Clear communication among oncologists, primary care physicians, and cancer patients is important throughout the entire cancer journey, but particularly when patients are using or thinking about complementary and alternative therapies. Use of complementary and alternative medicine (CAM) continues to gain popularity among cancer patients and survivors. CAM therapies provide a way for patients to manage their symptoms, regain a sense of control, improve their quality of life, and establish better pain management. Yet, as the prevalence of CAM use continues to grow, the communication gap between health care providers and patients widens, as nearly half of those who use CAM therapies fail to report their use to their providers. In recognition of the important role communication plays in the relationship between providers and their patients, the Office of Cancer Complementary and Alternative Medicine (OCCAM) has developed a new patient education resource: Talking About Complementary and Alternative Medicine With Your Health Care Provider: A Workbook and Tips. (http://cam.cancer.gov/talking_about_cam.html)

There are several reasons patients fail to disclose their use of CAM therapies to their providers, such as: a fear of a negative response from their oncologist; a perception of physician unfamiliarity with CAM therapies; a failure of the physician to ask about CAM use; a disinterest among physicians about CAM; and a lack of awareness among patients that they should be disclosing CAM use. When patients wish to discuss their complementary treatments with their physician(s), it is often up to the patient to begin the dialogue. Regardless of who initiates the conversation, communication about CAM use is important because certain CAM therapies, like herbal or dietary supplementation, continue on next page.
may interfere with the effectiveness of prescription medications or conventional treatment, like chemotherapy.

OCCAM’s new publication attempts to reduce some of the miscommunication about CAM, through a series of interactive worksheets that encourage the patient to take an active role in their health care. This resource was created for health care providers and patients to strengthen the model of patient-centered care. *Talking About Complementary and Alternative Medicine With Your Health Care Provider: A Workbook and Tips* seeks to increase a patient’s confidence when talking to their provider about their use of complementary therapies by helping them understand their motivations for CAM use, the effects CAM therapies have on their symptoms, and the importance of disclosing herb, vitamin, and dietary supplement use. This resource also provides strategies on how to talk with health care providers about CAM use and a guide to understanding cancer CAM terms and therapies.

The workbook is a fifteen-page PDF designed to help providers understand the patterns of CAM use by cancer patients and survivors. Additionally, each sheet included in the workbook can also be individually downloaded from OCCAM’s website (http://cam.cancer.gov/talking_about_cam.html) allowing the user to customize this resource to best fit their needs. Through the use of health diaries, a tool successfully used in oncology practice to document pain management and patterns4, patients are able to record their nutritional supplement use, note different CAM therapies they’ve tried over the course of a month, and organize all of their conventional and complementary practitioners’ contact information. These tracking sheets provide an easy method to capture a patient’s health-related behaviors and have the potential to be integrated into a patient’s medical record.

During the workbook creation, the National Cancer Institute’s Office of Marketing Research and Evaluation and OCCAM conducted usability testing with nine cancer survivors. Each participant was asked to comment on the design, functionality, and content of two versions of the patient education workbook. Two versions of the workbook were tested to provide OCCAM with feedback on which design, layout, image selection, and content resonated most with the intended audience.

Nearly all participants felt OCCAM’s initiative would be useful for tracking CAM use, and also for engaging in conversations with their providers. Among the participants, the favorite workbook page was the medication log, which asks a person to think about all of the medications they are taking including prescriptions; over the counter medications; and vitamins, herbs and dietary supplements. One participant commented, “this is good because some people don’t see herbs as different and it’s good to break [this list] into three categories,” while another participant stated, “I don’t think of dietary supplements as medicine.”

Since the workbook was designed for both health care providers and patients, OCCAM also sought feedback from a variety of health care providers. Among the health care providers surveyed, a majority felt this resource would be helpful for patients who expressed an interest in CAM therapies. Many reiterated the importance of knowing all medications and supplements a patient uses, and felt the medication log would be the most utilized resource among health care providers.

Two rounds of pretesting were conducted to obtain feedback, which was representative of the patient and health care provider populations. Pretesting was conducted until the trends observed in the patient and provider populations mirrored one another. Among those who provided feedback, the majority felt OCCAM’s publication was simple, organized, and helpful in fostering CAM conversations and would be a useful resource both during and after cancer treatments.

*Talking About Complementary and Alternative Medicine With Your Health Care Provider: A Workbook and Tips* was designed to complement NCI’s existing patient education resource, *Thinking About Complementary & Alternative Medicine: A Guide for People with Cancer*. This book provides questions to ask your doctor about CAM, tips on how to choose the therapies and practitioners that are right for you, and resources for finding more information about CAM. Together, these resources encourage patients and providers to communicate about CAM use both during and after cancer treatments and to recognize the importance of involving a patient as an active participant in decisions about their treatment plans.

We encourage both patients and health care providers to download this new workbook to use during office visits. It may also be added to an office waiting room library. Patients are encouraged to use these sheets prior to an appointment when they are interested in discussing CAM. They are a skillful way to organize one’s thoughts and get ready for dialogues with a health care professional.  

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What types of dietary intervention studies have you overseen in your laboratory and can you share some of the results?

