Alpha-Lipoic Acid Plus Low-Dose Naltrexone Reviewed for Cancer Treatment

A panel of researchers and clinicians was convened by the National Cancer Institute (NCI) on March 19, 2012 for presentations and a roundtable discussion about “The State of the Science of Alpha-Lipoic Acid plus Low-Dose Naltrexone for the Treatment of Cancer.” The meeting was hosted by the NCI Office of Cancer Complementary and Alternative Medicine (OCCAM) and the Cancer Therapy Evaluation Program (CTEP), both part of the NCI Division of Cancer Treatment and Diagnosis (DCTD).

The meeting provided an opportunity for NCI staff and outside experts to review and discuss case reports from Dr. Burton M. Berkson, an integrative medicine physician and Ph.D. in Biological Sciences, and Adjunct Professor at New Mexico State University. Dr. Berkson presented on his experience treating patients with alpha-lipoic acid (ALA) plus low-dose naltrexone (LDN) for various cancers and autoimmune diseases. The group also heard from Dr. Renee N. Donahue, Research Fellow in the Laboratory of Tumor Immunology and Biology at the NCI Center for Cancer Research, about her pre-clinical research on the efficacy and proposed mechanism of action of LDN for the treatment of cancer.

Dr. Farah Zia, Director of OCCAM’s Case Review and Intramural Science Program, noted, “The cases being presented today by Dr. Berkson were submitted and given rigorous scientific evaluation under the NCI Best Case Series (BCS) protocol. The ultimate goal of the BCS is to identify those complementary and alternative medicine (CAM) interventions that have enough evidence to support NCI-initiated research.” Dr. Zia also noted two ongoing NIH-supported clinical trials of naltrexone in cancer patients. The first is taking place at the University of Minnesota for patients with breast cancer and the second is running at Duke University for glioma patients.

Dr. Berkson presented seven case reports on patients with advanced cancers (pancreatic and lymphomas) that he had treated over the past 10 years with a combination of ALA (intravenously and orally) and LDN (orally), along with diet, vitamins, and lifestyle changes. Earlier in his medical career, Dr. Berkson reported success using ALA to repair liver damage in patients from mushroom poisoning or chronic infections with hepatitis C virus. He also cited a number of research articles in European medical journals showing ALA’s beneficial effects on cancer.

Dr. Berkson learned about the use of LDN for treating cancer from a patient with advanced prostate cancer. He reported to Dr. Berkson after the successful

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therapy with LDN of both the patient’s cancer and rheumatoid arthritis (RA). Subsequently, Dr. Berkson offered LDN to his patients with RA and other autoimmune diseases. “Within about a month, most of the patients were off all drugs and feeling completely normal on just LDN, at $15 a month,” he recalled. In his presentation of the case reports, Dr. Berkson reported uniformly positive responses and low toxicity from the ALA/ LDN regimen for each of the seven cancer patients. Of the seven cases presented by Dr. Berkson, four had pathology specimens reviewed through the NCI Best Case Series protocol. NIH and NCI specialists in radiological imaging (Dr. Elizabeth Jones) and pathology (Dr. Avi Rosenberg) reviewed the available medical imaging studies and pathology slides of the four cases. Of the four cases reviewed, three had confirmed pathologic diagnosis while one had a diagnosis that could not be definitively confirmed.

Dr. Berkson commented, “I try to discourage many cancer patients who call my office because I’m not an oncologist; however, I do work with cancer patients who are also seeing an oncologist.” He acknowledged that the ALA/LDN protocol works better for rheumatoid disease, “but I think it deserves some type of clinical trial in cancer patients as well.”

Dr. Gregory Plotnikoff, from Allina Hospitals System in Minneapolis, Minnesota reported that his hospital has 36 advanced cancer patients using LDN with and without ALA on a compassionate-use basis as well as an open-label study of the LDN treatment for aromatase inhibitor-induced pain in breast cancer. “The oncologists there are intrigued and anxious to do rigorous trials because they believe that there is something here that they have not seen from any other therapies,” he said.

Dr. Donahue presented findings from her research as a doctoral graduate student at the Penn State College of Medicine in the lab of Dr. Patricia J. McLaughlin and Dr. Ian S. Zagon. The lab’s research focused on the role of the cellular peptide opioid growth factor (met5-enkaphalin) – or OGF – and the OGF receptor (OGFR) axis in cancer and autoimmune diseases.

