCAM with valuable information to both public comment sessions. Opinions received on the utility of and need for nationally representative data on CAM use among U.S. cancer patients will add to the ongoing dialogue within OCCAM on this topic. Comments about collaborations between cancer researchers and CAM practitioners helped to shape the agenda and discussion topics for the October 22-23, 2007 OCCAM conference, *Cancer Researchers and CAM Practitioners: Fostering Collaborations; Advancing the Science* (http://www.cancer.gov/cam/news/conference2007.html).

In addition, OCCAM expanded its outreach efforts through exhibiting or sending publications to the following professional meetings during FY 2007:

- Society for Integrative Oncology – November 2006
- American Association for Cancer Research – April 2007
- Oncology Nursing Society – April 2007
- American College for the Advancement of Medicine – May 2007
- American Society of Clinical Oncology – June 2007
- American Association of Naturopathic Physicians – August 2007

Practice Assessment Program

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

In September 2007, Farah Zeba Zia, M.D., became the new director of PAP. Dr. Zia works with PAP Coordinator, Commander (U.S. Public Health Service) Colleen Lee, M.S., CRNP, AOCN®, to find the most appropriate projects that may warrant further investigation within NCI. In 2003, Dr. Zia completed a fellowship at NCI and the National Heart, Lung, and Blood Institute, where she worked in the oncology and hematology wards as well as developed and implemented clinical trials with the breast oncology team. After her fellowship, Dr. Zia became a full-time staff oncologist with the Mid-Atlantic Permanente Medical Group, practicing in northern Virginia hospitals. Her extensive background in oncology and clinical trials is a great asset to OCCAM and PAP.

Mixed Bacterial Vaccines as Cancer Therapy Meeting

On November 17, 2006, OCCAM hosted *Mixed Bacterial Vaccines as Cancer Therapy*, a half-day meeting to which staff members from NCI, NIH, and academia were invited to review and discuss information about the historical and current use of mixed bacterial vaccines as cancer therapy. The primary goal of the meeting was to provide Hal Gunn, M.D., CEO of Canada's Centre for Integrated Healing, with feedback on the strengths and weaknesses of his theory on the anti-cancer effects of these vaccines and to suggest and examine potential next steps in research on this topic. This meeting was planned as a result of an ongoing dialogue between Dr. Gunn and OCCAM, which started when he submitted data on the therapy to the NCI BCS Program in 2002.

OCCAM Participation at Major Professional Conferences

OCCAM staff members are active in both domestic and international professional conferences through presentations and by engaging in dialogue with cancer CAM researchers, practitioners, and patient advocacy groups. (See in Training and Conferences on pg. 17). During FY 2007, staff members participated in several important meetings:

- Dr. Wendy B. Smith, RDSP director, gave a presentation via videoconferencing at the *Complementary Therapy Research-Tackling the Challenges* conference in December 2006.
- Dr. Jeffrey D. White, OCCAM director, gave a presentation at the *12th International Congress on Biological Cancer Therapy*, in Heidelberg, Germany, on May 11-13, 2007.
- Dr. White also gave a presentation at the *Ovarian Cancer Alliance Annual Conference*, in Washington, D.C., on July 11, 2007.

Working with Advocates

In FY 2007, OCCAM staff had several opportunities to work with representatives of the cancer patient advocacy community.

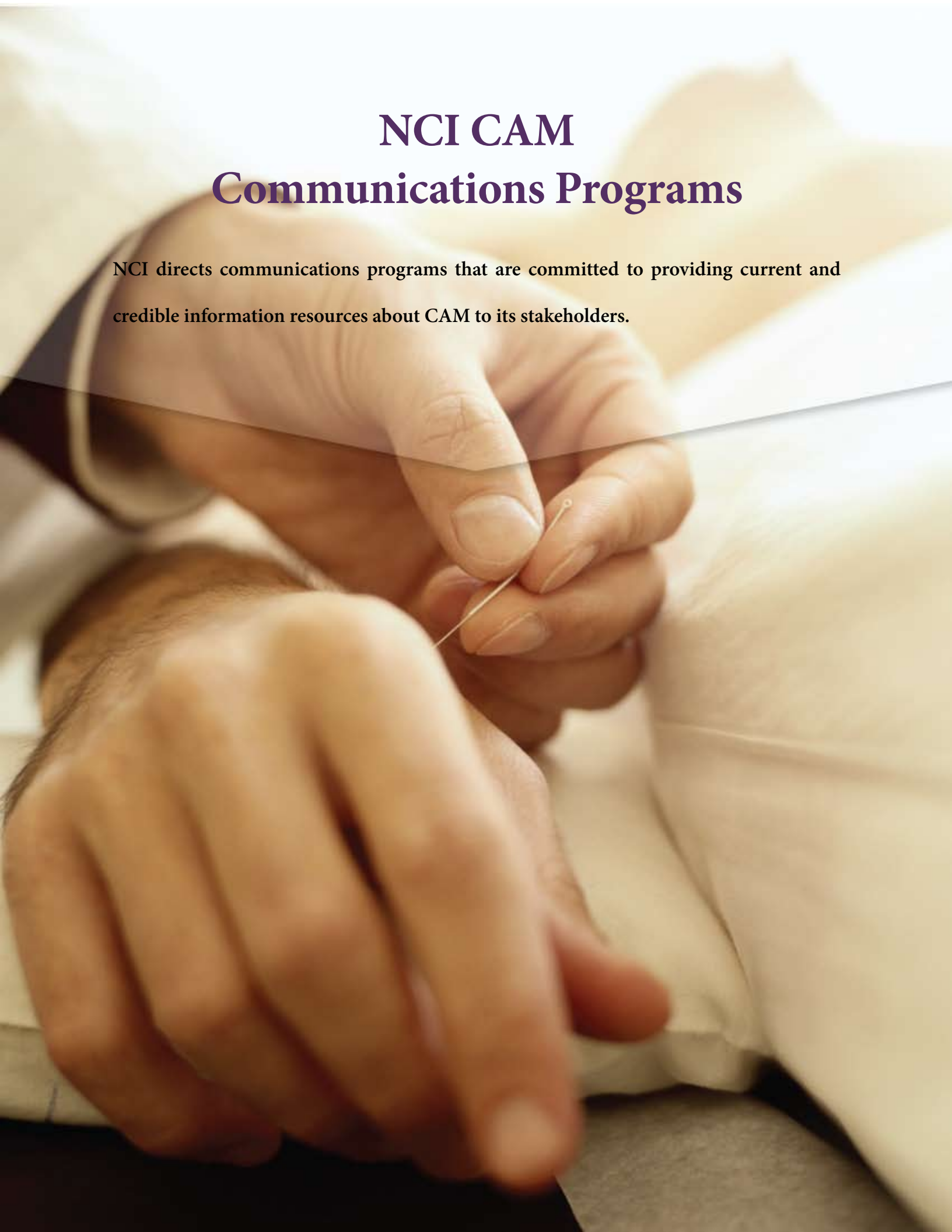
On November 7, 2006, OCCAM Director Dr. Jeffrey D. White participated in the Office of Liaison Activities (now the Office of Advocacy Relations) program series *Understanding NCI Teleconference*. The teleconference title was "What Advocates Should Know About Complementary and Alternative Medicine." Dr. White discussed the basics of CAM for cancer patients and gave an overview of OCCAM and the research funded on CAM throughout the NCI Divisions. Dr. White was followed by patient advocate Ms. Martha Powell who discussed how she has been involved in a CAM project with OCCAM. People who had called into the teleconference asked Dr. White questions about their concerns on using CAM. The CAM teleconference had one of the highest number of participants of any in the series.

For more information on the NCI teleconference series, please visit http://ola.cancer.gov/activities/teleconferences.

Advocates were also involved in the review of NCI's CAM Annual Report. In FY 2007, OCCAM solicited feedback from five Consumer Advocates in Research and Related Activities (CARRA) members who agreed to review a draft of the FY 2006 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 of these CARRA members improved the quality of the *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2006*.

OCCAM Staff List: FY 2007

Jeffrey D. White, M.D.	Director, OCCAM
Wendy B. Smith, Ph.D., B.C.I.A.C.	Director, RDSP
Farah Zeba Zia, M.D.	Director, PAP
Colleen Lee, M.S., CRNP, AOCN®	Coordinator, PAP
Shea Buckman, M.A.	Coordinator, COP
Christina Armstrong	Administrative Program Specialist
Ashanti Certain	Office Assistant
Phil Tonkins, Dr.P.H.	Scientific Program Analyst
Dan Xi, Ph.D.	Scientific Program Specialist
Oluwadamilola Olaku, M.D., M.P.H.	Scientific Program Specialist
Libin Jia, M.D.	Health Scientist Administrator
Tai N. Baker, M.P.H.	Communications Analyst
Stephen Graff, B.S.	Health Communications Intern
Karen Alladin, M.S.	Cancer Research Training Award (CRTA) Fellow
Elisabeth Beaver, M.S.	CRTA Fellow
Pia Chowdry, B.A.	CRTA Fellow
Therese Lizardo-Escano, B.A.	CRTA Fellow
Mariaah Williams	CRTA Fellow



NCI CAM Communications Programs

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

Providing Information Online

OCCAM's Web site at http://www.cancer.gov/cam serves as NCI's information hub on CAM issues. It provides a wealth of information resources about NCI CAM activities including publications and other educational material, research results, grant opportunities, lectures and other special events, and databases.

The site includes links to NCI-produced resources on CAM including fact sheets and Physician Data Query (PDQ®) summaries.

During FY 2007, NCI released the patient and health professional versions of PDQ summaries for *Antineoplastons* therapy (http://www.cancer.gov/cancertopics/pdq/cam/antineoplastons) and the health professional PDQ summary for the *Gerson Therapy* (http://www.cancer.gov/cancertopics/pdq/cam/gerson/HealthProfessional). With the addition of these resources, the number of CAM therapies covered in PDQ summaries increased to 18.

The NCI fact sheet "Complementary and Alternative Medicine in Cancer Treatment: Questions and Answers" was viewed 24,737 times in FY 2007. To read this fact sheet, please visit http://www.cancer.gov/cancertopics/factsheet/therapy/cam.

NCI's PDQ Cancer Clinical Trials Registry can be accessed at http://www.cancer.gov/clinicaltrials/search. In FY 2007, this registry included approximately 4,500 abstracts of protocols that were open and approved to accept patients, including 79 NCI-sponsored clinical studies on CAM approaches for cancer (See appendix). The PDQ registry is used by health professionals and patients alike and may be searched a number of ways including by diagnosis, treatment modality, locality, or a combination of these search criteria.

Also on the OCCAM Web site, a search table provides direct access to the entire list of cancer CAM clinical trials, including those trials which have already closed. The search table also allows users to view active CAM clinical trials by either cancer type or an associated symptom.

In FY 2007, there were active CAM clinical trials on 15 cancer types. Examples:

- Bladder cancer
- Head and neck cancer
- Lung cancer
- Prostate cancer

There were active CAM clinical trials for six common symptoms or treatment side-effects:

- Anorexia
- Hot flashes
- Fatigue
- Nausea
- Pain
- Oral complications

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

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

Producing Publications

In addition to online resources, NCI provides printed educational materials on CAM for health professionals, people affected by cancer, and consumers. These CAM materials are developed by various offices within NCI.

NCI's Annual Report on CAM

OCCAM *published NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2006*, 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/CAMAnnualReportFY2006.pdf.

Newsletter on NCI's CAM Activities

OCCAM's biannual newsletter *NCI CAM News* provides the latest information on NCI-sponsored research, funding opportunities, and meetings and workshops, as well as educational information on cancer and CAM. *NCI CAM News* also includes features on cancer CAM projects that represent the full range of NCI's cancer CAM activities as well as OCCAM program updates.