We have researched bean diet interventions modeled after the successful 4-year, 4000 participant Polyp Prevention Trial. Studies in the LCP lab have demonstrated that the diets enriched by beans (whole and fractionated) attenuated colon carcinogenesis in genetically obese mice. They also revealed potential serum biomarkers of efficacy. Short-term human feeding studies in collaboration with Drs. Lanza and Hartman (Antioxidant Status, Diet, and Early Pregnancy [5 M01 RR010732 15]) of Penn State University revealed several serum biomarkers of bean diet uptake/compliance as well as potential markers of efficacy. In addition to bean diets, we have used flavonol components of beans, particularly isorhemnitin, as well as resveratrol from grapes in intervention studies to prevent colon carcinogenesis in the AOM-DSS mouse model. These studies, some of them currently in progress, are revealing biomarkers that are serum proteins or metabolites. In addition, unlike the situation with small molecular targeted drugs, the target of dietary interventions is not always known. Although some of the targets of resveratrol are known, our studies have provided new knowledge of targets whose inhibited activity may be responsible for the chemopreventive activity of isorhemnitin and resveratrol.

In collaboration with Gary Stoner, now at the Medical College of Wisconsin,
we published on biomarkers of berry interventions in colon cancer patients (Prevention of Esophageal Cancer with Berries [SR01CA103180-08]). We have extended this collaboration and are currently measuring the effects of berries on serum metabolites both in patients with Familial Adenomatous Polyposis (a condition where patients are genetically prone to developing colon polyps that may progress to carcinomas) and in mice. We are also now working with Giorgio Trinchieri, M.D., in the CCR Cancer and Inflammation Program to determine the effects of diet and Traditional Chinese Medicine (TCM) on the gut microbiome and colon cancer, as well as general health. Without the ongoing funding from the DCP as well as from the ODS and OCCAM we could not have contemplated embarking on these rewarding discoveries.

Please talk a little about what prompted your labs’ recent interest in studying compounds from Traditional Chinese Medicine.

Over the years the LCP has had a number of postdoctoral fellows from China who understood TCM and introduced us to the concepts and practice. NCI scientists Zack Howard, Ph.D., and Joost J. Oppenheim, M.D. introduced us to their studies of TCM and to some of their collaborators at the Guang’anmen Hospital, China Academy of Chinese Medical Sciences in Beijing, China. We then met with Libin Jia of OCCAM and discussed projects of mutual interest. We are pleased that Weidong Li, from Guang’anmen Hospital, has joined us and is finding significant chemopreventive activity of TCM in the colon cancer models that we use, including using berberine (an isoquinoline alkaloid isolated from plants) which possesses anti-tumor, as well as anti-inflammatory and anti-diabetic, properties.

We are currently setting up a Cooperative Research and Development Agreement (CRADA) with Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing and the Center for Advanced Pre-clinical Research at NCI to study TCM in a pre-clinical mouse model of lung cancer.

Given your dedicated career to NCI and your imminent retirement, as you look back on your work, can you reflect on some of the changes in research of dietary interventions for cancer prevention, and how the field has grown?

I remember early in my career in 1979-83 when I served on the NIH Chemical Pathology (Carcinogenesis) Study Section. I worked reviewing grants and performing site visits to researchers investigating food factors for their role in causing or preventing cancer. There were a number of international conferences on food factors and cancer in the 1980s and 1990s. It was clear then that the major causes of cancer were all kinds of environmental exposures including cigarette smoke, water contaminants, hormones, and dietary factors. The quality of the early dietary research was uneven and in some quarters acquired a reputation for not being rigorous science. Of course there were many challenges to working with the mixtures found in foods. Sometimes, as with other natural products, the chemopreventive activity of foods was lost by purification to single compounds. Over time, the field attracted outstanding molecular biologists and animal researchers who were fascinated by the lack of toxicity and apparent efficacy of dietary interventions. In most cases, a chemopreventive food works by hitting a number of targets but none of them too hard. The field of dietary chemoprevention is now well-regarded and offers much opportunity to investigators whether early in their career or seasoned. We can envision a future in which cancer, like cardiovascular disease, can be prevented altogether in many people and in others can be kept at bay for decades with appropriate combinations of low-dose non-toxic drugs and diet.

As a mentor, do you have words of advice for young investigators starting in the field of complementary and alternative medicine research?

Get rigorous training in how to experimentally address the provocative questions in cancer research. Put the scientific method to work beginning with articulating the question clearly and designing experiments to address the question. Learn how to assess your own work as if you were a wise reviewer of your manuscript or proposal. Make sure to reach out and connect to those who have the most to offer you either as consultants or collaborators. It takes the right funding and the right people to make your research successful. Learning from one another is key.

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Chronic pain affects 100 million Americans. Costs associated with pain are estimated to be $560-635 billion annually, mainly due to medical costs and decreased productivity. Although pain is a side effect of many diseases studied at the National Institutes of Health (NIH), there is not a center at NIH devoted specifically to pain research. As a result, the NIH Pain Consortium, made of members from all Institutes and Centers at the NIH, was established in 1996 to identify key areas of pain research and to create a long-term plan for pain research at the NIH.

In May 2012, the Consortium held its 7th Annual Symposium. Dr. Nora Volkow, Director of the National Institute on Drug Abuse, kicked off this year’s Symposium providing an overview of the Consortium as well as the state of funding for pain research. She noted that $386 million dollars were spent on pain research in 2011, which represents a greater than 50% increase since 2006.

