National Cancer Institute

# NCI CAM News

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The Newsletter of the Office of Cancer Complementary and Alternative Medicine

## Collaboration at top of the agenda at the China-U.S. Symposium on Traditional Chinese Medicine and Cancer

**In this issue:**




*Participants at the 2011 China-U.S. Symposium on Traditional Chinese Medicine*

In July 2011, Dr. Jeffrey D. White, OCCAM Director, and Dr. Libin Jia, who manages many of OCCAM's international research collaborations, attended the 2011 China-U.S. Symposium on Traditional Chinese Medicine (TCM) and Cancer in Beijing, China. The theme of this meeting was "Confluence and Innovation—Building a Collaborative Bridge between China and the United States on TCM."

Although this meeting was suggested by Hongsheng Lin, the Director of the Oncology Department at Guang'anmen Hospital, Beijing, China in the fall of 2010, its origins date back to 2006, when OCCAM hosted the conference, "Traditional Chinese Medicine and Cancer Research: Fostering Collaborations; Advancing the Science." The OCCAM conference brought together researchers from around the world with common interests so they could learn about one another's work. As a result of this conference, research collaborations were initiated which are still ongoing, including one between the National Cancer Institute and Guang' anmen Hospital.

OCCAM worked with the Guang'anmen Hospital staff as well as Dr. Julie Schneider, now with NCI's Center for Global Cancer Research, and Dr. Elizabeth Yuan, the U.S. Health and Human Services Health Attaché in China, in making the China-United States Symposium a reality. "The meeting was about collaboration between the United States and China on cancer research. We [OCCAM] support several activities which involve such collaborations and we were able to recommend researchers involved in those projects. In addition, we have experience both hosting collaborative projects here in the intramural program at NCI as well as the grant-funded extramural activities," said Dr. White.

The collaborative spirit of the meeting was evident even in the early stages of planning. "There were several long-distance conference calls and email exchanges," noted Dr. White. Dr. Jia helped to coordinate with Chinese

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

*from previous page*

staff from the Oncology Department at Guang'anmen Hospital. The U.S. Department of Health and Human Services provided funds to support travel for U.S. scientists and the State Administration of TCM of the People's Republic of China also provided support for several other U.S. and Chinese scientists to come to the meeting.

The presentations during the Symposium focused on international research collaborations between the United States and China, as well as the development of anti-cancer therapies using TCM. Dr. White gave an overview of the NCI CAM research activities and described botanical cancer research in the United States. Dr. Jia detailed United States-China collaborative research projects supported by NCI/OCCAM.

During the meeting, "there was a lot of interaction and exchange between Chinese and U.S. researchers with regard to research ideas and potential collaborations," said Dr. White. For example, there is one new research project that will be started at NCI — a post-doctoral researcher from Guang'anmen Hospital will be working with Dr. Nancy Colburn in the Center for Cancer Research's Laboratory of Cancer Prevention, examining the effects of certain herbal approaches in preventing colorectal cancer.

There were also discussions of potential collaborations in funding research between the State Administration for TCM, the Chinese Ministry of Science and Technology, and NIH. "We're continuing to discuss with them possibilities for working together on such co-funding," added Dr. White.

Although there are cancer-CAM meetings throughout the year, there are few opportunities for people from different countries with such specialized interests to meet in a concentrated, TCM-specific way, observed Dr. White. In addition, "there is not much awareness here of results of Chinese research being conducted on TCM — in part because many research results are published in Chinese-language journals."

According to Dr. White, "There are not many venues for this kind of dialogue. That's the significance of meetings like this: they help to raise awareness, increase the kind of dialogue at levels that could lead to concrete research activity, and build relationships that may generate real research products." He added, "This meeting may lead to the development of other forums that can expand on these ideas."

Dr. White notes that OCCAM "would be interested in finding ways to open up more dialogue and interactions with many more organizations and work with other institutes in China, and elsewhere, that are conducting research relevant to the use of traditional medical systems for the treatment of cancer patients."

"If opportunities like that become available, we would be glad to explore them," he concludes.

## CRADA mechanism allows businesses and NIH to work together

Private industry, academia, and government agencies have much to gain from one another when it comes to the advancement of science. Expertise lies in many areas of science and the advancement of cancer research can come from many locations.

Cooperative Research and Development Agreements (CRADAs) are mechanisms created under the Federal Technology Transfer Act of 1986 for the purpose of facilitating Government-Industry collaborations and technology transfer. CRADAs allow government facilities, intellectual property, and expertise to be available for collaborative interactions with outside industry or academic institutions to further develop scientific and technological knowledge into useful, marketable products. While serving the larger mission of NIH, members of the NIH community can join with researchers in private industry to promote technological competitiveness, transfer the findings of scientific research into the marketplace and public sector, and help advance the development and commercialization of new health care pharmaceuticals and products. Furthermore, CRADAs are authorized only with collaborators (e.g., non-government agencies, academia, private sector) who will make significant intellectual contributions to the research project undertaken or will contribute essential research materials or technical resources not otherwise available to NIH. Taking advantage of this research mechanism, NCI has launched discussions for a CRADA partnership with colleagues in China investigating the potential anticancer effects of an herbal mixture derived from traditional Chinese medicine.

Researchers in NCI's Laboratory of Molecular Immunoregulation (LMI), in the Center for Cancer Research, have collaborated over the past year and a half with clinician scientists from the Oncology Department at the Guang'anmen Hospital with the China Academy of Chinese Medical Sciences on the anticancer and pain-relieving affects of an herbal medicine known as KuShen Injection (KI). KI is an herbal mixture that is used in Chinese hospitals either alone or in combination with chemotherapy for

pain control and inhibition of tumor growth. KI is extracted from two herbs- Kushen *(Sophora flavescens)* and Baitulung *(Rhizoma Smilacis Glabrae*).