The following issues of *NCI CAM News* were made available online in FY 2007:

- Winter 2007 http://www.cancer.gov/cam/newsletter/2007-winter/home.html
- Fall 2007 http://www.cancer.gov/cam/newsletter/2007-fall/home.html

CAM in the NCI Cancer Bulletin

The *NCI Cancer Bulletin* is a biweekly online newsletter designed to provide useful, timely information about cancer research to the cancer research community. The Bulletin has over 30,000 subscribers from all over the country. Numerous cancer CAM studies featured in the *NCI Cancer Bulletin* during FY 2007 are listed below:

- *Promoting Health and Well-Being after Cancer*; October 17, 2006 (Volume 3, Number 40) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_101706/page4
- *Cognitive Behavior Therapy Helps Survivors Overcome Fatigue*; October 31, 2006 (Volume 2, Number 42) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_103106/page4
- *Cancer Prevention Stakes Are High for Dietary Intervention Research*; December 5, 2006 (Volume 3, Number 47) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_120506/page6
- *CCR to Sponsor Cancer Prevention Think Tank*; December 5, 2006 (Volume 3, Number 47) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_120506/page8
- *Low-Fat Diet May Help Prevent Breast Cancer Recurrence*; January 3, 2007 (Volume 4, Number 1) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_010307/page4
- *Calcium Offers Prolonged Protection From Colorectal Adenomas*; January 23, 2007 (Volume 4, Number 4) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_012307/page4
- *Many Advanced Cancer Patients in Phase I Trials Using CAM*; February 14, 2007 (Volume 4, Number 7) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_021407/page4
- *A Conversation with...Dr. Walter Willett*; February 27, 2007 (Volume 4, Number 9) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_022707/page5
- *High Doses of Vitamin D Hormone Boost Prostate Cancer Therapy*; February 27, 2007 (Volume 4, Number 9) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_022707/page4
- *Strenuous Long-Term Physical Activity Lowers Risk of Breast Cancer*; March 6, 2007 (Volume 4, Number 10) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_030607/page5
- *Unmasking Diet's Impact on Cells and Cancer Risk*; March 13, 2007 (Volume 4, Number 11) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_031307/page10
- *Nursing Lecture Describes Dietary Interventions and Physical Activity for Cancer Patients*; May 1, 2007 (Volume 4, Number 16) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_050107/page4
- *Study Measures Support Group Use by California Cancer Patients*; May 15, 2007 (Volume 4, Number 17) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_051507/page4
- *Folic Acid Study Shows Surprising Results*; June 12, 2007 (Volume 4, Number 19) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_061207/page4
- *Dietary and Herbal Therapy for Brain Cancer (Clinical Trial)*; June 12, 2007 (Volume 4, Number 19) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_061207/page7
- *Breast Cancer Survivors Test Diet High in Fruits, Veggies*; July 24, 2007 (Volume 4, Number 22) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_072407/page4
- *Education and Exercise to Prevent Lymphedema (Clinical Trial)*; July 24, 2007 (Volume 4, Number 22) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_072407/page8
- *Testing Carbohydrates as Cancer Biomarkers*; August 21, 2007 (Volume 4, Number 24) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_082107/page6

- *A Conversation with...Dr. LaSalle D. Leffall, Jr.*; August 21, 2007 (Volume 4, Number 24) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_082107/page7
- *Hypnosis before Breast Cancer Surgery Reduces Pain, Cost*; September 11, 2007 (Volume 4, Number 25) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_091107/page4
- *Pomegranate Juice for PSA-Only Prostate Cancer Recurrence (Clinical Trial)*; September 25, 2007 (Volume 4, Number 26) http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_092507/page9

Responding to CAM Cancer Inquiries

NCI's Cancer Information Service (CIS) serves as NCI's link to the public by interpreting and explaining research findings in a clear and understandable manner and providing personalized responses to specific questions about cancer. Highly trained cancer information specialists are available via phone, live online chat, mail, and e-mail to answer questions about cancer treatment and clinical trials, including CAM therapies. During FY 2007, CIS responded to 1,539 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.

Traditional Chinese Medicine Research Conference Highlighted

OCCAM sponsored NCI's first Traditional Chinese Medicine (TCM) oncology research conference in 2006. The TCM conference was highlighted in the July 2007 report *NCI's International Portfolio: Addressing the Global Challenge of Cancer* as an opportunity to educate NCI staff about the application of various TCM methods (e.g., herbs and other plant remedies, acupuncture) to prevent and treat cancer, as well as to manage symptoms. Conference organizers created a collegial environment to engage over 40 Chinese researchers and practitioners of TCM with researchers here in the United States and to facilitate discussion about the role that NCI should take in furthering research in this area.

The NCI report can be found at http://www.cancer.gov/nci-international-portfolio.

Training and Conferences

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

Training Opportunities at OCCAM

During FY 2007, OCCAM hosted the following Cancer Research Training Award (CRTA) fellows: Karen Alladin, M.S., Elisabeth Beaver, M.S., Pia Chowdry, B.A., Therese Lizardo-Escano, B.A., and Mariaah Williams. The goals for the fellows, who were mentored by OCCAM Director Dr. Jeffrey D. White, were to learn about the NIH grant process and to explore approaches to cancer CAM research. During the course of the fellowship, CRTAs assisted with tasks such as coding the CAM modality for each project in the NCI CAM research portfolio, providing support to the OCCAM programs, and working on literature review projects that may be submitted for publication.

In addition, OCCAM also hosted a Health Communications Intern, Stephen Graff, B.S., who helped organize and execute a scientific conference; wrote and edited articles for the newsletter *NCI CAM News,* other publications, and promotional materials; and assisted with the management of OCCAM's Web site. Mr. Graff also participated in professional meetings and NIH-sponsored training seminars.

NCI Lectures and Workshops on CAM

NCI provides educational opportunities for its scientific program staff, fellows, other staff members, and the public on topics related to cancer CAM. In FY 2007, the following seminars and lectures on CAM were held:

Division of Cancer Prevention

Nutritional and Molecular Biomarkers in Diet and Cancer Epidemiology (Stars in Nutrition and Cancer Series)
October 23, 2006
http://prevention.cancer.gov/newsandevents/eventsarchive/20061023

Omega-3 Fatty Acids in the Dietary Management of Pro-Inflammatory States: A Nutrigenomic Model (Stars in Nutrition and Cancer Series)
March 15, 2007
http://dcp.cancer.gov/newsandevents/eventsarchive/20070315

Nutrition and Cancer Prevention Research Practicum
March 19-23, 2007
http://prevention.cancer.gov/newsandevents/eventsarchive/20070319-23

A New Look into the Anti-cancer Action of Selenium Through the Lens of Endoplasmic Reticulum Stress (NCI Cancer Prevention and Control Colloquia Series)
March 28, 2007
http://www3.cancer.gov/prevention/pob/fellowship/colloquia2006-2007.html#march

Vitamin D and Cancer: Current Dilemmas/Future Needs Workshop
May 7-8, 2007
http://dcp.cancer.gov/newsandevents/eventsarchive/20070507-8

Diet Nutrition and Lung Cancer: Key Findings from a Systematic Review (NCI Cancer Prevention and Control Colloquia Series)
May 16, 2007
http://www3.cancer.gov/prevention/pob/fellowship/colloquia2006-2007.html#may

Diet, Epigenetic Events, and Cancer Prevention Symposium
September 26-27, 2007
http://prevention.cancer.gov/newsandevents/eventsarchive/20070926-27

Division of Cancer Control and Population Sciences

Vitamin D and Colorectal Cancer Visiting Scholars Seminar Series
December 5, 2006
http://epi.grants.cancer.gov/visiting/index2006.html

CAM Monthly Lecture Series at NCI

The OCCAM Monthly Lecture Series informs the NCI community about recent and ongoing research projects in cancer CAM. These hour-long lectures feature a fifty-minute presentation on a cancer CAM topic and allow 10 minutes for questions. The lectures, conducted by researchers from all over the

country, are open to the public and also are archived as videocasts on the OCCAM Web site at http://www.cancer.gov/cam/news/monthly-lecture-series.html.

During FY 2007, the series included the following lectures:

- Novel Stress Reduction Approach for Cancer Patients
- The Potential of Thundergod Vine in Cancer Research
- Effects of Dietary Bioactive Components and Herbal Ingredients on the Prevention and Treatment of Cancer
- A Food-Based Approach to the Prevention of Gastrointestinal Tract Cancers
- Dietary Supplement Milk Thistle Extract and Prostate Cancer: Mechanisms and Efficacy
- Cancer Chemoprevention with Glucosinolate-rich Broccoli Sprouts
- Cancer Chemoprevention by Resveratrol

Supporting Scientific Conferences

In FY 2007, NCI supported two CAM conferences:

- Peter Johnstone, Ph.D., from Emory University in Atlanta, Georgia received a grant for the *Fifth International Conference of the Society of Integrative Oncology*. This meeting took place November 20-21, 2008, in Atlanta, Georgia.
- Shivendra Singh, Ph.D., from the University of Pittsburgh, received a grant award for the first-ever international symposium on *Bioactive Food Components, Alternative Medicine, and Cancer Chemoprevention*, held in Greece in October 2007. The 2-day meeting drew almost 150 attendees and included presentations and discussions on recent advances in the field including studies on prostate cancer chemoprevention with genistein and resveratrol, anti-inflammatory and antioxidant agents present in dietary and medicinal plants, and mechanisms of cancer chemoprevention by grape seed extract.

CAM Breakout Session at NCI Cancer Survivorship Conference

On October 4-6, 2006, NCI, the American Cancer Society, and the Lance Armstrong Foundation co-sponsored the third biennial cancer survivorship research conference *Cancer Survivorship: Embracing the Future*. The conference convened 340 participants to explore innovative research advances in the field of cancer survivorship. CAM was the topic of one of the sessions, which was moderated by Meryl Sufian, Ph.D., NCI Office of Cancer Survivorship program director. (Selected presentations from this conference were published in a supplement to the journal *Cancer*, Volume 112/issue 11).

Conference Presentations by NCI Staff

RDSP Director Wendy B. Smith, Ph.D., gave a presentation via teleconference to the *Complementary Therapy Research-Tackling the Challenges* conference on December 12, 2006. Dr. Smith discussed CAM definitions and examples, functions of OCCAM, and research funding opportunities. She also explained that there are many funding opportunities available for CAM researchers outside of the United States. She suggested that international researchers should partner with U.S. research institutions as another strategy for obtaining grant funding from NIH.

OCCAM Director Jeffrey D. White, M.D. presented at the *12th International Congress on Biological Cancer Therapy* in Heidelberg, Germany, on May 11-13, 2007. He focused his talk on the communications between cancer patients who use CAM techniques and their physicians. The conference provided participants, both patients and physicians, an opportunity to learn how to interact more efficiently with one another.

Dr. White also presented at the *Ovarian Cancer Alliance Annual Conference* in Washington, D.C., on July 11, 2007, on "Approaches to Uncovering and Studying Unconventional Cancer Therapies: The U.S. National Cancer Institute Experience." Dr. White discussed the latest research in this field as well as therapies and approaches relevant to ovarian cancer patients.

NCI Research in Complementary and Alternative Medicine

The CAM Portfolio Analysis Process

How much money does NCI spend on CAM research each year? This is one of the questions most frequently posed to OCCAM. Researchers, cancer patient advocates, proponents of CAM, and Congress are interested in the answer, and 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. However, the vast majority of CAM projects are managed by other programs and laboratories throughout the Institute. After the close of each fiscal year, each of the seven NCI divisions generates a list of projects they managed within their portfolio or conducted that are coded as CAM. OCCAM compiles the lists of projects and manually reviews the project coding. This coding must be carefully examined, because CAM projects are sometimes incorrectly categorized. Once a project has the correct CAM designation, OCCAM also classifies each one into a sub-category to further define the purpose of the research.

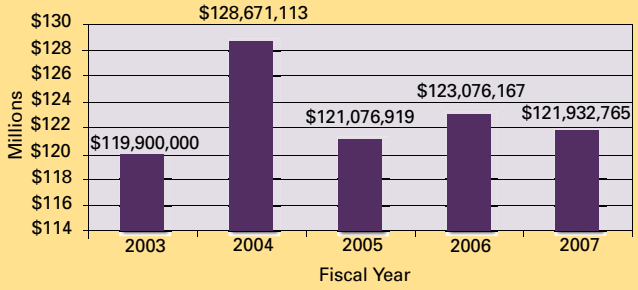
NCI's total CAM expenditure figure includes money awarded for intramural projects, extramural grants, cooperative agreements, contracts, and supplements. It is important to note that the reported figure for total CAM expenditure for a fiscal year does not include projects for which NCI is not the primary funder, nor does it include training grants such as T, F, K, and R25 awards.

NCI CAM Research Portfolio Analysis: FY 2007

TOTAL ESTIMATED CANCER CAM RESEARCH EXPENDITURE

In FY 2007, NCI invested an estimated $121,932,765 for 456 intramural and extramural research projects relevant to CAM. **Figure 3** shows the total CAM expenditures for FY 2003-2007.

Figure 3. NCI's CAM Expenditures FY 2003-2007*

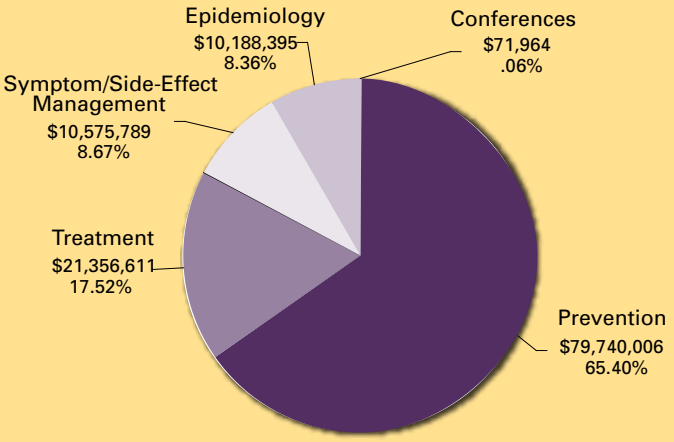


**Includes Grants, Cooperative Agreements, Intramural Projects, and Contracts*

BREAKDOWN BY RESEARCH TYPE

The accompanying pie-chart **(Figure 4)** shows the distribution of the projects according to research type (prevention, treatment, symptom/side effects management, epidemiology, and conferences). In FY 2007, 65.40% of cancer CAM-related research project funds went to various cancer prevention efforts, while treatment, symptom/side effects management, epidemiology, and conferences received 17.52%, 8.67%, 8.36%, and 0.06% respectively.