The Symposium included a session on complementary and alternative methods (CAM) to help treat chronic pain. Dr. Catherine Bushnell (McGill University) presented research showing that an individual’s psychological state may affect their pain experience. Studies have suggested that a person’s emotional state (for example, if they are in a good mood or a bad mood) will affect how much pain bothers them, while attention (whether or not they are distracted from pain) will affect how intensely they feel the pain. There are some CAM therapies that may change psychological state, including meditation and yoga. Meditation and yoga have been shown to change pain perception. In one study, yoga practitioners (those who have been practicing yoga for at least 6 years) and controls (non-practitioners) completed a cold pressor test to measure pain tolerance. In this task, participants place their hand in ice cold water for as long as they can. The results showed that yoga practitioners had a higher pain tolerance — they were able to keep their hands in the cold water for longer — than did controls. Dr. Bushnell also described ways in which chronic pain and some CAM therapies have opposing effects on brain anatomy. For example, chronic pain has been shown to result in thinner areas of brain gray matter while practicing meditation and yoga may result in thicker areas of cortex.

Dr. Dan Cherkin (University of Washington) presented data relating to CAM therapies — specifically acupuncture, massage, and yoga — for chronic back pain. Different types of acupuncture: individualized (acupuncture points were tailored to the patients), standardized (general acupuncture points were used), and simulated (a toothpick was used at acupuncture points instead of a needle), were compared with usual care for treating chronic low back pain in one study. Patients suffering from low back pain were randomized into one of four groups (individualized acupuncture, standardized acupuncture, simulated acupuncture, or usual care) and pain and gain of function were assessed at 8, 26, and 52 weeks. The three types of acupuncture were more effective in improving gain of function than was usual care (pain results were not presented).

Another study compared two types of massage (relaxation and focused
Vitamins, minerals, and botanicals in the spotlight: Annual research practicum offers comprehensive look at dietary supplements

Dietary supplements are a big business (in 2010, sales of dietary supplements in the United States were estimated to be $28.1 billion), but a confusing one. What exactly are dietary supplements? Who uses them? And perhaps, most importantly, do they even work? To help sort out these issues, the Office of Dietary Supplements (ODS) hosts an annual research practicum providing extensive background on dietary supplements, information on how they are regulated, and the latest research findings. The Mary Frances Picciano Dietary Supplement Research Practicum is an intensive, four day meeting featuring speakers from universities around the country, the NIH, and other government agencies, such as the Food and Drug Administration (FDA). The 6th annual practicum was held in 2012 with 147 attendees, including professors, dietitians, pharmacists, and graduate students.

Clifford L. Johnson, M.S.P.H, from the Centers for Disease Control and Prevention (CDC), introduced the National Health and Nutrition Examination Survey (NHANES), which is designed to “assess the health and nutritional status of adults and children in the United States.” The NHANES, used in some of the research presented at the practicum, consists of in-home interviews, medical examinations, and follow-up interviews. This survey provides information about health behaviors, nutritional status, and risk factors for diseases in the population. NHANES also provides a way to assess dietary supplement use in the United States.

Regan Bailey, Ph.D., from ODS, presented findings regarding who exactly is using dietary supplements, from data provided by NHANES. Dr. Bailey noted that the in-home interview format of the NHANES was important for assessing dietary supplement use because inside the homes the interviewers could actually see the supplement bottles used. In fact, the containers were seen 88% of the time in these interviews. Participants were asked if they had taken any vitamins, minerals, herbas or other dietary supplements in the past 30 days. They were also asked how long they had been using those products and how much they took. Results showed that from 1999 through 2010, supplement use was pretty stable, with females using supplements more than males. Older adults tended to use supplements more than younger adults – from 2003-2006, 70% of survey participants 60 years or age or older reported supplement use compared to 41% of respondents between the ages of 20-39. A further breakdown of age-related data showed that children used more supplements than teenagers and use increased among adults as they got older.

Dr. Natalia Morone (University of Pittsburgh), whose work is supported by the National Institute of Aging, spoke about challenges in using mind-body approaches for treating lower back pain in older adults. Researchers need to consider what postures to use when working with older adults. For example, it is often difficult to get elderly patients up from the floor after sitting or lying down meditation. Researchers also have to figure out the best ways to measure the effects of meditation during the length of their studies.

Dr. Diana Wilkie (University of Illinois at Chicago) described a study investigating effects of massage therapy on pain in patients dying of cancer who were in hospice care. In that study, patients received usual hospice care or usual hospice care in combination with five daily massages. The massage group reported lower levels of worst pain than did the usual care group. However, there were not significant differences between the groups in symptom distress or mood state.

Although more studies are needed to improve therapies for chronic pain, research presented at the Symposium suggested that non-pharmaceutical options may provide some relief for pain patients.
older. The most commonly reported supplements in the United States were multi-vitamin, multi-mineral products. Supplement use was also found to be highly correlated with education. According to Dr. Bailey, “those that have higher educational attainment tend to use more dietary supplements.”