OCCAM has contributed support for preclinical research being performed at NCI with KuShen Injection.* Dr. O. M. Zack Howard, staff scientist at LMI, is performing preclinical research using KI on mouse models. The model used is based on injecting mouse sarcoma cells near the common sciatic nerve. As the tumor grows, it presses on the nerve and increases temperature sensitivity, which mimics cancer nerve pain. Temperature sensitivity was determined by measuring the length of time (in seconds) the mouse kept its paw on a 55°C hot plate. The longer the paw remained on the hot plate, the less temperature-sensitive it was. Compounds known to reduce pain, Tylenol and Buprenex, reduced temperature sensitivity (that is, the mouse left its paw on the plate longer) but these compounds did not affect tumor growth (as measured by tumor weight). KI was tested at two different doses (25 mg/kg and 50 mg/kg) by intraperitoneal injection into the mouse and compared to 4 other groups: 1) a control mouse; 2) a sarcoma model mouse without treatment; 3) 100 ng/mouse dose of CpG ODN (Cytosine phosphodiester Guanine Oligodeoxynucleotides) used as a negative control, since it could activate neuron calcium flux to increase pain; and 4) a 300 ng/mouse Suppressive ODN (SupODN) group which blocks capsaicin-induced calcium flux, and could decrease pain. Results showed that KI reduced temperature sensitivity at both doses, and reduced tumor growth at the 50mg/kg dose. The SupODN group exhibited reduced temperature sensitivity and was the only other group to show significant results.

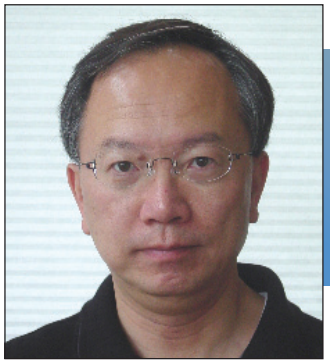
*The Kushen (Sophora flavescens) cultivation field in Changzhi, Shanxi Province of China*

A CRADA is under development with Guang'anmen Hospital to support further investigations. The project is intended to research the *in vitro* and non-human *in vivo* mechanism of action and dosing regimen for KI. To achieve these goals, the collaborators will study the ability of the injection to modulate cancer-induced temperature sensitivity/pain, tumor growth and metastases, and immune function in certain murine (mouse) tumor models.

While at the 2011 China-US Symposium on Traditional Chinese Medicine and Cancer, Drs. Libin Jia (OCCAM/NCI) and Zack Howard traveled to the KI manufacturing facility and the *Sophora flavescens* cultivation fields and spoke with scientists and manufacturers about the Good Manufacturing Process of KI. While at Zhendong Group, Dr. Howard had the chance to present her results to the producers of KI. Also, Dr. Jia was able to procure KI samples to bring back to NCI for potential use in further studies.

*A statue at the Zhendong Group manufacturing facility represents an ancient Chinese story about concocting medicine for a healthy, long life.*

*Project Number: ZIABC010707



*Dr. Shaw T. Chen*

## A Conversation with:

### Dr. Shaw T. Chen, MD, PhD
Botanical Drug Review Team, The Center for Drug Evaluation and Research (CDER), FDA

**What are botanical drugs?**

A botanical drug product is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans.

- A botanical drug product consists of vegetable materials, which may include plant materials, algae, macroscopic fungi, or combinations thereof.
- A botanical drug product may be available as (but not limited to) a solution (e.g., tea), powder, tablet, capsule, elixir, topical, or injection.
- Botanical drug products often have unique features, for example, complex mixtures, lack of a distinct active ingredient, and substantial prior human use. Fermentation products and highly purified or chemically modified botanical substances are not considered botanical drug products.

A botanical drug's special features require consideration and adjustment during the Food and Drug Administration (FDA) review process. The Center for Drug Evaluation and Research (CDER) issued a *Guidance for Industry-Botanical Drug Products (PDF)*[1] [Botanical Guidance] to take into consideration these features and to facilitate development of new therapies from botanical sources. The Botanical Guidance applies to only botanical products intended to be developed and used as drugs.

Up to this date, one botanical product fulfills the Botanical Guidance definition of a botanical drug product, and has been approved for marketing as a prescription drug (sinecatechins, Veregen®). There are some botanical drugs, including cascara, psyllium, and senna, that are included in the over-the-counter (OTC) drug review. For a botanical drug substance to be included in an OTC monograph there must be published data establishing a general recognition of safety and effectiveness, including the results of adequate and well-controlled clinical studies. The FDA regulates OTC drugs based on monographs which have been developed as a kind of "recipe book" covering acceptable ingredients, doses, formulations, and labeling required for OTC's. More information on OTC drugs are available at ***http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm093471.htm***

**What is the role of the Botanical Review Team in the US FDA?**

CDER established the Botanical Review Team (BRT) to provide additional scientific expertise on botanical issues to CDER and the reviewing staff and to ensure consistent interpretation and implementation of the Botanical Guidance.

**Please provide an overview of the Botanical Review Team and your role as Leader.**

The Botanical Team in CDER includes a Team Leader and a Pharmacognosy Reviewer. The Pharmacognosy reviewer serves as the botanical expert in the FDA and performs primary review of all botanical drug applications. The Team Leader performs secondary review for botanical applications, offers clinical perspectives in the implementation of Botanical Guidance, and consults with CDER leadership when necessary in the interpretation of botanical related policy.

**How did you first get interested in botanical drug products? How has that shaped your career?**

I share with many senior CDER staff their interests in facilitating development of new therapies for unmet medical needs. Many botanical products have been used in alternative medical systems extensively for long periods of time, and some may prove to be useful for serious conditions like cancer. That's why I joined the CDER working group to draft the Botanical Guidance in the mid- 1990s. I was appointed as the Botanical Team Leader in 2000 and charged with the assignment to set up the brand new Botanical Program in CDER. Although the pace of botanical new drug development is disappointedly slow, I've very much enjoyed helping investigators and companies in their research effort on botanical products.

**When researchers want to study the effects of a botanical drug, in most cases they have to apply for an Investigational New Drug (IND) application. Can you speak about the IND application process, particularly regarding any unique aspects of botanical drug applications?**

In general, the IND process for botanical products is no different from that of non-botanical drugs (please see detailed instruction on CDER website: ***http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/default.htm***). For botanical specific issues, you are referred to the Botanical Guidance at ***http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070491.pdf.***

[1] *http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070491.pdf*

## NCI grantee research shows improvements in quality of life of patients with breast cancer undergoing radiation therapy

Women undergoing radiation therapy for breast cancer can suffer from debilitating side effects that impact their quality of life (QOL). For example, treatments can leave women with fatigue, sleep disturbances, poor mental health, and unable to perform basic tasks of daily living. This isn't the way anyone wants to live, let alone someone battling breast cancer. Time away from treatments should bring solace and rejuvenation, not crippling fatigue.