“Our initial studies have shown that if you block the interaction between OGF and OGFR with an opioid receptor antagonist, such as naltrexone, you get an increase in cell proliferation,” Dr. Donahue reported. “However, subsequent studies have shown that if you use a lower dose of opioid receptor antagonist, such as LDN, you actually get the opposite effect, a decrease in cell proliferation.”

Dr. Donahue has also studied the effects of LDN or OGF in combination with common chemotherapy agents for cancer, such as taxol and cisplatin. She reported that LDN did not interfere with the tumor reduction effects of those drugs and, in one case, seemed to enhance the drug’s effect.

CTEP Director Dr. Jeffrey Abrams responded, “That could be a study design for a clinical trial that potentially could be attractive if we could show that that LDN and ALA are not going to hurt your chemotherapy, so you don’t have to worry about that. You can give chemo plus or minus LDN or LDN and ALA and see if we could really do a controlled study in cancer.”

As a result of this meeting, OCCAM will continue the Best Case Series Protocol evaluation process which requires cases to be reviewed by a panel of cancer specialists. These specialists will provide specific advice about whether NCI-initiated research is warranted. Discussion at NCI has focused on developing and presenting a phase 0/1 concept to the Division of Cancer Treatment and Diagnosis (DCTD) protocol concept review committee. The concept would investigate preliminary informational objectives in the utilization of low-dose naltrexone for the treatment of advanced/metastatic cancer in patients who have progressed on prior chemotherapy. If the concept is approved, the clinical trial would be conducted at the NIH Clinical Center, under the auspices of the DCTD Early Drug Development Clinic.
Please tell us about the Nutritional Science Research Group.

The Nutritional Science Research Group (NSRG) in the Division of Cancer Prevention (DCP) plans, develops, and coordinates external research programs in diet and nutrition as they relate to cancer prevention. The NSRG works with external researchers and internal NCI staff to foster the development of quantitative methods to monitor nutritional exposures, and to identify the molecular action of foods and their components.

For example, some of the NSRG projects focus on determining how essential nutrients (such as calcium in dairy products or non-essential components such as sulforaphane in broccoli) influence specific genes and ultimately the associated molecular targets. The overarching goal is to identify people who will benefit most and those who might be placed at risk due to dietary change. The NSRG has a diversified grant portfolio which includes research focused on ways in which the approximately 25,000 food components influence the cellular processeses that are key to influencing cancer risk and tumor behavior.

The NSRG publishes the quarterly Nutrition Frontiers newsletter (http://prevention.cancer.gov/programs-resources/groups/ns/nutrition-frontiers), runs the Frontiers in Nutrition and Cancer Prevention Online CME series (http://prevention.cancer.gov/programs-resources/groups/ns/webinars), and writes numerous fact sheets about cancer prevention (http://prevention.cancer.gov/programs-resources/groups/ns/factsheet). Many training and fellowship opportunities exist in cancer and nutrition research within the NRSG, including sabbatical opportunities for interested researchers (http://prevention.cancer.gov/programs-resources/groups/ns/training).

Can you share a few promising research projects funded by your office in the areas of nutrition, diet, and cancer prevention?

It is very difficult to say that one study is more important than another, but the ongoing VITamin D and OmegA-3 Trial (VITAL) study is unique because of its large size and the focus on both of these food components (vitamin D and omega-3 fatty acids) as potential promoters of health. VITAL is a research study of 20,000 men and women across the United States that investigates whether taking daily dietary supplements of vitamin D3 or omega-3 fatty acids reduces the risk of developing cancer, heart disease, and stroke, in people without a prior history of these diseases*. This is a large-scale U01 trial that is co-funded with The National Heart, Lung, and Blood Institute (NHLBI) and NIH Office of the Director (OD).