Christine L. Taylor, Ph.D., from ODS, discussed safety issues surrounding dietary supplements, including ways in which safety is measured and reported. There is a different approach to safety for dietary supplements than for drugs. Initially, drugs are assumed to be safe and do not require FDA approval to be sold. Once those products are on the market, however, the FDA monitors adverse event reports (for example, a life-threatening experience or birth defect) to determine if products need to be pulled off the shelves. To aid consumers in reporting problems associated with dietary supplements, the Dietary Supplement and Nonprescription Drug Consumer Protection Act was passed in 2006. As a result, dietary supplement labels must include contact information for reporting adverse events and companies must report adverse events within 15 days and keep records for at least 6 years. William J. Gurley, Ph.D., from the University of Arkansas for Medical Sciences, spoke about interactions that can occur when using herbs and drugs together. Very often, doctors and researchers are made aware of potential herb-drug interactions through published case reports. There are two main types of herb-drug interactions: pharmacodynamic, in which herbs have measurable effects on the body (e.g. changes in heart rate or blood chemistry); and pharmacokinetic, in which herbs affect drug absorption or metabolism. An example of a botanical with high potential for drug interactions is St. John’s Wort. This plant increases the activity of proteins responsible for drug metabolism. That increased activity leads to drugs being broken down faster than normal, so they have decreased effectiveness. Dr. Gurley described cases of transplant patients who had been taking cyclosporine (a routine drug used to prevent organ rejection) that had stopped working. It turned out that these patients were also using St. John’s Wort, which was interfering with the drug’s effectiveness.

Robert M. Russell, M.D., from Tufts University, provided information concerning requirements for conducting clinical studies using dietary supplements. If a researcher is interested in conducting a clinical trial testing an unapproved agent for treatment purposes or an approved agent for a new treatment (such as Saw Palmetto for treating symptoms of enlarged prostate or St. John’s Wort for treating depression), they must receive approval from the FDA. Information that must be provided in their application includes results of animal and toxicology studies, manufacturing information, and a detailed protocol for the proposed study.

The 2012 Dietary Supplements Research Practicum offered a comprehensive look at a number of issues associated with dietary supplements including how and why they are used as well as methods for researching them.

For information about the 2013 Practicum, go to http://odspracticum.od.nih.gov/.

Funding Opportunities

New Funding Opportunity: Physical Activity and Weight Control Intervention Among Cancer Survivors: Effects on Biomarkers of Prognosis and Survival (R01 & R21)

The NCI has recently released new R01 and R21 funding opportunity announcements (FOA) encouraging multidisciplinary and translational research projects to investigate the effects of physical activity or weight control on the biomarkers of cancer prognosis among cancer survivors. Potential research designs include, but are not limited to, clinical studies comparing the effects of exercise, weight control or both on cancer-related biomarkers, and the use of animal models to determine how physical activity or weight control affects tumor biology.

Examples of specific research questions this FOA seeks to address include, but are not limited to:

- Does the effect of weight loss on biomarkers differ for overweight/obese cancer survivors with different cancer subtypes (e.g. triple-negative compared to ER+ breast cancer)?
- How are the effects of physical activity on biomarkers different in older vs. younger adult cancer survivors or among those with multiple comorbidities?
- How can information learned from animal models be used to refine the testing of interventions in human cancer survivors?

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The National Cancer Institute (NCI) has released several requests for applications (RFA) to support research projects that address NCI’s Provocative Questions initiative. The newest RFAs utilize the R01 and R21 funding mechanisms and were originally released on September 21, 2012. The provocative question RFAs are arranged in four groups, A-D, to address the following cancer research related topics: cancer prevention and risk; mechanisms of tumor development or recurrence; cancer detection, diagnosis, and prognosis; and cancer therapy and outcomes. Investigators must propose to solve one of the provocative questions in their application for a R01 or R21 grant. Researchers are encouraged to direct additional questions about the R01 or R21 grant mechanisms in groups A-D to NCI’s Scientific/Research Contact, Emily J. Greenspan, Ph.D. at greenspanej@mail.nih.gov. More information about these RFAs is available on the following website: http://provocativequestions.nci.nih.gov/rfa.

Research Answers to NCI’s Provocative Questions- Group A

The provocative questions listed in Group A describe research initiatives for cancer prevention and risk. One provocative question in this group is: How does the level, type, or duration of physical activity influence cancer risk and prognosis?

To view the complete R01 funding announcement for Group A, visit the webpage: http://grants.nih.gov/grants/guide/pa-files/PAR-12-228.html. To view the R21 grant mechanism, visit the web page http://grants.nih.gov/grants/guide/pa-files/PAR-12-229.html. For any additional questions regarding these funding announcements contact either Catherine M. Alfano, Ph.D. at alfanoc@mail.nih.gov or Sharon A. Ross, Ph.D., M.P.H. at rosssha@mail.nih.gov.

Research Answers to NCI’s Provocative Questions- Group B

The provocative questions associated with Group B seek to investigate the mechanisms of tumor development or recurrence. One provocative question in this group is: Why do second, independent cancers occur at higher rates in patients who have survived a primary cancer than in a cancer-naïve population?

To view the complete R01 funding announcement for Group B, visit the webpage: http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-12-016.html.

Research Answers to NCI’s Provocative Questions- Group C

The provocative questions listed in Group C relate to cancer detection, diagnosis, and prognosis. One provocative question in this group is: What molecular events establish tumor dormancy after treatment and what leads to recurrence?

To view the complete R01 funding announcement for Group C, visit the webpage: http://grants.nih.gov/grants/guide/pa-files/PAR-12-228.html. To view the complete R21 funding announcement for Group C, visit the webpage: http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-12-019.html.