Dr. Lorenzo Cohen, Director of the Integrative Medicine Program at the MD Anderson Cancer Center in Houston, TX set out to tackle the issue by researching yoga as a potential method for improving women's QOL during cancer treatment. Dr. Cohen has recently been awarded a R01 grant* from the National Cancer Institute to further study incorporating yoga into cancer treatment. The research supported by this grant is just beginning and data from this project are expected in the next few years. However, much of the pilot data supporting the R01 was gathered from an R21** grant Cohen was also awarded. R21 grants support the development of pilot projects or feasibility studies that will support larger-scale creative and innovative research. Cohen presented data from the R21 project at the American Society for Clinical Oncology (ASCO) Annual Meeting in June 2011.

As part of the project, breast cancer patients with stage 0-III disease undergoing radiotherapy were randomly assigned to one of three groups: a yoga group, a stretching group, or a waitlist control group. Patients in both the intervention groups attended sessions 3 days a week throughout their 6-weeks of radiotherapy. Self-reported measures of fatigue, depression, QOL, benefit finding (ability to find meaning in the illness experience), and spirituality were completed and saliva samples and 10 minute recordings of ECGs showing heart activity were collected before treatment, at the end of treatment, and 1, 3, and 6 months after treatment. Results suggested that at the end of radiotherapy, the yoga and stretching groups had statistically significant lower levels of fatigue relative to the waitlist group and the yoga group had better cortisol (a biomarker associated with stress) regulation than did the other two groups. At the 1, 3, and 6 month post-treatment time points, the yoga group had a greater increase in physical functioning and reports of general health than both the stretching and waitlist groups. In addition, 3 and 6 months following radiotherapy, the yoga group reported higher levels of benefit finding than did the other two groups. There were no differences in spirituality or depression between the three groups. The investigators concluded that while stretching improved fatigue and physical functioning somewhat, yoga also produced beneficial changes in fatigue, QOL, and several other markers of stress and heart rate functioning.

Dr. Cohen notes that these findings "show the beneficial effects of yoga relative to both an active control group that engaged in stretching and a waitlist control group. The active control group is important as we now know there is something unique about the yoga program that goes beyond the benefits of simply stretching, which in and of itself was somewhat useful. Our subsequent study will enhance the control group to also include some simple relaxation techniques. At the completion of the phase III clinical trial, if yoga results in better outcomes than a stretching/relaxation group then it needs to be offered as part of the standard of care for women undergoing radiotherapy for breast cancer."

Program Director Ann O'Mara noted, "Fatigue remains one of the most commonly reported symptoms across all cancer types. Thus, these findings will be informative to a wide variety of patients undergoing treatment, with the potential of improving the quality of life of patients who have completed their treatments and are disease free."

* Grant number: 1R01CA138800-01A1
**Grant number: 5R21CA102385-03

## NCI funds largest cancer botanical research grant to study a complex multi-herbal intervention from traditional medical systems for cancer treatment

NCI is committed to multi-project and collaborative research. Bringing several scientists together to collaborate on complex problems is a time honored process and a mutually rewarding opportunity for experts to work together to further scientific discovery.

The P01 Research Program Project Grant mechanism supports integrated, multiproject research studies. Each Program Project application must consist of at least three component projects, which share a common central theme, focus, and/or overall objective. In September 2011, NCI, along with the National Center for Complementary and Alternative Medicine (NCCAM) and the NIH Office of the Director, funded a P01 project* grant to investigate the effectiveness of PHY906 as a modulator of the chemotherapy drug irinotecan in the treatment of patients with metastatic colorectal cancer. PHY906 is an extract of four herbs based on a formula of traditional Chinese medicine (TCM), known as Huang Qin Tang (HQT). HQT is used as a treatment for gastrointestinal ailments, including diarrhea, nausea, and vomiting. Preclinical data** suggests PHY906 can help improve the gastrointestinal side effects of irinotecan while simultaneously increasing the drug's anticancer activity.

The study, titled "Chinese Herbal Medicine as a Novel Paradigm for Cancer Chemotherapy," is led by Principal Investigator (PI) Yung-chi (Tommy) Cheng, Ph.D., of Yale University and the Yale Cancer Center's Developmental Therapeutics Program. He is joined by two other well-established Project leaders, Edward Chu, M.D. of the University of Pittsburgh Medical Center (UPMC), who also serves as Co-PI, and Hongyu Zhao, Ph.D. of the Yale School of Public Health.

The study has three main goals: 1) to confirm in humans that combining PHY906 with irinotecan may result in greater cancer-cell killing abilities of the chemotherapy drug, improve treatment side effects, and increase quality of life for the patients; (2) to explore the potential mechanisms of action of PHY906 by identifying specific molecular factors of the herbal mixture and their by-products; and (3) to develop novel and appropriate statistical and computational modeling methods for use in analyzing data from clinical effectiveness studies of herbal extracts. It is the hope of the scientists that this study may generate new methods for developing herbal or botanical medicines in combination with conventional chemotherapy for the treatment of cancer.

OCCAM Program Officer Dan Xi, Ph.D. stated, "This is the first NCI-funded clinical research Program Project grant studying a complex of multi-herbal mixtures from traditional medical systems (traditional Chinese medicine) for cancer treatment. The outcome of this research could lead to new therapeutic strategies for integration of traditional Chinese medicine with standard chemotherapy. The statistical methods being developed will likely provide useful tools for examining the clinical effects of multi-component natural products and their combination with conventional cancer therapies."

Further information on this project is available online, ***http://projectreporter.nih.gov/project_info_description.cfm?aid=8175586&icde=0***.

*Grant number: 1P01CA154295-01A1

** Lam W, Bussom S, Guan F, Jiang Z, Zhang W, Gullen EA, Liu SH, Cheng YC. The four-herb Chinese medicine PHY906 reduces chemotherapy-induced gastrointestinal toxicity. *Science Translational Medicine*. 2010 Aug 18;2(45):45ra59.

## OCCAM-funded grantee awarded additional funding to research ginger and lung cancer

An OCCAM-managed grant received supplemental funding from the NIH Office of Dietary Supplements (ODS). This collaborative effort is the first time that ODS has jointly co-funded an OCCAM-managed grantee. The Program Officer is Dr. Dan Xi, Ph.D., of OCCAM.