Figure 4. NCI CAM Research Projects FY 2007 by Research Type*

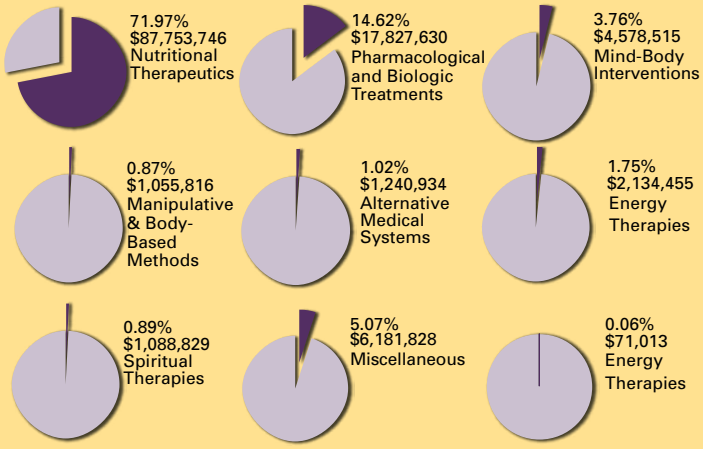


**Includes Grants, Cooperative Agreements, Intramural Projects, and Contracts*

BREAKDOWN BY MAJOR CAM CATEGORY

In FY 2007, NCI conducted or supported research addressing a variety of CAM therapies **(Figure 5)**. These CAM therapies fall into nine groups: alternative medical systems, exercise therapies, manipulative and body-based methods, mind-body interventions, nutritional therapeutics, pharmacological and biologic treatments, energy therapies, spiritual therapies, and miscellaneous. (See page 4 for definitions of CAM categories.)

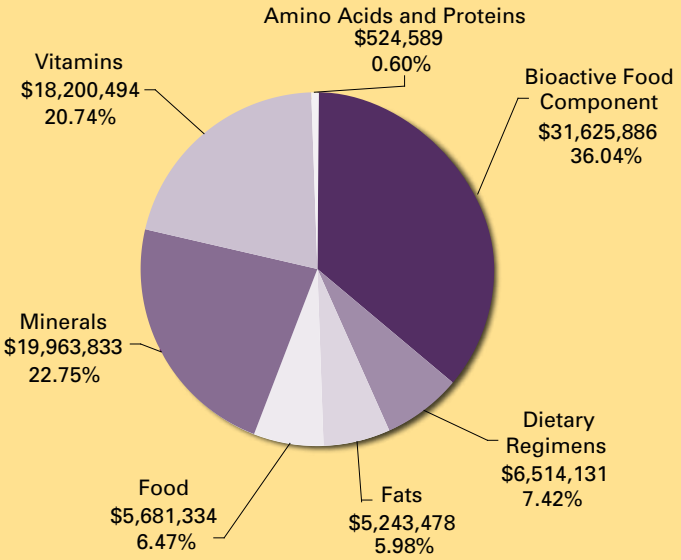
Figure 5. NCI Research by CAM Categories--FY 2007*



**Includes Grants, Cooperative Agreements, Intramural Projects, and Contracts*

The largest percentage (71.97%) of research funding went to projects that investigated nutritional therapeutics, which can be further broken out into subcategories of research on: food (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 6** shows the distribution of projects according to the subcategories of nutritional therapeutics.

Figure 6. NCI's FY 2007 CAM Nutritional Therapeutics Projects*



**Includes Grants, Cooperative Agreements, Intramural Projects, and Contracts*

BREAKDOWN BY CANCER TYPE

The research projects that make up NCI's FY 2007 CAM research portfolio address 19 categories of cancer types. Among these, prostate, breast, colorectal, and lung cancers received the largest amounts of cancer CAM research funding. Approximately one quarter of NCI's cancer CAM research funding was allotted for multiple types of cancer within the same project.

For a complete listing of the cancer type categories and estimated funding amounts, please see **Figure 7**.

Figure 7. NCI CAM Research Projects FY 2007 by Cancer Type*

Bladder	$206,834
Brain	$260,095
Breast	$20,154,436
Cervical	$1,371,435
Childhood Cancer	$156,789
Colorectal	$12,926,502
Esophageal	$881,995
Gastric	$2,201,222
Head and Neck	$2,254,009
Hematologic	$533,089
Liver	$1,201,004
Lung	$12,372,208
Melanoma, Skin	$2,124,141
Melanoma, Eye	$87,071
Multiple Types	$31,694,569
Ovarian	$211,519
Pancreatic	$1,595,359
Prostate	$28,137,106
Skin, Non-Melanoma	$3,563,384
TOTAL:	$121,932,765

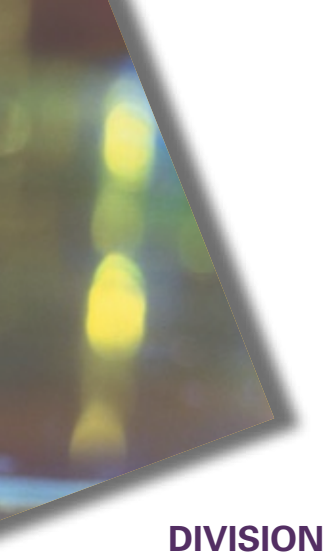
Highlights from NCI's Wide-Ranging CAM Research

The following research highlights are selected from the 456 CAM research projects that NCI supported during FY 2007 at laboratories within the Institute and at grantee institutions throughout the United States and the world. These research projects are organized under several categories reflecting NCI's comprehensive research focus into understanding the underlying mechanisms of cancer causation, prevention, treatment, and symptom management and palliation of the disease.

Abstracts for the research projects featured in this report can be found by searching the NIH Computer Retrieval of Information on Scientific Projects (CRISP) database at http://crisp.cit.nih.gov.

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.



Understanding the Role of Sphingolipids in Colon Cancer

DIVISION OF CANCER BIOLOGY

Sphingolipids are a class of molecules produced by the body and are also found in many common foods including dairy products and soy. These fatty molecules assist with many vital functions including blood vessel development and immune function. However, an excess buildup of some sphingolipids may also promote tumor development.

Julie Saba, M.D., Ph.D., at Children's Hospital Oakland Research Institute, is particularly interested in a sphingolipid called sphingosine-1-phosphate (S1P) and its potential role in the development of colon cancer. "It is a very important compound; if you don't make any of it, you can't survive," explained Dr. Saba. "On the other hand, it is a cell-survival molecule, and it prevents a form of cell death called apoptosis. So when S1P levels are too high in a tissue, they appear to promote cancer progression."

S1P normally exists in a delicate balance in the body, and this balance is regulated in large part by the enzyme S1P lyase (SPL), which breaks down the substance. Dr. Saba's laboratory is exploring how disruption of this balance, in particular down-regulation of SPL, may contribute to the formation of cancer cells.

In two recently published studies, Dr. Saba and her colleagues found that SPL is down-regulated in colorectal cancer cells taken from patients and in intestinal polyps found in a mouse model. The researchers also found that the enzyme that produces S1P may also play a role in intestinal tumor cell proliferation. "We found changes in the expression of these enzymes, so S1P starts to accumulate in the polyps," she explained. "If you genetically manipulate mice so that they can't accumulate S1P, the polyps don't enlarge. This finding supports the notion that the S1P pathway is feeding the progression of the cancer and that there are targets in this pathway that would be very important to block," she said.

Their current work, funded by NCI*, focuses on the hypothesis that SPL down-regulation occurs early in the formation of a colon tumor. The process leads to S1P accumulation – both S1P produced by the body and S1P coming from the breakdown of food in the intestines – in the mucosal lining of the intestine (the site where most colon cancer arises), activating cell signaling pathways that lead to tumor progression.

If the hypothesis is verified, future work will focus on how to target these abnormal pathways. "We would like to be able to activate SPL using drugs… and we'd also like to generate small molecules similar to sphingolipids that can inhibit cell growth and to find dietary sphingolipid components that imitate those effects," concluded Dr. Saba.

NCI Program Director Rihab Yassin, Ph.D., stated: "The knowledge gained from this research could outline an important role for SPL in metabolic tumor suppression and further our understanding of the biological basis of cancer." The research may also provide information that is relevant to the development of dietary interventions for the prevention of colon cancer. Dr. Saba plans to study the impact of adjusting levels of dietary sphingolipids on the rates of development of colon cancer in a mouse model of the disease.

*Grant number: 1R01CA129438-01A1

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.

Combination of Natural Compounds Studied for Prostate Cancer Prevention

DIVISION OF CANCER PREVENTION

Prostate cancer is the most common tumor among men in the United States. Fortunately, it is a cancer that scientists believe may be preventable, based on results in large epidemiological studies, as well as findings in animal and lab studies. One promising strategy which may help prevent precancerous cells in prostate tissue from progressing into cancer involves phytochemicals – compounds found naturally in plants and vegetables.

With grant support from NCI*, researchers at the Harvard Medical School, led by Jin-Rong Zhou, Ph.D., are simultaneously using two different antioxidant phytochemicals – silybin from the milk thistle plant and sulforaphane from broccoli sprouts, cauliflower, and other vegetables. Each of these phytochemicals possesses a distinct anti-cancer effect, and the researchers are testing if there is an enhanced preventative effect.

There are several reasons these two plant substances might have a "synergistic", combined effect, suggested Dr. Zhou, director of the Nutrition/Metabolism Laboratory at Beth Israel Deaconess Medical Center. The first reason, inherent to a lot of dietary and chemoprevention research, is that it can be hard to identify which components of a natural product are causing positive effects, and whether those effects may be dependent on other dietary or environmental factors that were not controlled for in the study. Secondly, both silybin and sulforaphane appear to be hitting different cellular pathways and targets, thus affecting different processes of a developing cancer.

After looking at a number of promising natural agents in laboratory studies using prostate cancer cells, "we decided that sulforaphane was the best agent to directly stop cancer cells from growing," explained Dr. Zhou. The researchers also found that "silybin best interfered with angiogenesis," the process by which blood vessels are created to supply tumors with oxygen and essential nutrients, he added. Another benefit of using the combination is that each of the compounds can be given at doses that are safe, Dr. Zhou reported. Many experiments with phytochemicals, vitamins, and dietary supplements show positive effects in mice or cancer cell cultures but only at dosage levels that would be toxic for humans.

The researchers are testing the two phytochemicals in male mice that have tumors derived from human cancer cells implanted directly into their prostate glands, so-called orthotopic tumors. This type of animal model is thought to be more similar to human prostate cancer than models in which the cells are implanted under the skin. The primary aim is to see if the treatment slows cancer progression. The researchers also hope to identify biomarkers – enzymes and proteins that could be detected easily in blood samples, for example – that would provide a way to tell when the treatments are effective and might also point to specific cellular markers and pathways that the two bioactive ingredients are affecting.

"Because prostate cancer may be in its earliest stages in so many older men," explained Zhou, "an alternative natural preventive treatment that is safe could dramatically impact public health in the U.S. and elsewhere." He is hoping that what they learn from these studies in cells and mice will lead to human clinical trials.

NCI Program Director Vernon Steele, Ph.D., commented: "The prevention of prostate cancer is a critical area of needed research. Finding agents to prevent this cancer has been difficult, with few successes. Dr. Zhou's project with two natural compounds, silybin and sulforaphane, may provide a safe and effective combination to prevent prostate cancer. The proposed animal testing would be critical for any decision to go forward with this approach."

*Grant number: 1R03CA130133-01

Green Tea Ingredient Studied for Men with High Prostate Cancer Risk

DIVISION OF CANCER PREVENTION

Prostate cancer can be fast acting and lethal or remain so slow-growing that it may never need to be treated. "We now know some of the signs for cases in which the disease threatens to develop into the more lethal type of prostate cancer," said Nagi Kumar, Ph.D., R.D., director of Nutrition Research at the H. Lee Moffitt Cancer Center. "We think we can interrupt the process by taking a page from TCM, where consumption of green tea may be one of the factors associated with why prostate cancer is not nearly the public health threat in China that it is here in the U.S."

With NCI funding,* Kumar and her colleagues at Moffitt and the Research Institute of South Florida are conducting a phase II clinical trial to test this chemopreventive idea. They are enrolling 240 men who have changes in the prostate tissue that are classified as high-grade prostatic intraepithelial neoplasia (HGPIN). Although not conclusive, some data suggest that patients with HGPIN have an increased risk of developing clinical prostate cancer within a year after biopsy.

The researchers are studying whether a combination of catechins naturally found in green tea including epigallocatechin gallate – the catechin that studies have shown to be the tea's most potent chemopreventive agent – can prevent or slow down the progression from HGPIN to prostate cancer in these high-risk individuals. All of the study subjects will be randomly chosen to take either the green tea catechins in the form of a pill (Polyphenon E) or a placebo daily for one year. The patients will not know whether they are receiving Polyphenon E or placebo.