Research Answers to NCI’s Provocative Questions- Group D

The provocative questions associated with Group D relate to cancer therapy and outcomes. One provocative
NIH opens pathways for collaborations between intramural and extramural investigators

In the world of NIH research, one is either an extramural (works in a lab outside of NIH) or intramural (works at the NIH) researcher, a distinction that provides different access to research resources. As intramural researchers, NIH scientists have access to numerous resources including equipment, technology, patient cohorts, and specimens. Most of these resources are normally off-limits to extramural researchers; however, a new grant program, “Opportunities for Collaborative Research at the NIH Clinical Center (U01),” has been established to encourage collaboration between extramural investigators and intramural NIH researchers and provide extramural researchers with an opportunity to utilize the vast research resources at the NIH Clinical Center.

Interested extramural researchers are encouraged to determine the NIH investigators they’d like to work with, by searching the National Intramural Database (NIDB) for a specific investigator (http://intramural.nih.gov/search/index.taf?UserReference=AD7D6C5DCD73B18F4F68A767). Researchers can also conduct searches, using specific key words or phrases to identify intramural research protocols aligned with their research area using the Search the Studies-NIH Clinical Research Studies website (http://clinicalstudies.info.nih.gov/index.html). Interested researchers can also search for a specific research resource by browsing the Resources page on the “Collaborating with NIH Intramural Investigators” website (http://clinicalcenter.nih.gov/translational-research-resources/resources.html). Examples of resources available to extramural researchers include equipment, technology and tools, such as radiology and imaging; biomedical specimens; protocol support and unique data sets; and databases of healthy volunteers.

Once an intramural researcher or a research resource is identified, extramural researchers are encouraged to contact the NIH investigator who oversees the specific resource. Before any collaborative scientific research may occur both the intramural and extramural investigators must sign the appropriate written agreements.

The collaborative science efforts and use of the Clinical Center resources are supported via two funding opportunity mechanisms:

- The “Opportunities for Collaborative Research at the NIH Clinical Center (U01),” which requires extramural investigators to collaborate with a Principal Investigator/Co-Investigator in the NIH Intramural Program and allocates $500,000 per year in direct costs for a period of three years. http://grants.nih.gov/grants/guide/pa-files/PAR-13-029.html.

- Administrative supplements for Bedside-to-Bench projects, which involve intramural and extramural collaboration for translational research projects and award $135,000 per year in direct costs for up to two years. http://clinicalcenter.nih.gov/ccc/btb/index.html.

The location of each collaboration is variable and may include, but is not limited to, the extramural investigator working at his/her home institution and the intramural researcher at the Clinical Center; the extramural researcher taking a sabbatical to conduct research at the Clinical Center; or a trainee/junior faculty member relocating to the NIH to manage or conduct a project. Extramural investigators who want to conduct research at NIH must apply for an NIH appointment.

Ultimately, this program provides investigators with an opportunity to work together, fostering new ideas and potentially new scientific discoveries as a result of collaborative efforts. To learn more about collaborating with NIH intramural investigators, visit http://clinicalcenter.nih.gov/translational-research-resources/index.html.
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Research Highlights

**NCI-funded international team investigates wild toad extract in combination with gemcitabine as potential pancreatic cancer treatment**

Toads may attract fairy tale princesses but research studies have suggested they may be even better at keeping certain cancers away. Huachansu, an injectable form of wild toad extract, is a Traditional Chinese Medicine used in China to treat liver, lung, pancreatic, and colorectal cancers. It is a standard treatment for advanced pancreatic cancer patients in China and preclinical research studies support its use. However, huachansu is not commonly used in Western countries. In a study* funded by NCI, scientists from the University of Texas MD Anderson Cancer Center and Fudan University in Shanghai, China investigated the effects of huachansu in combination with a conventional chemotherapy treatment in advanced pancreatic cancer patients.

In this study, patients were randomized to receive gemcitabine (standard chemotherapy treatment) along with huachansu or gemcitabine and a placebo. At the end of the study, median overall survival time was 160 days for patients that had received gemcitabine and huachansu and 156 days for patients that had received the placebo along with gemcitabine. When the researchers assessed progression-free survival in the study participants, they found that it was 99 days for patients in the huachansu group and 98 days for patients in the placebo group. Patients had also completed questionnaires about symptom severity and quality of life. According to the results, there were no differences in symptoms or quality of life between the two experimental groups at the end of the study.

*Project Number: U19CA121503-01
Improving cancer treatment side effects: The promise of the Traditional Chinese Medicine formulation, PHY906

One promise of complementary and alternative medicines is their ability to help alleviate cancer treatment side effects, and in some cases help enhance the efficacy of anticancer drugs. The herbal formula, PHY906, has been studied extensively through in vivo mouse models and human clinical trials to test its effectiveness at easing cancer treatment gastrointestinal side effects and its potential to improve the efficacy of cancer drugs. PHY906 is a pharmaceutical grade formulation (developed using technology that ensures consistency of different batches) of a Traditional Chinese Medicine, Huang-Qin-Tang (HQT) composed of four distinct herbs. The traditional HQT has been used for nearly 1800 years for treating gastrointestinal distress, such as diarrhea, vomiting, nausea, and extreme thirst. The four distinct herbs found in HQT and PHY906: the roots of Scutellaria baicalensis Georgi (skullcap); Glycyrrhiza uralensis Fisch (licorice); Paeonia lactiflora Pall (peony); and the fruit of Ziziphus jujuba Mill (Chinese date) each exhibit “a distinct pharmacological profile; [including] anticancer and antiviral activity, hematological and immunological modulation, analgesic activity, liver protection, and appetite improvement” (Liu & Cheng, 2012).