The R21 grant* was awarded to Shengmin Sang, Ph.D., of North Carolina Agricultural and Technical State University. The supplemental funding was provided to the project titled "Ginger Extract: Bioavailability Study and Lung Cancer Preventive Effect." Funding will support continued study on the bioavailability, biotransformation, and metabolic profile of ginger extract and its key constituents. Recent studies** have shown that ginger has antioxidant, anti-inflammatory, and anti-

tumor activities. Results from this study will aid in the development of methods for optimally preparing ginger extract that will be effective in the prevention of lung cancer, as well improve the quality of future clinical trials on chemopreventive effects through the use of standardized extracts. The parent project of this R21 supplement seeks to study the biological activities of ginger extract and its key constituents, [6]-gingerol and [6]-shogaol, and develop a ginger extract with high levels of shogaols that may help prevent lung cancer.

Further information on the project along with information on published results is available in the NIH RePORTER database: ***http://projectreporter.nih.gov/project_info_description.cfm?aid=8148074&icde=10022364.***

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* Grant number: 3R21CA138277-03s1

** Shieh PC, Chen YO, Kuo DH, Chen FA, Tsai ML, Chang IS, Wu H, Sang S, Ho CT, Pan MH. Induction of apoptosis by [8]-shogaol via reactive oxygen species generation, glutathione depletion, and caspase activation in human leukemia cells. *Journal of Agricultural and Food Chemistry*, 2010 Mar 24; 58 (6):3847-54.

Sang S, Hong J, Wu H, Liu J, Yang CS, Pan MH, Badmaev V, Ho CT. Increased growth inhibitory effects on human cancer cells and anti-inflammatory potency of shogaols from Zingiber officinale relative to gingerols. *Journal of Agricultural and Food Chemistry*, 2009 Nov 25; 57 (22):10645-50.

## Going Global: New NCI Center for Global Health aims to promote cancer research and reduce cancer deaths worldwide

It's time to dust off your passport — the National Cancer Institute (NCI) is about to go international with a new center devoted to global health. Announced during NCI Director Dr. Harold Varmus' first Town Hall Meeting, the NCI Center for Global Health (CGH) is a program that will focus on research efforts that may directly impact global cancer health. The Center will encourage collaborations between researchers and public health professionals in the United States and around the world, particularly in developing countries. In September, Dr. Edward L. Trimble, MD, MPH, was named Director of the Center.

Drs. Varmus and Trimble recently published a commentary[1] in the journal *Science Translational Medicine* about the new center. While global health initiatives in developing countries have been directed at topics such as infectious diseases and maternal and infant mortality, cancer deaths in those countries have been on the rise. Varmus and Trimble noted that approximately 7.6 million people died from cancer worldwide in 2008, but "by 2030, the number of cancer deaths may rise as high as 13.2 million, with 69 percent occurring in developing countries."

Varmus and Trimble wrote that NCI will not directly provide cancer care as part of the Center's goals, but because NCI is a research agency, it stands in a position to advance research related to global cancer care. They also observed that there is some overlap between the CGH and the new "Provocative Questions" project (for more information about the Provocative Questions project, see Page 10). For example, one of the questions directly related to global health issues asks why changes in cancer incidence occur when people move from one region to another.

For more information about the NCI Center for Global Health visit the Center's website, ***http://www.cancer.gov/aboutnci/globalhealth.***

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[1] Varmus H and Trimble EL. Integrating cancer control into global health. *Science Translational Medicine*. 2011; 3(101):101cm28. ***http://www.ncbi.nlm.nih.gov/pubmed/21937755***

## Funding Opportunities

### New funding opportunity: SBIR Phase IIB Bridge Awards to Accelerate the Development of Cancer Therapeutics, Imaging Technologies, Interventional Devices, Diagnostics, and Prognostics Toward Commercialization (R44)

The National Cancer Institute (NCI) has announced a new funding opportunity that aims to accelerate development of novel cancer-related commercial products and technologies. This announcement is soliciting applications from small business concerns seeking additional funding to support projects previously funded by NIH Small Business Innovation Research (SBIR) Phase II awards. This new opportunity was created to foster later stage research and development and help applicants reach subsequent milestones required for commercialization. In order to accomplish this goal, the award strongly encourages partnerships between SBIR Phase II awardees and third-party investors and/or strategic partners.

Proposed projects must be applicable to one of the following areas:

- Cancer Therapeutics
- Cancer Imaging Technologies, Interventional Devices, and *In Vivo* Diagnostics
- *In Vitro* and *Ex Vivo* Cancer Diagnostics and Prognostics

View the complete funding announcement here: ***http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-12-001.html*** and further questions can be directed to NCI Scientific/Research Contact Andrew J. Kurtz, Ph.D., kurtza@mail.nih.gov.

### New Funding Opportunity: Advancing Novel Science in Women's Health Research (ANSWER) (R21)

A new funding opportunity announcement (FOA) has become available sponsoring innovative and interdisciplinary research relating to women's health and sex/gender differences. The Office of Research on Women's Health, along with several participating Institutes and Centers, including the National Cancer Institute, initially released this funding opportunity in July, 2010. The FOA will use the NIH Exploratory/Developmental (R21) award mechanism, and direct costs are limited to $275,000 over a two-year period.

Some areas of interest include: diseases and conditions that affect women; prevention, treatment, and treatment outcomes; and health disparities/differences and diversity. Researchers conducting interdisciplinary research investigating how sex and gender factors affect women's health are encouraged to apply.

The deadline to submit a new application is October 16, 2012 and the deadline for resubmission applications is November 16, 2012.

For more details and information on how to apply, go to ***http://grants.nih.gov/grants/guide/pa-files/PAS-10-226.html*** and/or contact the FOA's NCI Research Contact, Karen Parker, Ph.D, at klparker@mail.nih.gov.

## Research Resources

### Stay on top of grant application submission changes

Researchers- both new and veteran- know that submitting grant applications to NIH is exhilarating and nerve-racking, but this activity also keeps them on their toes because of changing submission guidelines. Researchers interested in submitting grant applications to NIH are always encouraged to read all application guides thoroughly to get the latest information on page limits, deadlines, and new initiatives.