"Population studies in Asian men have shown the protective effects of green tea," said Kumar. "And laboratory studies have shown that green tea polyphenols can selectively kill cancer cells and in other ways slow down the progression of cancer in a number of cancer types, including lung, skin, and breast."

Part of the work they plan to do involves analyzing blood and tissue samples before and after a patient receives the Polyphenon E. This kind of science will help shed more light on the pathways the compound follows to do its preventive work. The study might also reveal changes in the body that could signal to doctors the state of cancer progression. Such early warning biological signs are especially important in cancers, like prostate cancer, that develop slowly and where mortality can be reduced by identifying the earliest possible signals that the disease is threatening to progress.

"If our study demonstrates that Polyphenon E slows the progression of prostate cancer and is safe," said Kumar, "we will recommend a larger, phase III study of men who have HGPIN to assess Polyphenon E's clinical impact on their risk for prostate cancer." NCI Program Director Howard Parnes, Ph.D., said, "The current study is designed appropriately to generate meaningful data about the compliance, symptoms, and toxicity of green tea polyphenols' use for prostate cancer. Its clinical effectiveness will then need to be proven by a larger study."

*Grant number: 1R01CA122060-01A1

A Closer Look at the Role of Selenium in Intestinal Inflammation and Cancer

DIVISION OF CANCER PREVENTION

The dietary supplement selenium has long been the focus of research and hope due to initial findings of its effectiveness as a preventive agent against several types of cancer. However, researchers have yet to clearly understand the process by which the compound may work against cancer and other diseases.

Linda A. Jelicks, Ph.D., associate professor at the Yeshiva University Albert Einstein College of Medicine in New York City, is taking a two-fold, closer look at those basic mechanisms by which selenium affects the cancer disease process. The goals of her NCI-supported study* are to use noninvasive magnetic resonance imaging (MRI) methods in combination with micro-positron emission tomography (PET) scans and biological assays to evaluate the role of selenium supplementation in mouse models of intestinal inflammation and colon cancer.

"My expertise is in the imaging of mice," Dr. Jelicks noted. Her group is repeatedly imaging the genetically-engineered mice after putting them on a selenium-enriched diet, using a version of the compound found in garlic – compared with other mice given a non-selenium-containing control diet. The researchers are monitoring all of the mice, looking for tumors and evidence of inflammation. "What we're really hoping to develop is a method where we can overlay the MRI and the micro-PET images," she explained. "We'll have the MRI in gray scale and the PET in color so that you can track development of the inflammation and development of tumors over time."

The study is currently ongoing. At the 8-month point in the feeding cycle, PET scans show "the small group of selenium-treated mice seems to have less inflammation than the control group," Dr. Jelicks reported. "I'm going to compare that to the MRI images which will let me detect the tumors. That way, we can see if there are particular areas of inflammation where tumors are growing."

If the current study shows positive results, Dr. Jelicks is planning a follow-up study to treat mice *in utero*. "The mothers will be fed selenium, and after the pups are born and weaned, they will go onto a selenium diet. The selenium diet will be compared to a control diet to see if the selenium actually delays onset of tumors in the mice," she said. In the long term, such treatments "could be significant for people with hereditary high risks or family histories of colon cancer to protect themselves and their offspring by selenium supplementation before, during, and after pregnancy," Dr. Jelicks said.

"We're also very excited about the possibilities of combining the two imaging modalities in the clinical care of human patients," she added. "It may prove a helpful method to identify more aggressive tumors and to see where inflammation is found and where gastrointestinal tumors may develop."

*Grant number: 1R21CA123334-01A1

Fish Oil Studied for Possible Prevention and Treatment of Pancreatic Cancer

DIVISION OF CANCER PREVENTION

Pancreatic cancer remains an almost universally fatal disease with an overall median survival of less than 6 months after diagnosis. As part of the effort to prevent and better treat the disease, researchers are investigating preliminary evidence that the omega-3 polyunsaturated fatty acids (PFAs) found in fish oil may play a beneficial role.

There are several epidemiologic and cohort studies suggesting that the high intake of fish oil correlates with decreased risk of developing certain cancers and certain inflammatory diseases. Based on those data, Guido Eibl, M.D., assistant adjunct professor at the David Geffen School of Medicine at the University of California, Los Angeles, has embarked on a 5-year study using lab cell cultures and animal models for pancreatic cancer to pinpoint the exact mechanisms of how omega-3 acids may affect development and progression of the disease.

With funding from NCI*, Dr. Eibl started by using pancreatic cancer cell cultures to study the effects of omega-3 PFAs compared with the effects of omega-6 acids found in more common cooking oils, such as corn oil. He and his colleagues found the omega-3 acids in fish oil decreased the growth of several types of pancreatic cancer cells, while the most common forms of omega-6 PFAs stimulated the growth of those same cancer cells.

The investigators have also conducted a study where human pancreatic cancer cells were transplanted into the pancreas of nude mice. They then started the mice on special diets which contained either high levels of corn oil or a fish oil-based diet. "What we found is that the tumors in the mice on the fish oil diet were significantly smaller than the tumors in the corn oil-fed mice," Dr. Eibl reported. The data from the mice study were published in the May 2008 issue of *Pancreas***.

As a next step, Dr. Eibl plans to study the two diets in genetically-engineered animals that rapidly develop pancreatic tumors and pre-cursor lesions called pancreatic intraepithelial neoplasias (PanINs). He will also investigate combinations of the diets, both fish oil and corn oil. "That is because patients will eat a variety of different oils in their regular diets," he noted. "So we'll try to figure out at what ratio you will see beneficial effects" against pancreatic cancer and PanINs.

He hopes that further studies will show fish oil omega-3 PFAs' value as a preventative agent in human disease: "If it proves to be successful, it would suggest the use of fish oil in high-risk human populations, such as those with chronic pancreatitis or with familial pancreatic cancer, so that they may add fish oil as part of their regular diet, which may have a beneficial effect."

Dr. Eibl believes the omega-3 acids may also have additive therapeutic impact on people diagnosed with pancreatic cancer. "We don't expect that fish oil will be the only therapeutic agent they'll be given," he explained. "But it could be given as a therapeutic supplement to current chemotherapies like gemcitabine. Perhaps omega-3 acids will have beneficial effects on their own and also increase the sensitivity of the tumors to respond to other chemotherapy agents."

NCI Program Director Sharon Ross, Ph.D., M.P.H., commented: "Dr. Eibl's research will assist in characterizing the molecular activity of omega-3 PFAs in pancreatic cancer prevention. His research application was submitted in response to an NCI initiative developed by the Division of Cancer Prevention entitled 'Molecular Approaches to Diet and Pancreatic Cancer Prevention.' Dr. Eibl's grant is a good example of an NCI-supported project that aims to help clarify the roles of diet and bioactive food components in pancreatic cancer development and prevention."

*Grant number: 1R01CA122042-01A1

**Funahashi, H, Satake, M, Hasan S, Sawai H, Newman, R, Reber, H, Hines, O, Eibl, G. Opposing effects of n-6 and n-3 polyunsaturated fatty acids on pancreatic cancer growth. *Pancreas*, May 2008;36(4):353-362.

Green Tea Extract and Erlotinib Explored for Prevention of Head and Neck Cancer

SPECIALIZED PROGRAMS OF RESEARCH EXCELLENCE

Carcinogens (cancer-causing agents) found in tobacco and alcohol products can affect large surfaces of tissue in the head and neck region. The carcinogens can cause precancerous lesions that may eventually lead to cancers in multiple sites. For example, a person may get both tongue and laryngeal cancer. Surgery can remove one cancerous spot at a time from these areas, but in many cases "you're just going to keep cutting and cutting," said Dong Moon Shin, M.D., principal investigator of the Head and Neck Specialized Program of Research Excellence (SPORE)* at Emory University.

Searching for a way to prevent these cancers from forming, Dr. Shin and his colleagues are testing a combination of green tea polyphenols – which contain a compound called epigallocatechin-3-gallate (EGCG) – and the small-molecule inhibitor erlotinib (Tarceva) as a chemopreventive therapy for patients with precancerous lesions of the head or neck. Both EGCG and erlotinib target a protein called the epidermal growth factor receptor (EGFR), which is overproduced in up to 90% of squamous cell carcinomas of the head and neck.

Recent laboratory work from Dr. Shin's group, published in the *International Journal of Cancer***, showed that the combination of EGCG and erlotinib was more effective than either compound alone at inhibiting cell growth, inducing apoptosis (a specific type of cell death) in cell lines, and suppressing tumor growth in a mouse model of head and neck cancer. Although both compounds target EGFR and the cell signaling pathways it controls, they do so in different and apparently complementary ways. Erlotinib inactivates the protein on the cell surface, and EGCG causes the protein to be absorbed back into the cell and destroyed, thereby starving some cancer cells of the EGCG they need to survive.

This year, the Emory SPORE will begin a phase I human clinical trial of the combination of EGCG and erlotinib in patients with precancerous lesions of the head or neck. Instead of synthetic EGCG, which had been used in previous research, the clinical trial will use green tea polyphenols, which may contain other anticancer compounds in addition to EGCG. Metabolism of EGCG from green tea polyphenols will be tested in blood samples taken from patients.

Their decision to use green tea polyphenols stems from disappointing results from other chemoprevention trials that used synthetic versions of natural compounds thought to have chemopreventive effects, explained Dr. Shin. "In the past, we did trials with synthetic EGCG. When you give very high doses, the patient can't tolerate it, and with low doses, the effect isn't there. With natural products, you can push the dose a little higher. In the chemoprevention field, I think natural products will ultimately prove more important than synthetic compounds."

*Grant number: 1P50CA128613-01

** Zhang X, Zhang H, Tighiouart M, Lee J, Shin H, Khuri F, Yang C, Chen Z, Shin D. Synergistic inhibition of head and neck tumor growth by green tea (-)-epigallocatechin-3-gallate and EGFR tyrosine kinase inhibitor. *International Journal of Cancer*, September 2008;123(5):1005-14.

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.

Lycopene Shows Promise as a Chemotherapy Adjunct for Prostate Cancer

DIVISION OF CANCER TREATMENT AND DIAGNOSIS

Men with hormone-refractory prostate cancer – cancer that does not respond or has stopped responding to treatment that lowers or eliminates male hormones in the body – have few therapeutic options available to them. Some patients receive chemotherapy with docetaxel, which is the most effective anticancer drug for prostate cancer available, but this treatment typically only extends survival by a few months.

"Any agent that could enhance the effect of docetaxel would be a significant improvement," noted Xiaolin Zi, Ph.D., assistant researcher in the Department of Urology at the University of California, Irvine (UCI). Dr. Zi and his colleagues are testing the effects of the addition of lycopene, an antioxidant found naturally in tomatoes and other foods, to the treatment of prostate cancer with docetaxel.

The popularity of lycopene supplements has already risen in men with prostate cancer after the publication of epidemiologic studies linking high levels of lycopene consumption to a lower risk of prostate cancer. The first studies of lycopene and docetaxel were performed to make sure that the supplement did not interfere with the effects of the chemotherapy drug.

Researchers have found that lycopene may actually increase the efficacy of docetaxel treatment. In a study presented at the 2007 meeting of the American Association for Cancer Research, Dr. Zi and colleagues showed that in a mouse model of prostate cancer the addition of lycopene to docetaxel treatment significantly enhanced tumor regression, producing an overall 36% increase in anti-tumor efficacy.

With NCI funding*, the UCI group conducted additional laboratory studies in prostate cancer cell lines that indicated the effect of lycopene may be linked to the amount of a protein called insulin-like growth factor-I receptor (IGF-IR) found in prostate-cancer cells. The more IGF-IR expressed by cells, the more likely that lycopene would suppress their growth. However, the exact molecular mechanism behind the effect of lycopene is not clear yet and is an area that needs further study, explained Dr. Zi.

Based on their positive laboratory results, Dr. Zi and colleagues have begun early planning for a phase II clinical trial that will randomly assign men with hormone-refractory prostate cancer to receive either docetaxel alone or docetaxel plus lycopene supplements. "It will be a practical trial to run," he commented. "Certified lycopene supplements are already on the market, and the patients would already receive docetaxel."

NCI Program Director Yali Fu, Ph.D., commented: "This study is a very good example of how traditional chemotherapy can be supplemented with another agent found in nutrition and diet. Dr. Zi's work demonstrated that these effects can be traced to the molecular level and thus promised to guide chemotherapy with the likely impact of reducing toxicity and increasing efficacy. We are looking forward to seeing clinical validation of this combination in improving hormone-refractory prostate cancer treatment."

*Grant number: 1R21CA129793-01

Chinese Herbal Remedy Studied for Prostate Cancer

DIVISION OF CANCER TREATMENT AND DIAGNOSIS

Men with prostate cancer who relapse after standard therapy or whose cancer does not respond to treatment have few therapeutic options. Because such patients often do not have success with traditional chemotherapy drugs, researchers are now exploring unconventional methods of treatment.