In a paper recently published in the Journal of Ethnopharmacology*, study authors reported on research supported in part from grants from the National Cancer Institute** and the National Center for Complementary and Alternative Medicine (NCCAM). The report provides an overview of preclinical studies using murine (mouse) tumor models and describes the PHY906 clinical program, consisting of five clinical trials conducted in the United States and Taiwan, examining three different types of cancers (liver, colorectal, and pancreatic).

In preclinical trials, PHY906 was used in conjunction with CPT-11 (irinotecan), commonly used for colorectal cancer. CPT-11 can cause severe late-onset diarrhea, and PHY906 was hypothesized to reduce the severity of this side effect. Mice bearing murine colon tumors were treated with a single high dose of CPT-11, either with or without daily administration of PHY906. Results indicated that PHY906 was able to “reduce CPT-11-induced body weight loss in a dose-dependent manner with maximum protective effect occurring at a PHY906 dose of 500 mg/kg” (Liu & Cheng, 2012). Also 100% of tumor-bearing mice survived with CPT-11 plus PHY906 treatment, while only 60% of mice treated with CPT-11 alone survived. PHY906 also increased the antitumor activity of CPT-11 in the mouse models of colon cancer, as well as in two other murine cancer models and chemotherapy drugs tested (hepatocellular cancer and capecitabine; and pancreatic cancer and gemcitabine).

The paper also outlines some of the findings of five clinical trials including: two phase I studies in advanced colorectal cancer; one phase I/II study in advanced hepatocellular carcinoma; one phase II study in advanced hepatocellular carcinoma; and one phase I/II study in advanced pancreatic cancer. These trials consisted of a total of 150 patients that received varying dose regimens of chemotherapy drugs and 200 mg capsules of PHY906. Discussion of one such trial, of patients with colorectal cancer using CPT-11, follows.

A clinical trial for patients with metastatic or unresectable malignancies was conducted at the Yale Cancer Center. This phase I study had the primary objective of determining the maximum tolerated dose of PHY906...
when combined with a standard dose of CPT-11. CPT-11 was administered intravenously, once every two weeks in escalating doses (180 mg/m² to 250 mg/m²). PHY906 was administered orally twice daily on days 1-4, every two weeks, with escalating doses (1200 mg twice daily to 2400 mg twice daily).

Results from the first twenty-five patients accrued to the Phase I study were reported at the annual American Society of Clinical Oncology conference in 2010. CPT-11 is commonly used at a dose of 180 mg/m² — higher doses are associated with diarrhea, as a dose limiting toxicity. In the above study, when combined with PHY906, patients were able to take up to 215 mg/m² of CPT-11, with no serious side effects (grade 3 or higher diarrhea). These results showed the positive effect PHY906 can have on cancer treatment side effects and indicated that higher doses of standard chemotherapies may be better tolerated by patients using the herbal formula.

The paper noted that it is important to understand that all of the PHY906 clinical studies, except for one, lacked appropriate control arms. Future phase II and phase III double-blind, randomized, placebo-controlled studies with sufficient patient populations will be required to further push this herbal medicine forward.

More information about this research and the other preclinical and clinical trials reported in this article are available online by reading the full journal article: http://www.ncbi.nlm.nih.gov/pubmed/22326673.

New research identifies biomarkers that may help determine how useful berry-based treatments are for treating colorectal cancer

Research studies have suggested that eating freeze-dried black raspberries may provide benefits for colorectal cancer patients. However, biomarkers that help determine how effective the raspberry interventions really are need to be identified. There is increasing evidence that inflammation and cytokines (substances made by cells of the immune system) play a role in promoting many types of cancers, including colorectal cancer. In addition, black raspberries may inhibit colorectal cancer by changing concentrations of certain cytokines. In a recently published study*, funded by the National Cancer Institute of the U.S. National Institutes of Health**, scientists investigated whether consumption of black raspberries would lead to changes in cytokine concentrations and whether these changes may reflect improvements in colorectal tissue.

As part of the study, colorectal cancer patients drank a freeze-dried black raspberry powder mixed with water 3 times a day until surgery (approximately 3 weeks). Plasma and tissue samples were obtained before berry treatment (during colonoscopy), and at the end of the treatment.

Patients who drank the raspberry treatment for 10 days showed changes in plasma concentrations of interleukin 8 (IL-8) and granulocyte macrophage colony stimulating factor (GM-CSF). Previous research has suggested that GM-CSF may have anti-tumor effects by activating the immune system, while IL-8 may bolster cancer progression by decreasing cancer cell death. The results of the current study indicated that, following raspberry intervention, decreased cancer cell growth was related to increased plasma concentrations of GM-CSF and increased cancer cell death was related to decreased plasma concentrations of IL-8. According to the researchers, the "results suggest that changes in plasma concentrations of GM-CSF and IL-8 are associated with changes in colorectal tissue markers in response to the berry treatment."

The researchers concluded that "changes in plasma GM-CSF and IL-8 concentrations may serve as indicators of beneficial response to berry treatment and thus, may be useful as a means to monitor response to berry-based interventions for colorectal cancer."