The Office of Extramural Research (OER) hosts an informative website on the myriad of grants, guides, and timelines that make up the research funding activities of NIH. One of the most comprehensive guides is the SF424(R&R) Application and Electronic Submission Information guide. The SF424 application is the Standard Form for Research and Related Grant applications. The guide is available on the OER website: ***http://grants.nih.gov/grants/funding/424/index.htm***

Recently, the Research Strategy section of a majority of grant types has been shortened to 12 pages. Since this

new rule can be seen as a challenge or an opportunity to researchers, the National Institute of Allergies and Infectious Diseases (NIAID) has created a web page to help guide potential applicants. Four excellent grant applications have been made available for viewing to help researchers submit competitive grant applications in the shorter format. While the topic areas are not about cancer, the sample applications exhibit a clear grasp of the new guidelines and these examples aim to help applicants create similarly appropriate submissions.

Sample R01 summary statements and applications are available on the NIAID website: ***http://www.niaid.nih.gov/researchfunding/grant/pages/appsamples.aspx***. Applications are copyrighted and may be used for nonprofit educational purposes only.

Other helpful links for grant submission are available to potential researchers and are listed below.

Remember to check early and often!

- Standard Due Dates: ***http://grants.nih.gov/grants/funding/submissionschedule.htm***
- Page Limits: ***http://grants.nih.gov/grants/forms_page_limits.htm***
- Frequently Asked Questions about Grants: ***http://grants.nih.gov/grants/ElectronicReceipt/faq.htm***

## Helpful HINTS: Health information seeking data available to all researchers

Are you interested in how people find, use, and understand health information? Even if your research is not traditionally in this field, you may be interested to learn more about how patients, caregivers, and the general public interact with diverse sets of health data. Broadening your scope in this way could potentially impact your own work or how scientific findings are communicated to the public.

The Health Information National Trends Survey (HINTS) is a biennial, cross-sectional, nationally representative sample of American adults that measures how people access and use health information, information technology, and the degree to which people are engaged in healthy behaviors. Additionally, several items in the HINTS dataset are specifically focused on cancer prevention and control and cover several cancer types. For example, along with questions on information seeking, participants are asked specific cancer-related behavior questions such as "Have you ever had a mammogram?" and "Have you ever had a colonoscopy?" The answers may help determine the relevance of conducting specific projects in cancer research.

All data from the HINTS survey are available free on the HINTS website for public use and the website has recently been redesigned to allow for better ease of use and navigation. Visit the HINTS website (***http://hints.cancer.gov/***) for more information on how you can use this comprehensive and illuminating data in your own research.

Website updates include the ability to:

- Search HINTS by topic area and quickly access data, reports, and materials on all HINTS topics, ranging from patient-provider communication to cancer prevention.
- View HINTS questions at the item-level to find data displayed in a user-friendly format with associated charts and publications.
- See a list of citations for all the scientific articles published using a given HINTS item by clicking the "view related articles" link under each item's data chart.


## Summer school: Registration now open for NCI Summer Curriculum in Cancer Prevention 2012

Scientists, clinicians, and health care professionals interested in learning more about cancer prevention and control are urged to register for an exciting educational opportunity.

The National Cancer Institute (NCI) Cancer Prevention Fellowship will host two separate courses as part of the NCI Summer Curriculum in Cancer Prevention. "The Principles and Practice of Cancer Prevention and Control" is a 4-week course designed to provide participants a broad-based perspective on the current state of the science in cancer prevention. The course will be held July 9- August 3, 2012 in Rockville, Maryland with lectures from 8:30am-2:20pm.

The second course, "Molecular Prevention," is a 1-week course targeted in scope to give participants a

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stronger background in the molecular biology and genetics of cancer. Topics covered will include molecular epidemiology, chemoprevention, biomarkers, and translational research. This course will be held from August 6-August 10, 2012, in Rockville, Maryland, from 8:30am-2:30pm.

Visit the Cancer Prevention fellowship website, ***https://cpfp.cancer.gov/summer/summer.php***, for more detailed information and registration instructions.

The registration deadline is February 15, 2012 for international applicants, and March 15, 2012 for domestic (U.S.) applicants.

## NCI Provocative Questions Project hopes tough questions lead to exciting answers

Scientists are problem solvers—they try to cure diseases and figure out why cells behave in certain ways. However, the questions they ask are often just as important as the answers. Although crucial questions are asked often in the halls of the National Cancer Institute (NCI), the "Provocative Questions" Project was initiated to identify some of the most puzzling problems in cancer research and to help support creative and innovative ways to tackle those problems.

The 24 Provocative Questions are the product of a series of workshops that were held in 2010 and 2011, as well as suggestions submitted online. This was a collaborative effort, with not only researchers participating, but also advocacy groups, healthcare professionals, and members of Congress providing input.

Examples of the Provocative Questions include:

- What environmental factors change the risk of various cancers when people move from one geographic region to another?
- Since current methods to assess potential cancer treatments are cumbersome, expensive, and often inaccurate, can we develop other methods to rapidly test interventions for cancer treatment or prevention?
- Given the evidence that some drugs commonly and chronically used for other indications, such as an anti-inflammatory drug, can protect against cancer incidence and mortality, can we determine the mechanism by which any of these drugs work?

Information about the grant recipients and any provocative answers that result from this project will be featured in future editions of *NCI CAM News*.

All of the 24 questions and a message from NCI Director Dr. Harold Varmus are available at ***http://provocativequestions.nci.nih.gov/?cid=WTq_occam.***

# Research Highlights

## Vitamin E Supplements Tied to Increased Risk of Prostate Cancer

Reprinted from the *NCI Cancer Bulletin*, vol 8/ no. 20, October 18, 2011
***http://www.cancer.gov/ncicancerbulletin/101811/page4***

Men in a large prostate cancer prevention trial who took vitamin E supplements had a higher risk of developing the disease than men who took a placebo, according to extended follow-up of trial participants. Dr. Eric Klein of the Cleveland Clinic and his colleagues reported the finding October 12 in *JAMA*.

The results are from the Selenium and Vitamin E Cancer Prevention Trial (SELECT), which included more than 35,000 relatively healthy men at average risk for prostate cancer. The trial was stopped early in 2008, when a planned interim analysis indicated that vitamin E and selenium—whether alone or in combination—were unlikely to prevent prostate cancer.

At the time, participants were told to stop taking the supplements, and researchers continued to follow the men. The interim analysis also suggested that vitamin E might be associated with an increased risk of prostate cancer, though the result was not statistically significant at the time.

But with additional follow-up, the researchers detected a 17 percent increased risk of prostate cancer among men who took 400 international units of vitamin E per day (IU/d) compared with men who took a placebo, a difference that was statistically significant.