Jin-Rong Zhou, Ph.D., assistant professor of surgery at Harvard Medical School, and his colleagues are exploring the use of the Chinese herb *Oldenlandia diffusa* (OD) for prostate cancer treatment. OD is used in TCM as an anticancer agent, but its active components remain largely unknown. In addition, the molecular mechanisms behind the effects it may have on cancer cells are not understood.

"Early data from our lab showed that OD induces cell death and inhibits cancer cell invasion and blood vessel formation, but we don't know what active compounds in the herb are responsible for these effects," Dr. Zhou said.

With NCI funding*, his laboratory is exploring the effects of OD on prostate cancer cells, with four main goals:

- Identify the active components of OD that inhibit cell growth and invasion
- Formulate possible combination therapies consisting of these compounds that will target both cancer cells and surrounding epithelial cells that play a role in cancer progression
- Verify the effectiveness of candidate combination therapies in mouse models of prostate cancer
- Characterize the structures of OD's active compounds and the cellular mechanisms by which they inhibit prostate cancer progression

The investigators will test their combination regimens in mouse models of both hormone-dependent and hormone-independent prostate cancer. Hormone-dependent prostate cancer requires male hormones, known as androgens, to grow. Hormone-independent prostate cancer can grow without stimulus from these hormones and therefore does not respond to treatment with drugs that block androgens. Active compounds isolated from OD may have different effects on these two types of prostate cancer.

"If we can identify potent active compounds and verify the efficacy and synergy of their combinations in the preclinical animal models, the next step will be a clinical trial in humans," Dr. Zhou added. He and his colleagues are currently preparing their laboratory data for publication.

*Grant number: 1R21CA133865-01A2

Chinese Herbal Formula Studied for Breast and Lung Cancer

CENTER FOR CANCER RESEARCH

NCI scientists are joining with Chinese researchers to study the effects of a TCM herbal remedy called Sheng Qi Formula (SQF) as a possible complementary treatment to improve the quality of life and as a stand alone therapy for certain types of advanced breast and lung cancer.

The original formula for SQF was a water extract of milkweed vetch root and Chinese ginseng root. The SQF decoction is traditionally delivered orally to patients in China, where it is used to decrease the side effects of chemotherapy such as cisplatin and other drugs used to treat late-stage lung and other cancers.

O.M. Zack Howard, Ph.D., staff scientist in NCI's CCR has been working on the study at NCI* labs with a visiting researcher Jie Li, M. D., Ph.D., from Guang An Men Hospital in Beijing, China. The study at NCI has focused on the effects of SQF alone and in combination with chemotherapy in a mouse model of inflammatory breast cancer (called 4T1). Similar studies with non-small cell lung cancer will be performed next. In the initial breast cancer study, the researchers zeroed in on SQF's effects on a cell type called a myeloid immunosuppressive cell (MIC) which is a type of white blood cell that is generated by tumors. High levels of MICs suppress the immune system's ability to fight tumors and contribute to the inflammatory response.

"Following implantation of the 4T1 tumor, the MIC levels in a mouse spleen can go up to 70% of the total cells," Dr. Howard noted. "The SQF formula can decrease MICs by at least one-half the elevated levels directly after implantation. At 21 days following 4T1 implantation, SQF treatment alone reduced the tumor volume by 30%. So we have both an immunological and a therapeutic effect."

In China, SQF is also believed to enhance the effects of standard chemotherapeutic drugs in patients. Taxol is a widely used treatment in breast cancer patients, but it is not very effective in the 4T1 model of breast cancer. When combined with SQF, taxol reduced tumor growth in the mice better than either treatment alone, however the overall effect was modest. The tumors did not regress completely, Dr. Howard reported.

In the next phase of the study, the researchers tried SQF in combination with another chemotherapy drug gemcitabine, which has been used as part of chemotherapeutic regimens in numerous malignancies including non-small-cell lung cancer (NSCLC), ovarian, and breast cancer. "Gemcitabine recently has been reported to limit the production of MICs," Dr. Howard noted. "We hypothesize that combining gemcitabine with SQF would synergistically inhibit MIC numbers and decrease tumor growth."

The results showed that SQF and gemcitabine profoundly limited tumor growth, Dr. Howard reported. About 40% of the mice implanted with tumors showed complete tumor regression, "and all mice in the combination therapy group showed prolonged survival compared to untreated mice or mice receiving a single treatment," she added. Combining SQF and gemcitabine did not reduce the MIC below the effect of SQF alone. "We will now investigate the effect of SQF with other tumor models, beginning with NSCLC in the near future," Dr. Howard said.

*Project number: Z01BC010707

Milk Thistle with Vitamin D Studied to Treat Myeloid Leukemia

DIVISION OF CANCER TREATMENT AND DIAGNOSIS

Historically, doctors have cautioned patients receiving cancer chemotherapy to avoid taking antioxidants – natural and manufactured substances like vitamins A, C, and E; beta-carotene; lycopene; and plant-derived phytochemicals such as carnosic acid (from rosemary) and silibinin (from milk thistle). The concern is that many anti-cancer drugs produce oxygen-based compounds that can damage DNA and might be partly responsible for the therapeutic effect of these drugs. By blocking the production of these oxidizing compounds, antioxidants might interfere with the beneficial effects of chemotherapy.

Recent work, however, suggests that certain antioxidants might actually counter the toxic effects of chemotherapy drugs and thus allow patients to safely receive larger doses. "This combination approach also looks promising for vitamin D," said George P. Studzinski, M.D., Ph.D., professor of Pathology and Laboratory Medicine at the University of Medicine and Dentistry of New Jersey. Vitamin D is an important nutrient, producing a steroid hormone the body uses to metabolize calcium, and it also fights cancer cells.

"The evidence is strong," asserted Studzinski, that larger amounts of the active form of vitamin D_3 in the body – 1α, 25-dihydroxyvitamin D_3 ($1,25D_3$) – can reduce the incidence of breast, prostate, and colon cancer. He believes that acute myeloid leukemia (AML) might well be added to that list for the benefits of vitamin D, if researchers could overcome one major hurdle. "The amount of synthetic $1,25D_3$ we need to kill the AML cells produces too much calcium in the bloodstream," he explained. Excess calcium levels can make people feel tired, confused, and depressed and cause nausea, abnormal heart rhythms, pancreatitis, and kidney stones.

While not all of the genes and pathways involved have been fully described, researchers know that $1,25D_3$ fosters a natural process known as cell differentiation (when a cell gets a more specific job), which prevents some types of cancer cells from multiplying. Normal hematopoietic stem cells develop into red and white blood cells and platelets, but when the stem cells fail to fully differentiate, myeloblasts can accumulate and may evolve into leukemia cells.

The $1,25D_3$ triggers these damaged cells to differentiate and die. The problem has been that so far the treatment of AML with vitamin D – in mice and in donated human blood cells – has succeeded only at concentrations people might find toxic. This is where the silibinin could prove beneficial by enhancing stem cell differentiation and at the same time slowing down calcium production in patients taking high levels of vitamin D.

Studzinski's lab is using an NCI grant* to try to figure out the best synthetic $1,25D_3$ and the most effective combination therapy using vitamin D and silibinin for treating AML. In collaboration with Michael Danilenko, Ph.D., of Ben Gurion University in Israel, they are developing a specific mouse model that better reflects the way that actual human myeloid blood cells behave. By networking with the clinical and research centers around the

United States that specialize in AML, Studzinski and colleagues have developed a bank of leukemia cells to study the molecular and genetic mechanics that are at play. "It wouldn't be surprising if we are able to identify certain subtypes of AML where the combination therapy is more effective," he said.

Studzinski hopes this work will eventually lead to a clinical trial testing the vitamin D–silibinin combination in AML patients. He also foresees a potential use for this therapy as a preventive treatment for childhood cancer survivors. "As more children survive cancer, they face a lifetime of increased risk for certain cancers from their original treatments, and leukemia is one of the more common," Studzinski noted. "We might put them on a fairly high dose of the silibinin therapy to prevent or lower the risk for leukemia later in life, if we can develop a version of the combination treatment without many side effects."

NCI Program Director Yali Fu, Ph.D., commented: "In recent years, there has been a number of interesting research results on the antiproliferative effect of silibinin, a naturally occurring flavonoid antioxidant, on both blood and solid tumors. Employing clinically relevant models to determine the cellular effects and the efficacy of vitamin D3 derivative and its combination with silibinin is important. Dr. Studzinski's work is a step in this direction and should shed light on the molecular basis of responsive subtypes of AML."

*Grant number: 1R01CA117942-01A2

Resveratrol and Curcumin Studied for the Treatment of Acute Lymphoblastic Leukemia

DIVISION OF CANCER PREVENTION

Cases of acute lymphoblastic leukemia (ALL) that carry a genetic mutation called the t(4;11) translocation are especially common in infants – 60 to 80% of ALL cases in infants have this mutation. Unfortunately, t(4;11) ALL has a very poor prognosis and upon relapse, is highly resistant to traditional chemotherapy drugs.

The laboratory of Susan Zunino, Ph.D., research molecular biologist at the U.S. Department of Agriculture's Western Human Nutrition Research Center, is focusing on whether resveratrol and curcumin – antioxidant molecules found in red wine and the spice turmeric, respectively – can kill t(4;11) ALL cells.

Dr. Zunino and her colleagues' *in vitro* work shows promise. In leukemia cell lines derived from patients with highly treatment-resistant ALL, both resveratrol and curcumin induced a type of programmed cell death called apoptosis. The compounds appear to work by damaging the cancer cells' mitochondria– the structures in cells that produce the energy necessary for all cellular functions.

Resveratrol and curcumin, when taken up by a cancer cell, cause the membranes surrounding the mitochondria to lose their natural polarity – normally one side of the membrane has a positive electrical charge and the other side has a negative charge – which in turn triggers apoptosis. The *in vitro* dose levels of resveratrol and curcumin that cause apoptosis in only the cancer cells have been found.

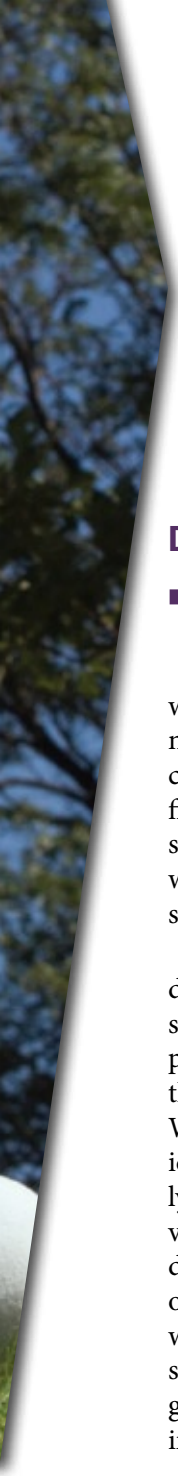
Dr. Zunino and her colleagues are now extending their work with NCI funding* to include animal studies. They are first injecting immunodeficient mice with leukemia cells, either from a cell line established in culture from a patient with t(4;11) ALL or from biopsy specimens from patients with t(4;11) ALL. When leukemia develops, the investigators will treat the mice with one of four injected regimens – a placebo, the chemotherapy drug vincristine, resveratrol, or curcumin – and compare survival between the groups. In a second set of experiments looking at resveratrol and curcumin for preventing relapse, mice will receive vincristine along with either resveratrol or curcumin in their diet.

"If resveratrol and curcumin are effective in preventing the growth of the leukemia, these agents might be useful in the clinical setting in conjunction with other anti-leukemic agents," Dr. Zunino noted. "But caution in any such speculation is warranted until further animal, and eventually human, studies are performed to determine optimal doses, treatment regimens, and synergistic effects with standard chemotherapeutic agents."

*Grant number: 1R21CA122117-01A1

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.



Relieving Chronic Stress Enhances the Immune System in Cervical Cancer Patients

DIVISION OF CANCER CONTROL AND POPULATION SCIENCES

The body's immune system can be crucial in fighting cancer. Lari Wenzel, Ph.D., and Edward L. Nelson, M.D., from the University of California, Irvine believe the link might be the "mind-body" connection. They are exploring whether the evolving field of psychoneuroimmunology might provide insights to help patients cope with the stress of cancer, while at the same time fortifying their immune response to cancer cells.

"Many cancer survivors continue to experience disrupted quality of life long after cancer treatment," said Dr. Wenzel. "If quality of life (QOL) disruptions persist over time, patients may be able to benefit from the kind of psychosocial support that we provide." With NCI funding*, she and Dr. Nelson tested this idea recently by enrolling 50 women who had recently been treated for cervical cancer. Women with cervical cancer experience greater and more prolonged disruption in their QOL than do patients with many other types of cancer. The investigators found that women who received telephone counseling had a significantly improved QOL compared to those who got "usual care," who generally experienced either no improvement or even a decline in QOL.