**Project Numbers: CA103180 and CA148818
Multicultural Outreach: Native Americans and Cancer

Cancer affects thousands of Americans every year and minority communities can be particularly susceptible to cancer health disparities. The NCI Multicultural Media Outreach Program works to provide culturally-relevant, evidence-based cancer information and educational resources to media outlets that target minority audiences. One such resource is the Lifelines video series, a part of the Lifelines education series that includes print, radio, web, and broadcast resources free to the public and to multicultural media outlets.

The Office of Cancer Complementary and Alternative Medicine (OCCAM) Director, Dr. Jeffrey D. White, is featured in the latest Lifelines video targeted to the Native American community. “Connecting Complementary & Alternative Medicine and Traditional Native American Healing Practices” features Dr. White speaking with Jeffrey A. Henderson, M.D., M.P.H, President and CEO of the Black Hills Center for American Indian Health. Drs. White and Henderson discuss cancer research and practice as it relates to complementary and alternative medicine (CAM) in the Native American community. Dr. Henderson, a NCI grantee, also discusses how Native American traditional healers can be seen as allies to help Native American patients find resources about cancer and screening and in some cases even help patients learn about clinical trials.

The complete video, along with all the Lifelines videos, can be viewed on the NCI YouTube channel: http://www.youtube.com/user/NCIcancertopics.

In further outreach to the Native American population, Dr. White was featured on the national radio talk show program, Native America Calling, where he was the special guest in a show titled, “Holistic Approach to Cancer.” Dr. White spoke about CAM use, clinical trials, and the importance of discussing your CAM use with your doctor. To listen to the program, or read the transcript, visit the OCCAM website: http://cam.cancer.gov/drwhite_radio.html.

James Alexander, team lead for the Multicultural Media Outreach Program notes: “Our job is to communicate cancer information in a culturally relevant way to minority and underserved populations. Whether it is an educational video, an outreach article, or an informational audio segment for radio and online posting, the content we create, which we call Lifelines, is part of helping people in minority and underserved communities understand cancer disparities. Our work is also about helping multicultural communities connect with NCI and the resources it offers. The support of Dr. White and his office has been instrumental in helping us to extend our reach, especially recently to more of the Native American community.”

Webinars offer another way to learn about NCI CAM research and funding opportunities

NCI-funded researchers can tell you of the trials, successes, and challenges of submitting grants to the NIH. Getting helpful tips and focused guidance is an integral part of a successful submission. At times, NIH staff will present grant writing workshops across the United States, which help deliver information on program funding and grants administration. While this is a wonderful way to connect researchers and NIH staff, these in-person meetings may not always be the most cost or time-efficient way to reach geographically diverse audiences.

One solution is a webinar. Webinars are a practical way to reach broad audiences and deliver information in a free-to-use and timely manner. Viewers can log on from the privacy of their home or office to view the webinar without having to travel to conferences and meetings; all they need is a computer and two hours of time. Also, presentations can be stored online for archiving and reviewed at a later date.

OCCAM took part in one such webinar to educate viewers on “Complementary and Alternative Medicine Cancer Research and the National Cancer Institute,” with a special focus on CAM grant funding. Dr. Jeffrey D. White, Director of OCCAM, and Dr. Dan Xi, Program Director, represented OCCAM and discussed NCI-funded CAM research. Topics ranged from specific funding announcements to guidance on the NIH grants process, and answers to some frequently asked questions. The webinar also included a presentation from NCI grantee, Dr. Lorenzo Cohen from the MD Anderson Cancer Center, in Houston, Texas. During his presentation, he discussed Traditional Chinese Medicine and his view of the NIH grants process including grantsmanship, NIH study sections, and communication with Program Officers.

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Some call New Mexico “The Land of Enchantment” and for attendees of the Society for Integrative Oncology ninth international conference in Albuquerque, New Mexico, this enchanting city played host to three days of research collaboration and cutting-edge science. The Society for Integrative Oncology (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 meeting, held from October 8-10, 2012, focused on the overarching theme of “Honoring Diversity in Cancer Prevention and Control,” with speakers presenting basic science, preclinical, and clinical research in fields ranging from acupuncture, Traditional Chinese Medicine, mind-body approaches, and much more. OCCAM showed a strong research presence at this year’s SIO. The office sponsored an exhibit booth where attendees could speak with OCCAM staff about funding, patient education, and receive grant application guidance. In addition to the booth, OCCAM staff members both presented and moderated panels.

Drs. Farah Zia, Oluwadamilola Olaku, and Jeffrey D. White, conducted a workshop entitled the “NCI Best Case Series Protocol: How to Move Research Forward.” The workshop highlighted the case series submitted to the NCI Best Case Series (BCS) Program by the P. Banerji Homeopathic Research Foundation in Calcutta, India.

The workshop had several goals including stimulating discussion specific to the available evidence for the homeopathic Banerji Protocol therapy. In addition, NCI BCS investigators, Drs. Zia and Olaku, engaged participants in discussions about the utility of the protocol design in assessing medical cases and its use as justification for further research. An overarching goal of the workshop was to encourage the integrative oncology community to conduct collaborative research, specifically linking the clinical practitioners with the researchers to build strong bridges to future investigations.

Drs. Prasanta and Pratip Banerji, of the P. Banerji Homeopathic Research Foundation, along with Dr. Barbara Sarter, Associate Professor, Hahn School of Nursing and Health Sciences, University of San Diego, and Dr. Iris R. Bell of the University of Arizona, presented their involvement with the cases, including direct clinical care and/or research regarding homeopathic remedies.