VITAL is a 5-year study headed up by JoAnn Manson, M.D., and Julie Buring, Sc.D. at Brigham and Woman’s Hospital, in Boston, Massachusetts. Gabriela Riscuta, M.D., CNS, is the Program Director of the VITAL trial within the NSRG. The study is recruiting incredibly well and although it is only in its initial phase, everything we have been hearing from the study group sounds promising. More information about VITAL is available on the VITAL website (http://www.vitalstudy.org/) and in the NIH Reporter Database (http://projectreporter.nih.gov/project_info_details.cfm?aid=8120386&icde=12225940).

We fund many other studies throughout the United States that have shown interesting results. We profile several of them in our Nutrition Frontiers quarterly newsletter that features studies and results that we find relevant and useful to researchers and the public.

We recently profiled a study by Li-Shu Wang and colleagues from the Ohio State University Comprehensive Cancer Center, which showed that black raspberries might modulate colorectal tumor development. This pilot study had patients consume 60 grams of black raspberry powder daily for an average of 4 weeks. After the treatment period, biopsies were performed on tumor tissue and adjacent normal tissue and revealed that black raspberries decreased cancer cell growth and tumor blood vessel formation and increased cancer cell death. While a pilot study, the findings are intriguing.

Do you find that conducting research on bioactive food components poses any significant challenges?

A challenging question related to nutrition research is: “When does a food component become a drug?” This is a situation that has profound regulatory issues for the Food and Drug Administration. For example, if resveratrol (found in red wine) has an active anticancer effect on the body, how much wine does someone have to consume to achieve those beneficial effects? In addition, if you cannot consume wine or in the quantity needed, yet you can take it in pill form with exaggerated amounts, is it now considered a drug? We must be aware of the amounts and duration of exposures that are required to bring about a response and thus if this is a physiological or pharmacological response.

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We are also perplexed by inconsistencies in the research literature about the importance of specific dietary components, just as people may be seeing in the media or hearing from their doctors. For example, some research studies suggest fish oil (omega-3 fatty acids) may help to inhibit cancer while others provide no evidence for a benefit. Many other foods and beverages (such as fruit or coffee) suffer from the same inconsistencies in findings. Part of the reason for this is because historically we’ve done a rather poor job of assessing nutritional intake. In addition, we have not considered individuality in response, that is, that different people respond to food and bioactive food components in different ways that likely depend on their genes. Both of these issues can lead to mixed messages about how important diet is in our lives — especially as a deterrent to cancer.

Overall, we believe that over 30% of cancers are preventable by dietary change; however, that does not mean that every person needs to adhere to the same type of diet plan. Certain people will likely get more benefit from a specific dietary change, say a vegan diet, than someone else. That second person may respond better to different dietary change including increased fish intake. The science is headed in the direction of personalized nutrition and the idea that some subpopulations may be more responsive to certain diets than others. Identification of these folks will be done through the practice of nutrigenomics, or the study of the interactions of food and their active components with a person’s particular genes. If one knows something about a person’s genes and how they are functioning, then predictions about whether or not one will benefit from specific foods can be made.

What would you say are some common misconceptions people have about nutrition and its role in cancer prevention, and what does the research say about these misconceptions?

The number one misconception is the idea that “one size fits all” for nutrition. The other common misconception with nutrition and cancer prevention is “if a little is good, a lot is even better.”

Nutrition is a complex area of study. There are over 25,000 bioactive food components, at least, and the diet we eat is not simple. While there is an overall 20% increase of cancer incidence in those that are obese, certain types of cancer are much more affected by obesity than others.

Information about how food and bioactive food components affect you and your cancer risk are available from lots of different sources. We in the NSRG have a set of fact sheets that give basic information about vitamin D and cancer prevention, calcium and cancer prevention, garlic and cancer prevention, and several others. View all the factsheets here: http://prevention.cancer.gov/programs-resources/groups/ns/factsheet.

Where do you think nutrition research will go next?

There is certainly growing recognition about how excess calories can negatively affect disease risk, including cancer. It might not always be the excess calories, it may be that when you are consuming excess calories you are not consuming something else, thus creating an inadequacy of one or more nutrients.

Also, from my perspective we are incorporating a personalized approach to health promotion, and moving away from this “one size fits all” belief. Multiple factors, including the microbiome (the environment of microbes and viruses that are in our gastrointestinal tracts), can be influenced by the types of foods that we consume and, in turn, influence the response to our foods. This area deserves additional attention.