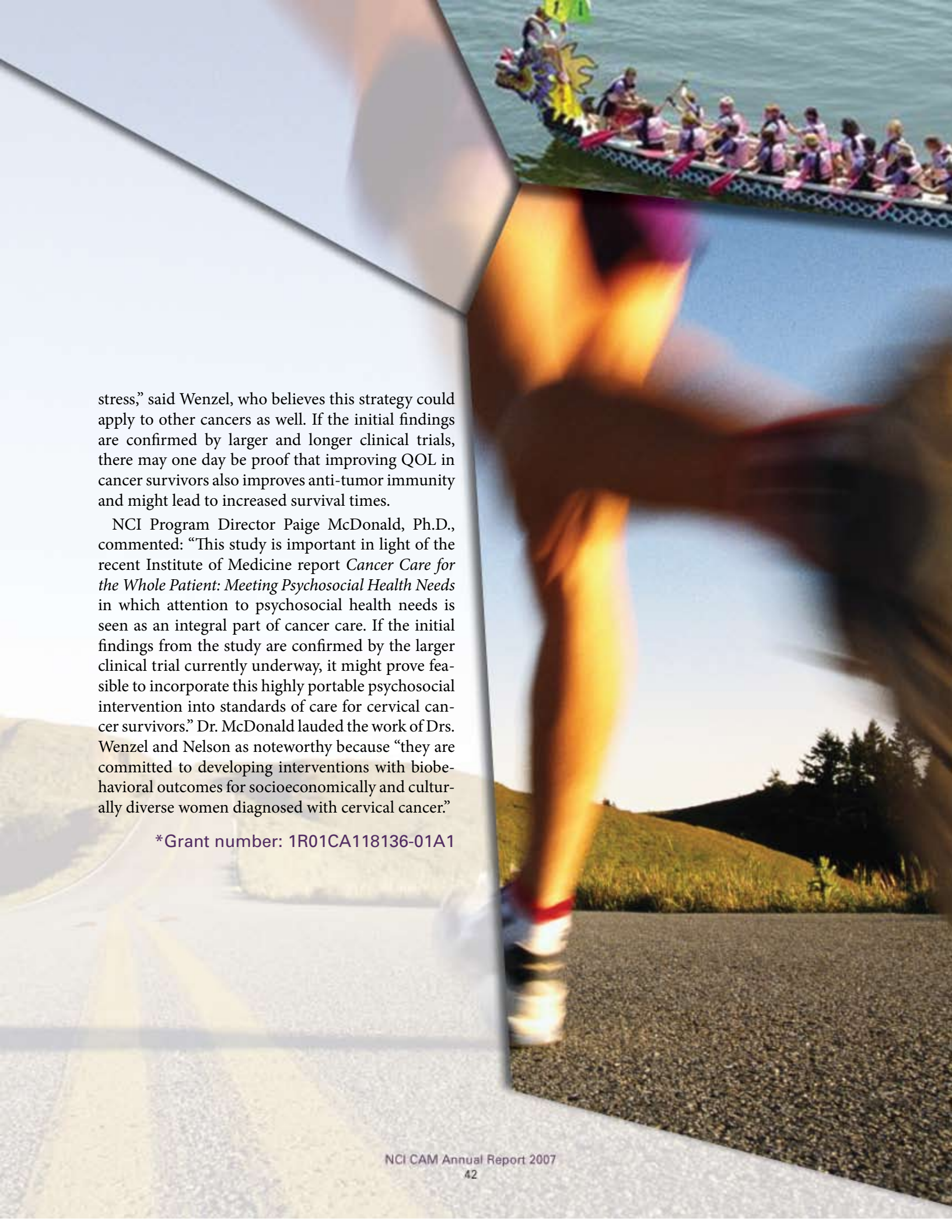
"These patients are suffering from chronic stress," explained Dr. Wenzel. Dr. Nelson pointed out that chronic stress affects the body's psychoneuroimmune axis by encouraging the immune system to make more antibodies and fewer "killer" cells– what researchers classify as a T helper type 2 (Th2) immunologic response. In contrast, a Th1 immune response produces more killer cells and is better for controlling cancer. Since the immune system produces effects throughout the body, the Th1 response may be effective against cancer cells that have begun to spread from the primary tumor site. "Prominent Th1 immunity in tumors has been associated with improved disease control and survival in a recent report of colon cancer patients," Nelson noted.

The researchers used saliva and blood samples of patients who received phone counseling as well as those who had not, hoping to see whether they showed different proteins and hormones that measure both stress and Th1 or Th2 immunity. "We were surprised that, even with this small number of patients who were counseled, improvement in QOL was associated with an increase in the Th1 capacity of the immune system," said Nelson.

While other biobehavioral research has shown direct effects on the immune system, the interventions have usually been directed at so-called "acute" stressors, explained Wenzel. But the situation with cervical cancer is different, she noted, "because these cancers are being detected earlier and more effectively treated. Thus, a growing population of survivors is faced with chronic, long-term stresses associated with their diagnosis and treatment, including socioeconomic and cultural barriers and sexual and reproductive concerns. If a fortified immune system can produce what scientists call longitudinal improvements in QOL, those patients might actually live longer."

The researchers hope the encouraging results from this NCI-supported feasibility study will be pursued. "The shift in the immune system that we have identified appears to be related to a decrease in chronic

continued



stress," said Wenzel, who believes this strategy could apply to other cancers as well. If the initial findings are confirmed by larger and longer clinical trials, there may one day be proof that improving QOL in cancer survivors also improves anti-tumor immunity and might lead to increased survival times.

NCI Program Director Paige McDonald, Ph.D., commented: "This study is important in light of the recent Institute of Medicine report *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs* in which attention to psychosocial health needs is seen as an integral part of cancer care. If the initial findings from the study are confirmed by the larger clinical trial currently underway, it might prove feasible to incorporate this highly portable psychosocial intervention into standards of care for cervical cancer survivors." Dr. McDonald lauded the work of Drs. Wenzel and Nelson as noteworthy because "they are committed to developing interventions with biobehavioral outcomes for socioeconomically and culturally diverse women diagnosed with cervical cancer."

*Grant number: 1R01CA118136-01A1

Dragon Boat Racing May Help Cancer Survivors Thrive

DIVISION OF CANCER CONTROL AND POPULATION SCIENCES

The ancient Chinese sport of dragon boat racing has been catching on in the cancer survivor community in recent years. A new study is examining whether this team-oriented activity can enhance the quality of life for survivors.

In recent years, researchers have documented the benefits of general physical activity in improving outcomes for some cancer survivors. Building upon that research, Cynthia Carter, Ph.D., assistant professor at the Hollings Cancer Center at the Medical University of South Carolina, is investigating whether physical activity conducted within the context of social support of a dragon boat team contributes "synergistically" to improved overall quality of life. "We think the collective experience of dragon boating is likely enhanced by team sport factors such as cohesion, teamwork, and the goal of competition and by paddling on the water creating greater feelings of inner peace and harmony," she explained.

Dragon boat racing is documented as far back as 400 B.C. in China. "It has wonderful myths and a lot of pageantry that are incorporated into modern-day dragon boating festivals," Dr. Carter added. The sport has grown increasingly popular in North America. It was first adopted by cancer survivors in 1996 when a sports medicine physician Don McKenzie, M.D., in Vancouver, Canada, began treating a breast cancer survivor for a shoulder injury. The patient was unable to perform the standard weight-lifting exercises for the injury because of concerns about lymphedema in women who have had breast surgery and who later lift more than a certain amount of weight.

Dr. McKenzie thought that the paddling exercise involved in dragon boat racing might be an acceptable alternative for building upper body strength in former breast cancer patients. He set up the very first all-women, breast cancer survivor team to compete in local festivals. "It became such a positive experience for these women that they set about spreading the word," Dr. Carter noted. "Dragon boat racing grew very quickly in the survivor community and eventually made its way into the United States."

In the small study, funded by a grant from NCI*, 124 cancer survivors (men and women) choose to participate twice a week in either an 8-week dragon boat paddling program (experimental group) or an organized walking program (control group). At the conclusion of study period, the dragon boat participants compete in a local race. "There is an established dragon boat survivor program here in our community, so the study participant teams compete against our other survivor dragon boat teams in the area," said Dr. Carter.

Although the study is still ongoing, Dr. Carter reported, "So far we have found that the survivors choosing to participate in both study arms look very similar in terms of demographics."

Physical activity is becoming more of a standard of care recommendation for post-treatment cancer survivors. "What I hope that our study can add to the conversation is the idea that this type of activity is enhanced by a team-oriented program," Dr. Carter added. "When we get kids playing sports, they don't seem to have a hard time sticking with their exercise activities, because it's social, team-oriented, and fun. Adults aren't that different, and I think we'll find that aspect actually has a very positive impact on adherence to physical activity in adults as well."

NCI Program Director Diana Jeffery, Ph.D., added: "Team sports engender social support, which we know can be instrumental in helping cancer survivors learn about available resources. Overall, the expectation of this study is to improve quality of life and promote physical function and emotional well-being."

*Grant number: 1R03CA128482-01

SCIENTIFIC PUBLICATIONS

This is a selected list of some of the most important peer-reviewed scientific articles about the findings and analyses of NCI-supported CAM research studies published during FY 2007. The articles are classified and grouped according to research type: cancer prevention, cancer treatment, and cancer side effect/symptom management.

Article citations marked with an asterisk (*) are the results of studies featured in the *NCI's Annual Report on Complementary and Alternative Medicine: Fiscal Year 2006* which can be read and downloaded at http://www.cancer.gov/cam/attachments/CAMAnnualReportFY2006.pdf.

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

Cancer Prevention

Barnard RJ, Leung PS, Aronson WJ, Cohen P, Golding LA. A mechanism to explain how regular exercise might reduce the risk for clinical prostate cancer. *European Journal of Cancer Prevention*, October 2007;16(5):415-21.

Chen S, Oh SR, Phung S, Hur G, Ye JJ, Kwok SL, Shrode GE, Belury M, Adams LS, Williams D. Anti-aromatase activity of phytochemicals in white button mushrooms (Agaricus bisporus). *Cancer Research*, December 2006;66(24):12026-34.

Grau MV, Baron JA, Sandler RS, Wallace K, Haile RW, Church TR, Beck GJ, Summers RW, Barry EL, Cole BF, Snover DC, Rothstein R, Mandel JS. Prolonged effect of calcium supplementation on risk of colorectal adenomas in a randomized trial. *Journal of the National Cancer Institute*, January 2007;99(2):129-36.

* Hudson TS, Hartle DK, Hursting SD, Nunez NP, Wang TT, Young HA, Arany P, Green JE. Inhibition of prostate cancer growth by muscadine grape skin extract and resveratrol through distinct mechanisms. *Cancer Research*, September 2007;67(17):8396-405.

Khan N, Afaq F, Kweon MH, Kim K, Mukhtar H. Oral consumption of pomegranate fruit extract inhibits growth and progression of primary lung tumors in mice. *Cancer Research*, April 2007;67(7):3475-82.

Kaur M, Singh RP, Gu M, Agarwal R, Agarwal C. Grape seed extract inhibits in vitro and in vivo growth of human colorectal carcinoma cells. *Clinical Cancer Research*, October 2006;12(20 Pt 1):6194-202.

* King ML, Murphy LL. American ginseng (panax quinquefolius L.) extract alters mitogen-activated protein kinase cell signaling and inhibits proliferation of MCF-7 cells. *Journal of Experimental Therapeutics and Oncology*, 2007;6(2):147-55.

* Lawson KA, Wright ME, Subar A, Mouw T, Hollenbeck A, Schatzkin A, Leitzmann MF. Multivitamin use and risk of prostate cancer in the National Institutes of Health–AARP Diet and Health Study. *Journal of the National Cancer Institute*, May 2007;99(10):754-64.

Raina K, Singh RP, Agarwal R, Agarwal C. Oral grape seed extract inhibits prostate tumor growth and progression in TRAMP mice. *Cancer Research*, June 2007;67(12):5976-82.

Syed DN, Afaq F, Kweon MH, Hadi N, Bhatia N, Spiegelman VS, Mukhtar H. Green tea polyphenol EGCG suppresses cigarette smoke condensate-induced NF-kappaB activation in normal human bronchial epithelial cells. *Oncogene*, February 2007;26(5):673-82.

* Ward MH, Cross AJ, Divan H, Kulldorff M, Nowell-Kadlubar S, Kadlubar FF, Sinha R. Processed meat intake, CYP2A6 activity and risk of colorectal adenoma. *Carcinogenesis*, June 2007;28(6):1210-6.

Cancer Treatment

Adhami VM, Malik A, Zaman N, Sarfaraz S, Siddiqui IA, Syed DN, Afaq F, Pasha FS, Saleem M, Mukhtar H. Combined inhibitory effects of green tea polyphenols and selective cyclooxygenase-2 inhibitors on the growth of human prostate cancer cells both in vitro and in vivo. *Clinical Cancer Research*, March 2007;13(5):1611-9.

Agarwal C, Tyagi A, Agarwal R. Gallic acid causes inactivating phosphorylation of cdc25A/cdc25C-cdc2 via ATM-Chk2 activation, leading to cell cycle arrest, and induces apoptosis in human prostate carcinoma DU145 cells. *Molecular and Cellular Biochemistry*, December 2006;5(12):3294-302.