**The Evidence on Vitamin E**

In reporting their results, the researchers noted that, by and large, vitamin E has failed to show a benefit for preventing a number of diseases. "The totality of the evidence shows that vitamin E does not prevent other diseases, and we now have evidence that it may increase the risk of prostate cancer," said Dr. Klein.

Consumers need to be skeptical of health claims for over-the-counter products when strong evidence of a benefit demonstrated by clinical trials is lacking, the study authors stressed.

"Studies like SELECT make us take a step back and realize that any pharmaceutical agent we give has the potential for benefit and, as remote as it may be, also the potential for harm," said co-author Dr. J. Michael Gaziano of Brigham and Women's Hospital.

"That's why we engage in these large-scale randomized studies, especially for agents that are in widespread use," he added.

More than half of all men over age 60 in the United States are taking supplements containing vitamin E, and 23 percent are taking the dose used in SELECT, the study authors noted. Therefore, the finding of an increased risk of prostate cancer has "substantial implications."

The increased risk of prostate cancer emerged only after the men had stopped taking the supplements. "These agents seem to have longer-lasting effects," said Dr. Klein, noting that researchers who design clinical trials need to consider this possibility.

"This study is yet another cautionary tale about the potential risks of high-dose nutritional supplements," said Dr. JoAnn Manson of Harvard Medical School, who was not involved in the research. "We've seen this before, and it shows why it is so important to have these randomized trials."

In the early 1980s, she noted, beta-carotene was widely regarded as "a magic bullet for good health" until clinical trials showed that it was harmful to those at elevated risk for lung cancer, particularly smokers.

Another large randomized trial, the Physicians Health Study II, linked vitamin E to an increased risk of bleeding-related strokes.

Although deficiencies in certain nutrients can cause health problems, high doses of supplements may have health risks that outweigh the benefits, noted Dr. Manson, who is leading a large randomized trial of vitamin D and omega-3 fatty acids.

"With many nutrients, there is an optimal range of intake and blood levels, and more is not necessarily better," she added.

**Most Prostate Cancers Found Early**

More than 400 sites in the United States, Canada, and Puerto Rico participated in SELECT, which was coordinated by SWOG, a federally funded cancer research cooperative group. Doctors monitored the participants according to contemporary community standards of screening and biopsy. This ensured that, as in general practice, some men had PSA tests and others did not.

During the 7 years of the trial (5.5 years of taking supplements and 1.5 years of not taking them), doctors diagnosed 65 cases of prostate cancer for every 1,000 men in the placebo group. In comparison, doctors diagnosed 76 cases for every 1,000 men in the vitamin E-only group.

Most of the detected cancers were found early, and therefore "the risk of a man dying from the disease is not very great," said co-author Dr. Ian Thompson of the University of Texas Health Science Center at San Antonio.

He pointed out, however, that most men diagnosed with prostate cancer in the United States end up being treated with surgery or radiation, which can impair a man's sexual and urinary functions.

"If a man is taking vitamin E, he should either stop taking it or talk to his doctor about a reason he should take it," Dr. Thompson said. "And I can't think of a reason he should take it."

It is not clear why SELECT showed an increased risk for prostate cancer when earlier studies that led to the randomized trial showed that vitamin E protected against the disease. The study populations were different, however, and the original results may have been chance findings, the researchers said.

In fact, the prospective randomized trial, the gold standard in medical evidence, was launched precisely because the earlier studies were not definitive and needed to be confirmed.

The SELECT investigators have biological samples from the participants, and they intend to explore questions raised by the trial. For instance, men who took both supplements did not have an increased cancer risk, so there may have been an interaction between selenium and vitamin E.

The current results are an example of "rigorous scientific exploration," noted Dr. Howard Parnes of NCI's Division of Cancer Prevention, another co-author. "The idea of science is to put your observations to the test and see if they are correct," he said. "You often learn the most from the studies that overturn conventional wisdom."

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## Soy isoflavones may help improve radiation therapy used for lung cancer

Lung cancer is the leading cause of cancer deaths in the United States. The majority of lung cancers are non-small cell lung carcinomas (NSCLC) and patients with NSCLC commonly receive chemotherapy in combination with radiation treatment. However, the radiation can damage surrounding healthy lung tissue and can result in severe lung damage leading to breathing problems and a decreased quality of life for the patient. Research studies have suggested that soy isoflavones (the active components in soy) may help to increase the effectiveness of radiation therapy and reduce some of the side effects. In a recently published, NCI-funded study*, Dr. Gilda Hillman and her colleagues in the Department of Radiation Oncology, Wayne State University School of Medicine, investigated the effects of soy isoflavones on radiation therapy in a mouse model of lung cancer.

In this experiment, mice were injected with lung cancer cells. Then, each mouse was assigned into one of four groups: a control group (no treatment), radiation only, daily soy isoflavone supplement, or both radiation treatment and the soy supplement. At the end of the experiment, the mice's lungs were examined.

The mice that received combination radiation treatment and soy supplements exhibited much less radiation-induced damage to healthy lung tissue compared to mice that received only radiation therapy. In addition, there was more damage to the lung tumors in mice that received combination treatment than in mice who received only radiation, soy, or no treatment at all. Previous work by Dr. Hillman's team has also shown that the isoflavone genistein is able to enhance the cancer-killing effect of radiation therapy in animals with prostate and kidney tumors.

To read more about this research finding, go to ***http://www.ncbi.nlm.nih.gov/pubmed/22079530.***

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* Grant #R21CA155518

## Read all about it! CAM research highlighted at NCI-designated Cancer Centers

The NCI Office of Media Relations works tirelessly to keep track of the multiple NCI-designated Cancer Centers, academic centers, grantees, and principal investigators that are researching NCI-supported science around the United States. Stories and press releases come out daily describing exciting advancements in cancer treatment and prevention, and NCI strives to provide this information to the public as quickly and accurately as possible.

In recent months, several scientific findings have been published relating to complementary and alternative medicine (CAM). Cancer CAM related stories from the Office of Media Relations are organized on the OCCAM website in the NCI CAM news section (***http://www.cancer.gov/cam/news_stories.html***). All of the NCI Cancer Center News articles are available on the Media Relations News Center website (***http://www.cancer.gov/newscenter***).