Lastly, I think more and more people are becoming aware of a “transgenerational effect” between diet and disease. The transgenerational effect posits that what one does influences his/her offspring and their offspring. For example, there is some evidence that a parent’s diet may influence their child’s subsequent risk of disease state, including cancer, and that depending on the food item this can happen from both the father’s or mother’s side. Overeating in animals seems to lead to overeating in the offspring for multiple generations. So we must begin to ask what the impact of the current obesity crisis will be, not only on us but on future generations as well. Hopefully, we will continue to make more discoveries and gain greater understanding of transgenerational effects of eating behaviors.

Where do you see the research from this office headed? Do you have goals when it comes to the types of research you would like to see coming through the Nutritional Science Research Group?

The NSRG continues to promote basic nutrition science since there is so much to learn about the actions of food components in healthy and unhealthy circumstances. Without understanding the variability in response, many may simply dismiss diet as one variable for health and disease prevention. We need knowledge about mechanisms and who benefits most if we are to translate science into appropriate advice for people about what to eat.

We are keen to learn more about the microbiome and its influence on the response to foods and their components. We want to know what the optimum time is for ingesting a specific food or bioactive food component to get the greatest response. This has to do with circadian rhythms — our 24-hour biological clock. Should one eat a specific food/component at one time of day or another, and/or with something else to obtain maximum benefit? In addition, we need to know how to optimize a cell and keep it resilient from any kind of damage, whether caused by excess calories, environmental toxins, bacteria, or viruses.

We are also exploring what specific cell types are most influenced by diet. For instance, we are intrigued with the potential impact of dietary components on stem cells, both normal stem cells and cancer stem cells. The stem cells in
Foods have multiple components that may act together to enhance or maybe suppress the effects of one constituent. Interactions between various nutrients are most assuredly an area of great interest to the NSRG. 

the tumor are abnormal because they are growing at an uncontrolled rate, but it can be argued that something similar is happening in normal cells that are involved with repairing tissue damage. We also need to understand why food components often seem to influence cancer risk in one type of tissue more than another. If the response were in stem cells, why would not all tissues respond identically?

The other big area that always surfaces is how do isolated food components compare with the whole food. We are often asked, “Is a supplement the same as a food?” We just do not have as much data as needed to answer that question.

Plenty of Food for Thought Served Up at the Nutrition and Cancer Prevention Research Practicum

From March 12-16, 2012 a select group of participants attended the Nutrition and Cancer Prevention Research Practicum hosted by the Nutritional Science Research Group (NSRG) within the Division of Cancer Prevention. The practicum began nine years ago with sixteen dietetic interns and gradually grew as others expressed interest in attending. This year’s participants included graduate students, dietetic interns, Registered Dietitians, post-doctoral research fellows, physicians, and a Registered Nurse. “Interest in this practicum has expanded beyond NIH. Participants have come from all over the country, and in recent years, we’ve had a number of international attendees from countries including Brazil, Italy, Ireland, and Mexico,” noted Elaine Trujillo, M.S., RD, CSND, a nutritionist with NSRG who organized the practicum.

The practicum offered an intense week of learning about the latest research in nutrition science and cancer. According to Dr. John Milner, Chief of the NSRG, the goal of the practicum was “to promote a greater understanding of the complex relationship between diet and cancer prevention and to encourage individuals to actively participate in research that will help provide clarification about the specific role of foods and food components as modifiers of cancer risk and tumor behavior.”

The week’s speakers included researchers from NSRG, NIH Program Officers, and representatives from advocacy groups. Many of the lectures dealt with specific foods, their effects on cancer, and their role in cancer prevention. Participants got a good overview of the latest research on potential anti-cancer effects of tomatoes, soy, cruciferous vegetables, and green tea, among other topics. Gabriela Riscuta, M.D., CNS (from NSRG) spoke about health benefits of mushrooms, focusing on β-glucans that are found in mushroom cell walls. She also described two epidemiological studies that showed consumption of mushrooms may lower the risk of developing breast cancer. The attendees also gained a sense from the presentations of how to interpret the findings, which were often inconclusive.