OCCAM’s webinar slides and speaker contact information are available online: http://cancercenters.cancer.gov/Webinar/OCCAM/OCCAMWebinar.html.

Shannon Silkensen, Ph.D., Program Officer in the Office of Cancer Centers, discusses the utility of the webinar series: “OCC is excited to bring this Webinar Series to the Cancer Center Members. We believe that by linking the researchers with the NCI Program Staff, better, more mission-targeted science will be accomplished. We were delighted that Dr. White and his team were able to participate in our Webinar Series and highlight funding opportunities for our Center Members in this growing area of research.”

Meetings

OCCAM represents NCI at leading Integrative Oncology conference

From left to right, Drs. White, Zia, Banerji, Olaku, Sarter and Bell take questions from the audience

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Dr. Sarter spoke about her time working with the Drs. Banerji: “In February 2008, I took a sabbatical from my faculty position in the Department of Family Medicine at the University of Southern California in order to learn the Banerji Protocol in Calcutta at the PBH Research Foundation. I had received a diploma in classical homeopathy before I went to Calcutta, but never truly embraced this system of medicine until I spent those five months with the Banerjis. Since then, I have directed my time and abilities to advancing the research effort and data mining at the Foundation.”

Dr. Bell presented her research on “Homeopathic Remedies as Nanoparticles.” She discussed the properties of nanoparticles, such as their high surface area to volume ratio, a characteristic that changes their material properties. In her presentation she explained that nanoparticles have “high bioavailability; easily cross cell membranes as well as the blood-brain barrier; require smaller and less frequent doses, [and have] lower side effects.”

Dr. Farah Zia, Director of the Case Review and Intramural Science Program (CRISP) at OCCAM, and moderator of this workshop, noted that: “The Banerji case series is a prime example of a seemingly successful ‘Best Case Series’ deserving of further laboratory and clinical research. The mission of CRISP is to improve the quality of care of cancer patients by a rigorous scientific evaluation of cancer CAM interventions and by facilitating prospective research for certain CAM interventions with the goal of developing them into novel therapeutics. In order to achieve this objective, we must foster the building of bridges between the clinical and research communities. We applaud researchers, such as Dr. Bell, whose research is exciting, innovative, and forms the platform on which further ideas will be built; furthermore, we encourage practitioners to submit their best cases of cancer patients treated with an unconventional cancer treatment to the NCI Best Case Series Protocol. More information is available at http://cam.cancer.gov/best_case_protocol.html. Continued dialogue among and between the practitioner and research communities, such as the current workshop, will continue to shed light on ways to achieve our unified goal.”

Dr. Libin Jia, Health Scientist Administrator at OCCAM, moderated two separate sessions entitled “Clinical Science Abstracts: Methodological Issues in Integrative Oncology Research” and “Evaluation of Herbal Medicine: A Cross-Cultural Discussion.”

Dr. Jia noted that the presentations in the Clinical Science Abstracts session represented a wide variety of methodological approaches in research focused on Traditional Chinese Medicine, exercise interventions, and yoga practices, among others. Dr. Misha Cohen, OMD, LAc from University of California at San Francisco explored methodological challenges of clinical Chinese herbal medicine. She stated that proper provision of the Certificates of Analysis (COA) and documentation for Investigational New Drugs (IND) is critical to Chinese herbal medicine research in oncology settings.

Dr. Jia also co-moderated the round table session titled “Evaluation of Herbal Medicine: A Cross-Cultural Discussion.” Speakers from the United States, China, and other countries exchanged ideas on herbal medicine in terms of quality control of the starting materials, and the policy and regulations among different entities such as the United States, European Union, and China. Themes that emerged included the need for emphasis on the standardization of the herbal medicines in the research and clinical setting and interest in knowing more about safety issues surrounding the use of herbal medicines in the United States and abroad.

Dr. Jeffrey D. White, OCCAM Director, was part of a plenary discussion on “Funding in Integrative Oncology Research” that overviewed three different funding streams from the government, for profit, and non-profit sectors. Dr. White gave a brief summary of the NCI grant application and review process and answered several questions as part of a panel of the session speakers which included Eveline Mumenthaler from the Gateway for Cancer Research and Kerri Diamant, Founder and Executive Director, AlterMed Research Foundation.

Ms. Elizabeth Austin, M.S., Coordinator of OCCAM’s Communications and Outreach Program, was an invited speaker as part of the “Exploring Web-Based Information Resources on Complementary and Alternative Medicine information summaries (http://www.cancer.gov/cancertopics/pdq).”

Several new summaries have been added in the past year including “Prostate Cancer, Nutrition, and Dietary Supplements (PDQ®),” featuring information about the use of nutrition and dietary supplements for reducing the risk of developing prostate cancer or for treating prostate cancer.

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Other resources highlighted included the Memorial Sloan Kettering “About Herbs” website: http://www.mskcc.org/cancer-care/integrative-medicine/about-herbs-botanicals-other-products and the CAM-Cancer resource of information summaries hosted by the National Information Center for Complementary and Alternative Medicine (NIFAB) at the University of Tromsø, Norway (http://www.cam-cancer.org/CAM-Summaries).

Each year the SIO conference brings together some the most experienced researchers and practitioners of integrative oncology. For more information about the society visit: http://www.integrativeonc.org/.

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