### Recent highlights of cancer CAM research include:

#### University of Michigan Study Finds Ginger Root Supplement Reduced Colon Inflammation Markers

Ginger supplements have been shown to reduce markers of colon inflammation in a select group of patients, suggesting that the supplement may have potential as a colon cancer preventative agent, according to a study performed at the University of Michigan Medical School.
(***http://www.cancer.gov/newscenter/pressreleases/2011/MichiganGingerRootStudy***)
*NCI Cancer Center News*, October 12, 2011

#### UCLA study finds primary component of turmeric kicks off cancer-killing mechanisms in human saliva

Curcumin, a component of the spice turmeric, has been found to suppress a cell signaling pathway that drives the growth of head and neck cancer,

according to a study performed at the UCLA Jonsson Comprehensive Cancer Center.
(***http://www.cancer.gov/newscenter/pressreleases/2011/UCLAStudyTurmeric***)
*NCI Cancer Center News*, September 14, 2011

### Mayo Clinic study finds flaxseed no help for hot flashes during breast cancer or menopause

A randomized, placebo-controlled study of 188 women in 2009 found no statistically significant difference in hot flashes between woman taking flaxseed and those taking a placebo. Previous research in 2007 suggested that consuming 40 grams of crushed flaxseed daily might help manage hot flashes.
(***http://www.cancer.gov/newscenter/pressreleases/2011/MayoClinicFlaxseed***)
*NCI Cancer Center News*, September 9, 2011.

## CAM Information

### New database makes it simple to search for dietary supplements research

Searching for information specifically about dietary supplements can be arduous. The Office of Dietary Supplements (ODS) at NIH has made the task easier thanks to the new PubMed Dietary Supplement Subset.

The PubMed Supplement is a partnership between ODS and the National Library of Medicine (NLM) to create a dietary supplement subset of NLM's PubMed scholarly biomedical journal search database. PubMed (***http://www.pubmed.com***) includes links to abstracts and full text articles and other related resources.

This subset will limit searches to articles related to dietary supplement research including research on vitamins, minerals, phytochemicals, and botanical and herbal supplements in human nutrition and animal models.

This database replaces a previous resource, The International Bibliographic Information on Dietary Supplements (IBIDS), which was a collaboration between ODS and the US Department of Agriculture's National Agricultural Library. The replacement occurred to create a more user friendly and comprehensive database. While the majority of citations in the IBIDS originally came from PubMed, ODS worked with NLM to create an even more comprehensive search strategy to better limit searches to dietary supplement-related citations, resulting in the PubMed Dietary Supplement Subset.

For more information about this resource and guidance on sample searches and search strategies visit the ODS web page: ***http://ods.od.nih.gov/Research/PubMed_Dietary_Supplement_Subset.aspx.***

### Sign-up for OCCAM's Listserv

Stay up-to-date on the latest cancer CAM news at NCI with OCCAM's listserv, *OCCAM Announcements*. As a listserv subscriber, you will receive a monthly email about upcoming workshops and lectures, new funding opportunities, publications, and other resources. To subscribe, simply visit OCCAM's web site: ***http://www.cancer.gov/cam/news_listserv.html.***

## Meetings

### OCCAM leads workshop at the Eighth International Conference of the Society for Integrative Oncology

For the past eight years, national and international researchers with an interest in integrative oncology have gathered to present the latest research in this burgeoning field. The Society for Integrative Oncology (SIO) held its Eighth International Conference in Cleveland, OH, on November 10-12, 2011. This year's conference included over 500 attendees, and 3 days of oral and poster presentations. The conference theme of "Innovating Integrative Oncology: New Science, New Solutions" spoke to the wide array of attendees, including researchers, funding agencies, health care professionals, patients, and advocates. SIO is a non-profit professional society committed to the research and application of complementary therapies and botanicals for cancer treatment and recovery.

This year's keynote speaker was National Institutes of Health (NIH) Director Francis S. Collins, M.D, Ph.D. His talk, "Seeking Out the Most Effective Interventions for Cancer Prevention and Treatment," focused on what NIH and NCI are currently funding in the

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field of integrative cancer treatment and prevention, along with a look at the NCI Cancer Genome Atlas (***http://cancergenome.nih.gov/***). Dr. Collins emphasized NIH's commitment to the field of integrative oncology and encouraged researchers to forge ahead with their work in the face of shrinking budgets.

OCCAM presented a 90-minute workshop, "One-on-One with the National Cancer Institute Office of Cancer Complementary and Alternative Medicine." OCCAM staff Oluwadamilola "Dami" Olaku, M.D., Elizabeth Austin, M.S., Libin Jia, M.D., and Dan Xi, Ph.D. participated on the panel. Each panelist represented one of OCCAM's main program areas and presented a brief talk on their respective program and recent projects underway at the Institute. The session was intended for attendees interested in funding opportunities from NCI, in learning more about how to submit cases to the NCI Best Case Series Program, and for those seeking information about communication and international activities originating from OCCAM. OCCAM staff was also available throughout the conference for more in-depth one-on-one conversations at the OCCAM exhibit booth throughout the 3-day conference.

Communications and Outreach Program Coordinator Elizabeth Austin, M.S., who moderated the OCCAM workshop, stated, "The workshop gave the audience a basic overview of our office and programs. Each program area was able to present our key initiatives and then sit back and let the audience dive into their areas of interest through their questions. We were available to set up meetings during the conference with attendees and provide detailed feedback to questions at the end of our session and throughout the conference. It's our hope that by attending prominent CAM or cancer conferences we are better able to interact with researchers, on a one-on-one level, and share information about the CAM funding available from NCI and the diverse ways NCI is supporting cancer CAM research."

*SIO attendees gather for a presentation*

Dr. Libin Jia, of OCCAM, also moderated a panel of oral presentations titled, "Addressing Side Effects of Conventional Therapies." Dr. Jia noted that presentations in his session covered a wide range of topics related to treating chemotherapy and radiation side effects with botanical and herbal products, including mushrooms and "miracle fruit" (the African fruit Synsepalum dulcificuma), among others. "Since side effects from chemotherapy can negatively affect quality of life of many cancer patients, finding therapies to ease or improve these side effects becomes an important issue for clinical practice. Even though the clinical trials of many of the therapies presented are still in early phases, the primary positive outcomes are encouraging," said Dr. Jia.

The Eighth International Conference of Society for Integrative Oncology was funded in part by a R13 conference grant from the National Cancer Institute (1R13CA144223-01A1), and further information about the conference is available on the Society for Integrative Oncology website (***http://www.integrativeonc.org***).