Some common themes apparent in the lectures, besides the enthusiasm of all of the speakers, were that methods of preparation (such as cooking food versus eating raw food) may affect activity of nutritional components and that bioactive food components will affect individuals to varying degrees. For example, researchers are increasingly looking at how individual genetics affect responses to bioactive food components and why some people may have a greater response than others to those components. Brooke Savage, a graduate student at the University of Massachusetts, Amherst, was impressed by the lectures. “It’s great to see my education come together and how it applies to real-world situations,” she said.

There were a number of lectures that stepped out of the lab and focused on various topics of interest to the attendees. For instance, speakers presented information about numerous resources (such as databases and websites) available for researchers and clinicians. There were also talks about obtaining grant funding from the NIH, which featured discussions of different award mechanisms available, and ways to communicate research findings to patients and the public.

The practicum was not just a week of lectures and classroom-based learning. The week’s events also included a trip to Beltsville, Maryland and a Nutrition Research Day at the Clinical Center on NIH’s Main Campus. In Beltsville, the attendees took a tour of the U.S. Department of Agriculture (USDA) Human Nutrition Research Center. During the tour, they learned about the different types of clinical studies

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Antioxidants help prevent the damage that can occur to cell membranes and DNA by highly chemically active molecules called free radicals. Many cancer patients take antioxidants while undergoing conventional treatment, although it is unknown how helpful — or harmful — those supplements may be. On the one hand, antioxidants may help protect healthy (non-cancerous) cells from damage caused by chemotherapy or radiation. On the other hand, antioxidants may also be protecting the cancer cells targeted by those treatments. Published studies support both sides of the argument. A new review article*, authored by OCCAM Director Dr. Jeffrey D. White, former OCCAM contractor Akiko Nakayama, and interns Karen P. Alladin and Obianuju Igbokwe, evaluated studies that investigated the effects of antioxidants administered alongside chemotherapy or radiation. Among the studies reviewed, the majority used the antioxidants glutathione (GSH), different types of vitamin E, or N-acetylcysteine (NAC). Analysis of the studies revealed a number of deficiencies. For example, many studies did not disclose product details (such as manufacturer information) or why a specific dose of antioxidant was used. The primary end points of the studies also differed: some measured the response of the tumor to the treatments while others assessed symptom/side effect management. There were also numerous combinations of antioxidant, chemotherapy, and radiation treatments used in the studies. According to the authors of the review, “Among the 52 clinical trials we reviewed, only five studies of glutathione and two studies of NAC used exactly the same antioxidant and conventional cancer therapy doses and regimens in the same cancer types.”

The variations in study design and absence of important information make it difficult to reach a consensus about how useful antioxidants are when taken alongside chemotherapy or radiation. The authors concluded their review by providing suggestions for establishing evidence-based clinical guidelines for antioxidant use during cancer treatment. They noted that more research is needed identifying mechanisms of actions of antioxidants and the optimal doses and formulations required for patients. The authors point to an example from colorectal cancer, combining folinic acid with fluorouracil (5-FU). Many studies have investigated this combination and the mechanism through which folinic acid affects 5-FU is now well known.

To read more, go to http://www.ncbi.nlm.nih.gov/pubmed/22085269.


The practicum did not exactly provide participants with a checklist of foods they should add to their diet to reduce their risk of developing cancer. It raised more questions than it answered, hopefully providing potential research ideas — and lots of food for thought — for the attendees.

Visit the Nutritional Science Research Group’s website, http://prevention.cancer.gov/nutrition, for information about next year's practicum and how to apply.

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Funding Opportunities

NCI–wide Omnibus Funding Announcements (R21/ R03)

NCI has announced new R21 and R03 funding opportunities. These new program announcements (PAs) are NCI–wide and solicit applications in all areas of cancer research relevant to the mission of NCI, including complementary and alternative medicine. The new awards will replace many existing PAs, including OCCAM’s expiring program announcements: Developmental Projects in Complementary Approaches to Cancer Care and Treatment (R21) PA-09-167 and Developmental Projects in Complementary Approaches to Cancer Care and Treatment (R03) PA-09-168.

NCI Exploratory/Developmental Research Grant Program (NCI Omnibus R21)

This R21 mechanism promotes the early and conceptual stages of research efforts on novel scientific ideas that have the potential to substantially advance cancer research in all areas relevant to the mission of the NCI. By using the R21 mechanism, this funding opportunity announcement (FOA) will support “Exploratory/Developmental” projects and may involve basic, translational, clinical, and/or population research in areas of cancer biology, cancer control, cancer diagnosis, cancer disparities, cancer prevention, or cancer treatment.