Kweon MH, Adhami VM, Lee JS, Mukhtar H. Constitutive overexpression of Nrf2-dependent heme oxygenase-1 in A549 cells contributes to resistance to apoptosis induced by epigallocatechin 3-gallate. *Journal of Biological Chemistry*, November 2006;281(44):33761-72.

Khan N, Hadi N, Afaq F, Syed DN, Kweon MH, Mukhtar H. Pomegranate fruit extract inhibits prosurvival pathways in human A549 lung carcinoma cells and tumor growth in athymic nude mice. *Carcinogenesis*, January 2007;28(1):163-73.

Kumar NB, Krischer JP, Allen K, Riccardi D, Besterman-Dahan K, Salup R, Kang L, Xu P, Pow-Sang J. A Phase II randomized, placebo-controlled clinical trial of purified isoflavones in modulating steroid hormones in men diagnosed with localized prostate cancer. *Nutrition and Cancer*, 2007;59(2):163-8.

Limtrakul P, Chearwae W, Shukla S, Phisalphong C, Ambudkar SV. Modulation of function of three ABC drug transporters, P-glycoprotein (ABCB1), mitoxantrone resistance protein (ABCG2) and multidrug resistance protein 1 (ABCC1) by tetrahydrocurcumin, a major metabolite of curcumin. *Molecular and Cellular Biochemistry*, February 2007;296(1-2):85-95.

Ou L, Ip C, Lisafeld B, Ip MM. Conjugated linoleic acid induces apoptosis of murine mammary tumor cells via Bcl-2 loss. *Biochemical and Biophysical Research Communications*, May 2007;356(4):1044-9.

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

Zhang H, Wang X, Chen F, Androulakis XM, Wargovich MJ. Anticancer activity of limonoid from Khaya senegalensis. *Phytotherapy Research*, August 2007;21(8):731-4.

Cancer Side Effects/Symptom Management

Antoni MH, Lechner SC, Kazi A, Wimberly SR, Sifre T, Urcuyo KR, Phillips K, Glück S, Carver CS. How stress management improves quality of life after treatment for breast cancer. *Journal of Consulting and Clinical Psychology*, December 2006;74(6):1143-52.

Antoni MH, Wimberly SR, Lechner SC, Kazi A, Sifre T, Urcuyo KR, Phillips K, Smith RG, Petronis VM, Guellati S, Wells KA, Blomberg B, Carver CS. 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(10):1791-7.

Cruciani RA, Dvorkin E, Homel P, Malamud S, Culliney B, Lapin J, Portenoy RK, Esteban-Cruciani N. Safety, tolerability and symptom outcomes associated with L-carnitine supplementation in patients with cancer, fatigue, and carnitine deficiency: a phase I/II study. *Journal of Pain and Symptom Management*, December 2006;32(6):551-9.

Dibble SL, Luce J, Cooper BA, Israel J, Cohen M, Nussey B, Rugo H. Acupressure for chemotherapy-induced nausea and vomiting: a randomized clinical trial. *Oncology Nursing Forum*, July 2007;34(4):813-20.

Spiegel D, Butler LD, Giese-Davis J, Koopman C, Miller E, DiMiceli S, Classen CC, Fobair P, Carlson RW, Kraemer HC. Effects of supportive-expressive group therapy on survival of patients with metastatic breast cancer: a randomized prospective trial. *Cancer*, September 2007;110(5):1130-8.

Appendix

PDQ Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
PEDIATRIC TRIALS					
Phase II Randomized Study of a Therapeutic Music Video Intervention Versus Listening and Discussing Books on Tape for Increased Resilience and Quality of Life of Adolescents and Young Adults Undergoing Myeloablative Autologous or Allogeneic Transplantation for Cancer	COG-ANUR0631	Educational/ Counseling/ Training	11 to 24	NINR; NCI	Phase II
Pilot Study of Educational and Promotional Materials Development for Use in Promoting Physical Activity in Community-Based After-School Programs by Multiethnic, Urban Adolescents	MSUHNS-0003669	Prevention; Educational/ Counseling/ Training	11 to 14	NCI	No phase specified
Randomized Prospective Pilot Study of Acupressure in Preventing Chemotherapy-Associated Nausea and Vomiting in Pediatric Patients with Cancer	CCCWFU-02104	Supportive care	2 to 21	NCI	No phase specified
Randomized Study of Traumeel® S for the Prevention and Treatment of Mucositis in Pediatric Patients Undergoing Hematopoietic Stem Cell Transplantation	COG-ACCL0331	Supportive care	3 to 25	NCI	No phase specified
Randomized Study of Electroacupuncture for Treatment of Delayed Chemotherapy-Induced Nausea and Vomiting in Patients with Newly Diagnosed Pediatric Sarcoma, Neuroblastoma, Nasopharyngeal Carcinoma, Germ Cell Tumors, or Hodgkin Lymphoma	NCCAM-02-AT-0172	Supportive care	5 to 35	NCCAM; NCI	No phase specified
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	MCC-0402	Supportive care; Treatment	3 to 20	NCI	Phase III
Phase I Study of Beta-Glucan and Rituximab in Pediatric Patients with Relapsed or Progressive CD20-Positive Lymphoma or Leukemia or Post-Allogeneic Stem Cell Transplant-Related Lymphoproliferative Disorder	MSKCC-03095	Treatment	Under 22	NCI	Phase I
ADULT TRIALS					
Bladder					
Phase II Randomized Study of Neoadjuvant Genistein in Patients Undergoing Surgical Resection for Bladder Cancer	WCCC-CO-04307	Biomarker/ Laboratory analysis; Treatment	18 and over	NCI	Phase II
Brain					
Pilot Study of a Stress Reduction Program in Patients with Malignant Brain Tumors and Their Family Caregivers	CASE-CCF-2306-CC052	Supportive care	18 and over	NCI	No phase specified
Phase II Randomized Study of Boswellia serrata and Standard Treatment Versus Standard Treatment Alone in Patients with Newly Diagnosed or Recurrent High-Grade Gliomas	CASE-CCF-7348	Treatment	18 and over	NCI	Phase II

PDQ Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Pilot Study of Regulatory T-Cell Inhibition With Daclizumab During Antitumor Immunotherapy Targeted Against Cytomegalovirus in Patients With Newly Diagnosed Glioblastoma Multiforme and Therapeutic Temozolomide-Induced Lymphopenia	DUMC-PRO00000581	Treatment; Diagnostic	18 and over	NCI	No phase specified
Breast					
Pilot Study of Restorative Yoga for Symptom Management and Stress Reduction in Women with Ovarian or Breast Cancer	CCCWFU-02403	Educational/ Counseling/ Training	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	Educational/ Counseling/ Training; Treatment	18 and over	NCI	No phase specified
Randomized Study of the Effect of a Reduced-Calorie Diet and/or Exercise Program on Risk Factors for Breast Cancer Development in Overweight or Obese Postmenopausal Women	FHCRC-PHS-1960.00	Prevention; Biomarker/ Laboratory analysis; Behavioral study	50 to 75	NCI	No phase specified
Randomized Study of Exercise in Preventing Breast Cancer in Healthy Young Women	UMN-0505M69867	Prevention; Diagnostic	18 to 30	NCI	No phase specified
Phase I Pilot Chemoprevention Study of IH636 Grape Seed Proanthocyanidin Extract in Healthy Postmenopausal Women at High Risk of Developing Breast Cancer	CHNMC-IRB-03178	Prevention	40 to 75	NCI	Phase I
Phase II Randomized Study of Genistein in Women at High Risk for Breast Cancer	NU-NWU03-1-04	Prevention	25 and older	NCI	Phase II
Randomized Pilot Study of Hypnosis in Controlling Hot Flashes in Women Who are Breast Cancer Survivors	S-WHITE-8165	Supportive care	Over 18	NCI	No phase specified
Randomized Pilot Study of the Effect of Healing Touch in Women with Breast Cancer Experiencing Radiotherapy-Induced Fatigue	VU-VICC–SUPP-0633	Supportive care	21 to 75	NCI	No phase specified
Randomized Study of Hatha Yoga in Improving Physical Activity, Inflammation, Fatigue, and Distress in Postmenopausal Female Breast Cancer Survivors	OSU-2007C0004	Supportive care; Biomarker/Laboratory analysis	21 and over	NCI	No phase specified
Pilot Study of Soy-Based Meal Replacement (Almased®) as a Weight Loss Intervention in Patients with Estrogen Receptor/Progesterone Receptor-Negative Stage I-III Breast Cancer in Complete Remission	CCCWFU-98904	Supportive care; Educational/ Counseling/ Training; Behavioral study	21 and over	NCI	No phase specified
Phase II Randomized Study of Soy Protein in Postmenopausal Women with Breast Disease Taking Tamoxifen and Experiencing Hot Flashes	CALGB-79805	Supportive care	Postmenopausal (20 and over)	NCI	Phase II
Phase II Study of Hypericum Perforatum (St. John's wort) in Postmenopausal Women with Non-Metastatic Breast Cancer Suffering from Hot Flashes	CCCWFU-98301	Supportive care	18 and over	NCI	Phase II
Phase II Randomized Study of Three Different Programs of Paced Breathing in Women Breast Cancer Survivors with Hot Flashes	MAYO-MC06C8	Supportive care	18 and over	NCI	Phase II

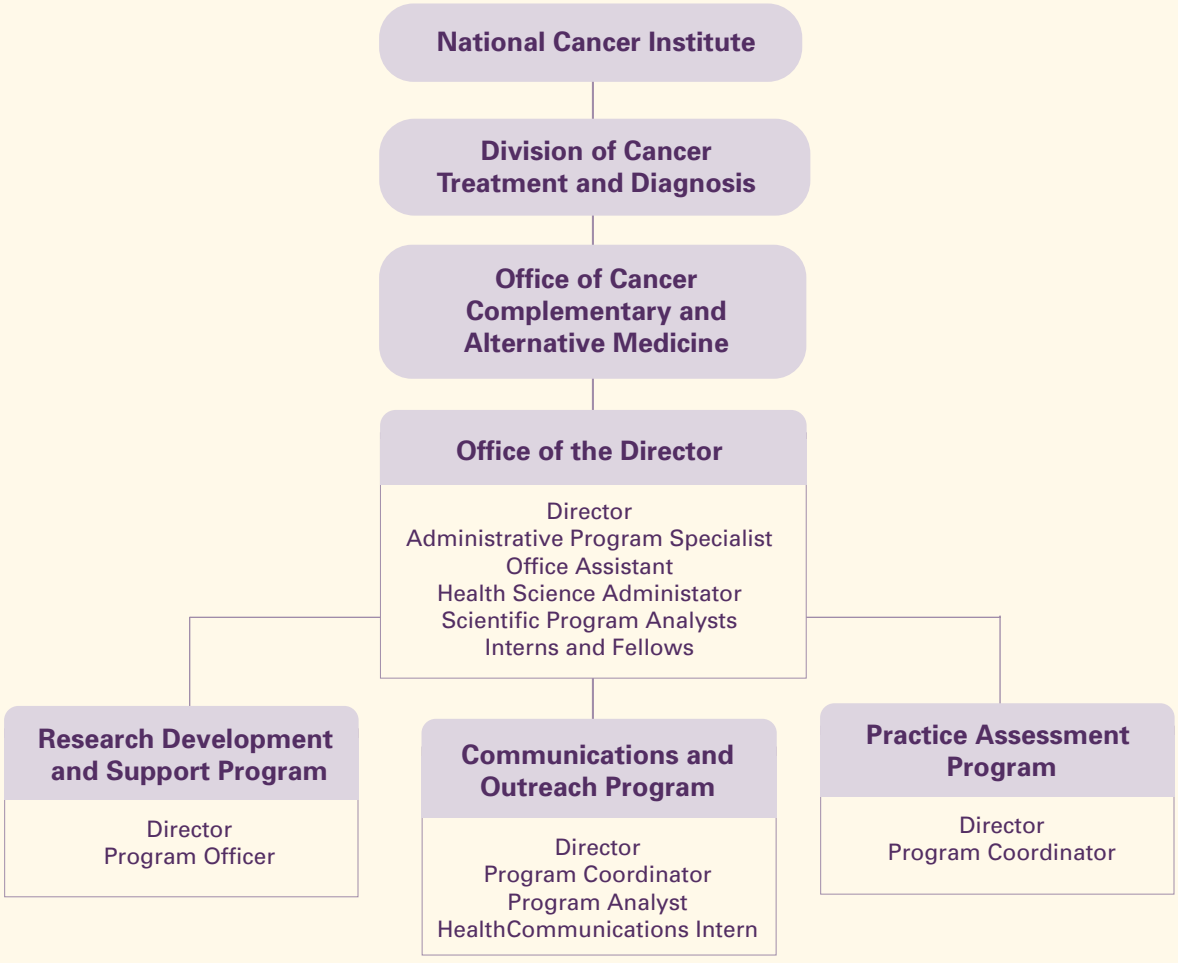
PDQ Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Phase I Randomized Study of Green Tea Catechin Extract (Polyphenon E) in Women with a History of Hormone Receptor-Negative Stage I-III Breast Cancer	MDA-MDA04-4-01	Treatment; Prevention; Biomarker/ Laboratory analysis	21 to 65	NCI	Phase I
Phase II Study of Gemcitabine Hydrochloride and Genistein in Women with Stage IV Breast Cancer	WSU-C-2597	Treatment	18 and over	NCI	Phase II
Cervix					
Randomized Study of Mindfulness-Based Stress Reduction Versus General Health Education in Improving Immune Response to Human Papilloma Virus in Patients with Cervical Dysplasia	FCCC-06851	Behavioral study; Educational/ Counseling/ Training; Biomarker/ Laboratory analysis	18 and over	NCI	No phase specified
Phase II Randomized Study of Green Tea Extract (Polyphenon E) for the Prevention of Cervical Cancer in Patients with Human Papillomavirus (HPV) and Low-Grade Cervical Intraepithelial Neoplasia (CIN 1)	UARIZ-UAZ03-1-02	Prevention	18 and over	NCI	Phase II
Colon/Rectum					
Phase II Randomized Chemoprevention Study of Atorvastatin Versus Oligofructose-Enriched Inulin (Raftilose Synergy 1) Versus Sulindac in Patients at Increased Risk of Developing Sporadic Colorectal Neoplasia	MAYO-030103	Prevention; Biomarker/ Laboratory analysis	40 and over	NCI	Phase II
Phase III Randomized Study of Selenium in Patients with Adenomatous Colorectal Polyps	UARIZ-00-0430-01	Prevention	40 to 80	NCI	Phase III
Phase II Randomized Study of Acupuncture in Reducing Postoperative Ileus in Patients Who Have Undergone Segmental or Subtotal Colectomy for Colorectal Cancer	MSKCC-06145	Supportive care	Over 18	NCI	Phase II
Phase I Study of Resveratrol in Patients with Resectable Colorectal Cancer	CCUM-TASK2B	Treatment; Biomarker/ Laboratory analysis	Over 18	NCI	Phase I
Phase II Chemoprevention Study of Curcumin in Current Smokers with Aberrant Crypt Foci	UCIRVINE-UCI04-2-01	Prevention; Biomarker/ Laboratory analysis	40 and over	NCI	Phase II
Espohagus					
Phase IB Randomized Study of Green Tea Extract (Polyphenon E) in Preventing Esophageal Cancer in Patients with Barrett's Esophagus	MDA-03101	Prevention	18 and over	NCI	Phase I
Head and Neck					
Randomized Pilot Study of Electroacupuncture for Chronic Radiation-Induced Xerostomia in Patients with Head and Neck Cancer	MAYO-MCS285	Supportive care	21 to 89	NCI	No phase specified
Phase I Randomized Study of Antioxidant-Deficient Diet in Controlling Cachexia in Patients with Oropharyngeal Cancer Receiving Chemoradiotherapy	UNC-LCCC-0523	Supportive care; Biomarker/Laboratory analysis; Treatment	Over 18	NCI	Phase I