## Two OCCAM fellows present original research at the American Public Health Association Annual Meeting

One of the most diverse and well-rounded public health meetings in the United States, the 139th Annual Meeting and Exposition of the American Public Health Association, drew crowds of over 13,000 to Washington, DC. National and international health care professionals, researchers, students, and interested members of the public gather each year to present current research findings in public health.

This year, two OCCAM fellows, Miriam Al-Keliddar, M.P.H. and Jeans Santana, B.A., presented their original OCCAM-supported research as part of the Alternative and Complementary Health Practices, Special Primary Interest Group session. Supported by their OCCAM mentors and other research experts, Ms. Al-Keliddar and Mr. Santana diligently researched and assembled their presentations to highlight their findings, as well as support the mission of OCCAM.

Ms. Al-Keliddar works with the Extramural Research Program at OCCAM and gave an oral presentation about the "Use of complementary and alternative medicine during active surveillance among prostate cancer patients." Ms. Al-Keliddar states, "Active surveillance is a form of expectant management that can be used by men with low-grade, localized,

asymptomatic disease, and consists of regular monitoring of disease progression through PSA (a biomarker of prostate cancer) tests and digital rectal exams, under the direction of an oncologist. Complementary and alternative medicine (CAM) use, such as soy or lycopene supplementation, may extend this asymptomatic period, delaying the necessity of treatment and its possible side effects." Methods for this research included a literature review of studies that focused on use and effectiveness of CAM during active surveillance among patients with prostate cancer (PC). Results revealed that genistein, a phytoestrogen and one of the active ingredients in soy, may reduce PSA levels and lengthen doubling time (a possible indicator of PC progression). Lycopene (an antioxidant found in tomatoes) and curcumin (a component of the Asian spice turmeric) have also been shown to lower PSA levels and possibly prevent the progression of PC. While the initial research is promising, some reviewed studies were inconclusive or showed no difference in PSA levels. Further studies are needed to maximize statistical power, better understand how various doses can affect biomarkers of PC, and gain a clearer view of efficacy.

Ms. Al-Keliddar will continue her research in this area while at OCCAM, and she will also investigate disparities in CAM use among PC patients and the potential utility of certain CAM approaches in patients with oral cancers. Ms. Al Keliddar hopes to put her experience at OCCAM to work in a career in dentistry, and has honed her research and scientific skills in the past two years to begin her journey to dental school. As for her oral presentation at APHA, Ms. Al-Keliddar notes, "The presentation gave me the opportunity to work on my public speaking skills and test my ability to make scientific research relatable to people from many different disciplines."

Mr. Santana works with the Case Review and Intramural Science Program at OCCAM and his research has focused on CAM use among Hispanics, as well as disparities in CAM use. His poster presentation, titled "Complementary and alternative medicine use by Hispanic cancer patients and the impact of acculturation: National Health Interview Survey 2007," described the prevalence of CAM use among U.S.- and foreign-born Hispanic adults diagnosed with cancer and analyzed how acculturation (the cultural modification of an individual or group in response to contact with another culture) affects CAM use. Discussions of limitations of the dataset and strategies were also included on the poster. Data from 129 Hispanic cancer patients from the 2007 National Health Interview Survey (NHIS) were analyzed to learn about CAM use. Results showed that Hispanics with cancer had a higher percentage use of manipulative modalities (including massage therapy) (16.3%), as compared to other modalities such as mind/body (for example, meditation) (9.3%) and biological (such as herbs) (1.6%). Results concluded that CAM use among Hispanic cancer patients is relatively low. The effect acculturation has on CAM-use patterns for foreign-born Hispanics was undeterminable due to small sample size (n=129). "The Hispanic community is quickly growing," Mr. Santana noted, "and they [Hispanics] are heterogeneous, descending from varying cultural histories and beliefs. Shedding light on CAM-use differences and similarities of these individuals will better equip health care providers who consult with Hispanic cancer patients."

During his time at OCCAM, Mr. Santana has assisted with the NCI Best Case Series (BCS) Protocol performing case report reviews and working with NCI BCS staff to determine the merit for prospective research of alternative therapies. Mr. Santana will be attending medical school in the fall, with current plans to focus on Latino and global health. "Hispanics aren't the only population with challenges, thus I think it will be to my benefit to be as culturally competent as possible once I begin to treat a diverse set of patients," Mr. Santana added.

Further information about the research presented by OCCAM at APHA is available by contacting the office at ncioccam1-r@mail.nih.gov.

## OCCAM Director Invited to Speak at the International Symposium on Malignant Mesothelioma

OCCAM Director Dr. Jeffrey D. White was invited to speak at the International Symposium on Malignant Mesothelioma 2011 meeting held on June 24, 2011 in Washington, DC. This event was sponsored by the Mesothelioma Applied Research Foundation, a nonprofit collaboration made up of patients, their families, physicians, researchers, and advocates who have the goal of eliminating mesothelioma.

Dr. White gave a talk titled, "Complementary and Alternative Approaches in Mesothelioma Treatment." His talk began with an overview of complementary and alternative medicine (CAM), highlighting various CAM modalities. He mentioned negative attitudes towards CAM but also described a "bright side of CAM," including increased NIH funding of CAM research and an increased number of CAM research results published in high quality medical journals.

Dr. White then focused on clinical trials. He mentioned resources that patients can use to find information about clinical trials and provided examples of cancer CAM clinical trials that are currently being supported by NCI. For example, a quick search for CAM trials associated with neuropathy (nerve damage that can occur after chemotherapy treatment) revealed studies using acupuncture to decrease symptoms.

Dr. White noted, "Mesothelioma is a relatively uncommon cancer and when it is not surgically cured the standard chemotherapy approaches have limited effectiveness. Though there is not much

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research of CAM approaches specifically for mesothelioma, much of the symptom management and quality of life research is very relevant for managing patients with this disease."

The presentation concluded with a question-and-answer session with the audience. Audience members asked a variety of questions ranging from information about specific CAM modalities (such as omega-3 fatty acids and acupuncture) to seeking more information about participating in clinical trials.

## Featured Scientific Meetings

| Date | Meeting | Location | OCCAM Staff Attending |
|---|---|---|---|
| February 17-18, 2012 | Prevention and Treatment on Cancer Intergrative Medicine | Tokyo, Japan | Dr. Jeffrey D. White |

**To obtain a copy of this newsletter or for inquiries on cancer and CAM, please contact 1-800-4-CANCER (1-800-422-6237).**

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