PDQ Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Phase III Randomized Study of Acupuncture Versus Standard of Care in Treating Pain and Dysfunction in Patients with Head and Neck Cancer Who Have Undergone Neck Dissection	MSKCC-03131A	Supportive care	Not specified	NCI	Phase III
Phase II Randomized Study of Fruit and Vegetable Extracts in Patients with Stage I-IVB Head and Neck Cancer	CCCWFU-0112	Treatment	18 and over	NCI	Phase II
Phase II Randomized Chemoprevention Study of Bowman-Birk Inhibitor Concentrate in Patients with Oral Leukoplakia	UCIRVINE-UCI-98-34	Treatment; Prevention; Biomarker/ Laboratory analysis	18 and over	NCI	Phase II
Hematologic					
Pilot Study of Healing Touch in Treating Patients Receiving Chemotherapy for Acute Myeloid Leukemia or Acute Lymphocytic Leukemia	CCCWFU-02305	Supportive care	18 and over	NCI	No phase specified
Randomized Study of Music in Reducing Anxiety and Perceived Pain in Adult Patients Who Are Undergoing Bone Marrow Biopsy for Hematologic Cancers or Other Diseases	CCCWFU-98306	Supportive care	18 and over	NCI	No phase specified
Kidney					
Phase II Pilot Study of Genistein and High-Dose Interleukin-2 in Patients with Metastatic Malignant Melanoma or Renal Clear Cell Carcinoma	NU-04V1	Treatment	18 and over	NCI; Pharmaceutical/ Industry	Phase II
Lung					
Chemoprevention Study of Broccoli Sprout Extract in Smokers	JHOC-J0427	Prevention	Over 18	NCI	No phase specified
Phase II Randomized Study of Green Tea or Polyphenon E in Preventing Lung Cancer in Former Smokers with Chronic Obstructive Pulmonary Disease	UARIZ-HSC-0353	Prevention; Biomarker/ Laboratory analysis	40 to 80	NCI	Phase II
Phase III Randomized Chemoprevention Study of Selenium in Participants with Previously Resected Stage I Non-Small Cell Lung Cancer	ECOG-5597	Prevention	18 and over	NCI	Phase III
Multiple					
Pilot Randomized Study of Cognitive-Behavioral Therapy Versus Standard Care in Patients with Advanced Gastrointestinal Cancer or Lung Cancer	MGH-2007-P-000368	Educational/ Counseling/ Training; Supportive care	Over 18	NCI	No phase specified
Phase I Study of Gemcitabine and Mistletoe in Patients with Advanced Solid Tumors	NCCAM-02-AT-260	Treatment	18 and over	NCCAM; NCI; Other	Phase I
Non-cancer					
Phase I Randomized Study of Garlic Supplements to Modulate Opioid Effects in Healthy Volunteers	FHCRC-2040.00	Natural history/ Epidemiology; Biomarker/ Laboratory analysis	21 to 45	NCI	Phase I

PDQ Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Phase I Randomized Study of Nutritional-Grade, Absorption-Enhanced Diindolylmethane (BR-DIM) in Healthy Volunteers	KUMC-HSC-9139-3	Biomarker/ Laboratory analysis; Prevention	18 to 70	NCI	Phase I
Ovary/Peritoneal Cavity					
Randomized Study of Hypnosis, Massage Therapy, and Healing Touch in Patients Undergoing Chemotherapy for Ovarian Epithelial or Primary Peritoneal Cavity Cancer	UMN-2000NT790	Supportive care	Any age	NCI	No phase specified
Pancreas					
Phase II Study of Genistein, Gemcitabine Hydrochloride, and Erlotinib Hydrochloride in Patients with Locally Advanced or Metastatic Pancreatic Cancer	WSU-2005-006	Treatment	21 and over	NCI	Phase II
Prostate					
Randomized Study of the Molecular Effects of Lycopene Versus Omega-3 Fatty Acid Nutritional Supplements in Patients with Stage I or II Prostate Cancer	UCSF-03553	Biomarker/ Laboratory analysis; Treatment	Not specified	NCI	No phase specified
Randomized Study of Fish Oil Supplements and Green Tea in Preventing Prostate Cancer in Patients Who Are at Risk for Developing Prostate Cancer	OHSU-CI-CPC-04131-LX	Prevention--	18 and over	NCI	No phase specified
Randomized Study of Lycopene in Preventing Prostate Cancer in Healthy Participants	UIC-2004-0217	Prevention; Biomarker/ Laboratory analysis	18 and over	NCI	No phase specified
Phase II Randomized Chemoprevention Study of Calcitriol in Patients with High-Grade Prostatic Intraepithelial Neoplasia	CINJ-080404	Prevention	18 and over	NCI	Phase II
Study of Acupuncture in Treating Hot Flashes in Patients with Prostate Cancer Undergoing Androgen Deprivation	OHSU-7235	Supportive care	Over 18	NCI	No phase specified
Phase III Randomized Study of Soy Protein/Isoflavones and Venlafaxine on Vasomotor Symptoms in Patients with Prostate Cancer Undergoing Hormonal Manipulation	CCCWFU-97405	Supportive care	21 and over	NCI	Phase III
Randomized Study of Polyunsaturated Fatty Acids in Patients with Prostate Cancer Undergoing Prostate Biopsy and/or Surgery	DFCI-03116	Treatment; Biomarker/ Laboratory analysis	Adult	NCI	No phase specified
Phase I Study of Nordihydroguaiaretic Acid in Patients with Nonmetastatic, Biochemically Relapsed Prostate Cancer	UCSF-035510	Treatment	Over 18	NCI	Phase I
Phase I Randomized Study of Neoadjuvant Diindolylmethane in Patients Undergoing Radical Prostatectomy for Stage I or II Adenocarcinoma of the Prostate	WCCC-CO05186	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase I
Phase I Study of Defined Green Tea Catechin Extract in Patients with Prostate Cancer Scheduled to Undergo Prostatectomy	UARIZ-UAZ05-6-01	Treatment; Biomarker/ Laboratory analysis	18 and over	NCI	Phase I
Phase II Randomized Pilot Study of Calcitriol and Dexamethasone Before Radical Prostatectomy in Patients with Localized Adenocarcinoma of the Prostate	RPCI-RP-0212	Treatment	18 and over	NCI	Phase II
Phase II Study of Licorice Root Extract and Docetaxel in Patients with Hormone-Refractory Metastatic Prostate Cancer	CINJ-5040	Treatment	18 and over	NCI	Phase II

PDQ Clinical Trials	Primary ID	Type of Trial	Age Range	Sponsor of Trial	Phase(s)
Phase II Randomized Study of Neoadjuvant Dietary Supplementation with Soy in Patients Undergoing Radical Prostatectomy for Localized Prostate Cancer	CCCWFU-98203	Treatment; Biomarker/ Laboratory analysis	Over 18	NCI	Phase II
Phase II Study of Cholecalciferol and Soy Supplementation in Patients with Biochemically Recurrent Prostate Cancer Following Failed Definitive Local Therapy	CCCWFU-85106	Treatment; Biomarker/ Laboratory analysis	Over 18	NCI	Phase II
Phase III Randomized Study of Pomegranate Juice in Patients with Rising Prostate-Specific Antigen Levels After Surgery or Radiotherapy for Localized Prostate Cancer	UCLA-0507059-01	Treatment	18 and over	NCI; Pharmaceutical/ Industry	Phase III
Not specified					
Randomized Study of Stress Management Therapy in Patients Undergoing Chemotherapy for Cancer	MCC-0501	Educational/ Counseling/ Training; Supportive care	18 and over	NCI	No phase specified
Randomized Pilot Study of Glutamine Supplementation for the Prevention of Paclitaxel-Induced Myalgia and/or Arthralgia in Patients with Cancer	OHSU-ONC-99037-L	Supportive care	18 and over	NCI	No phase specified
Randomized Study of the Effect of Animal-Assisted Therapy and Recreational Therapy on Distress in Cancer Patients Undergoing Treatment for Pain	NCI-05-CC-0093	Supportive care; Biomarker/Laboratory analysis	18 and over	NCI	No phase specified
Phase II Randomized Pilot Study of Massage Therapy in Patients with Cancer Pain	MSKCC-03046A	Supportive care	18 and over	NCI	Phase II
Phase II Randomized Study of Ginger in Patients with Cancer and Chemotherapy-Induced Nausea and Vomiting	CCUM-0201	Supportive care	18 and over	NCI; NCCAM	Phase II
Phase II Randomized Study of Hatha Yoga for Persistent Sleep Disturbance in Cancer Survivors	URCC-U3905	Supportive care	21 and over	NCI	Phase II
Phase II/III Randomized Study of Ginger for Chemotherapy-Related Nausea in Patients with Cancer	URCC-U1902	Supportive care	18 and over	NCI	Phase II; Phase III
Phase III Randomized Study of Valerian for Improving Sleep in Patients with Cancer Receiving Adjuvant Therapy	NCCTG-N01C5	Supportive care	18 and over	NCI	Phase III
Phase III Randomized Study of Levocarnitine (L-carnitine) for the Management of Fatigue in Cancer Patients	ECOG-E4Z02	Supportive care	18 and over	NCI	Phase III
Phase III Randomized Study of Alpha-Lipoic Acid in Preventing Platinum-Induced Peripheral Neuropathy in Cancer Patients Receiving a Cisplatin- or Oxaliplatin-Containing Chemotherapy Regimen	MDA-CCC-0327	Supportive care	Not specified	NCI	Phase III
Phase III Randomized Study of Vitamin E in Preventing Chemotherapy-Induced Peripheral Neuropathy in Patients Undergoing Curative Neurotoxic Chemotherapy for Cancer	NCCTG-N05C3	Supportive care	18 and over	NCI	Phase III
Randomized Study of Resistance Exercise via Negative-Eccentric Work (RENEW) in Improving Mobility and Reducing Fatigue and/or Weakness in Elderly Cancer Survivors	UUMC-R21CA114523	Supportive care	60 and over	NCI	No phase specified
Pilot, Randomized Study of Mindfulness Relaxation Versus Relaxing Music Versus Standard Symptom Management Education in Patients with Newly Diagnosed Solid Tumors Undergoing Chemotherapy	MDA-CCC-0106	Educational/ Counseling/ Training	18 and over	NCI	No phase specified

OCCAM Organizational Chart



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