NCI Small Grants Program for Cancer Research (NCI Omnibus R03)

This R03 mechanism supports discrete, well-defined projects in any area of cancer research that can realistically be completed in 2 years and that require limited levels of funding. Types of projects may include pilot or feasibility studies; secondary analysis of existing data; small, self contained research projects; development of research methodology; and development of new research technology.

Please view the FOA for specific submission details and dates: http://grants.nih.gov/grants/guide/pa-files/PAR-12-144.html.

New Funding Opportunity: Pilot and Feasibility Clinical Research Studies in Digestive Diseases and Nutrition (R21)

The National Cancer Institute (NCI), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the Office of Dietary Supplements (ODS) have recently released a funding announcement to investigate digestive and liver diseases and the nutritional disorders associated with them, including those associated with an increased risk of cancer. This R21 grant mechanism is limited to $275,000 of direct costs over a maximum, 2-year period. R21s provide flexibility for initiating preliminary, short-term clinical studies that allow new ideas to be investigated in an expedited manner thus encouraging investigators to pursue creative avenues of research.

This program announcement titled “Pilot and Feasibility Clinical Research Studies in Digestive Diseases and Nutrition (R21)” has four areas of research interest: the effects of diet on cancer risk and progression, rare or uncommon digestive diseases, hepatitis B and C, and the safety and efficacy of surgical and endoscopic techniques. The NCI is particularly interested in the effect of food and bioactive food components on cancer cells.

Appropriate research studies include, but are not limited to, those:

- Examining interactions between nutrients, such as antioxidants and micronutrients, on mediators of the inflammatory responses in digestive diseases, including cancer.
- Investigating the role of alterations of dietary fatty acids on clinical mediators of digestive diseases, for example, prostaglandins.
- Developing strategies using bioactive food components to examine biomarkers associated with cancer change and tumor behavior.

To view the complete funding announcement, visit the web page at http://grants.nih.gov/grants/guide/pa-files/PA-12-139.html or direct further questions to the NCI’s Scientific/Research Contact, Dr. Maria Agelli, ma215e@nih.gov.

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Research Resources

NIH Launches Clinical Research Trials Portal Website on NIH.gov

Are you interested in learning more about clinical research trials and how to participate in such experiments, but don’t know where to find reliable information? In an effort to help the general public understand the merits of clinical trials research, the NIH has launched a new website, “NIH Clinical Research Trials and You.”

The new portal describes clinical trials explaining how they help advance scientific knowledge, the phases of clinical trials research, potential risks and benefits associated with participation, and the ethical protection of research subjects. The website also features short testimonials from both researchers and volunteers regarding their involvement in clinical trials research. Promotional materials that help raise awareness of the benefits of participating in clinical trials research are also available for health care organizations.

Visit “Clinical Trials and You” (http://www.nih.gov/health/clinicaltrials/index.htm) to learn more about clinical trials or to find a clinical trial near you.

The Latest Information from NIH and NCI is Now Just a Tweet, Like, and Click Away

Whether you prefer to tweet, like, or view the latest cancer information, NIH and NCI maintain numerous online resources to keep you up-to-date on new cancer research and guidelines. In fact, the use of social media has continued to expand at the NIH and NCI, as more offices and centers have established Twitter accounts (or feeds), mobile applications (apps), Facebook pages, and YouTube videos and channels. The use of such sites enables patients, clinicians, and researchers to satisfy their growing appetite for up-to-the-minute information on cancer research.

As a patient, researcher, or clinician, you are bound to find an NIH-hosted online resource to meet your needs. The Office of Extramural Research’s Twitter account, @NIHforFunding, helps researchers learn about new funding announcements, requests for information, upcoming workshops, and changes made to new and existing grant solicitation programs. Another useful Twitter feed is the National Library of Medicine’s account, @PubMedHealth. This feed updates followers with the latest scientific publications and provides links to article abstracts when available.

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Similar to Twitter accounts, mobile apps are quickly establishing their presence among the health communication efforts of the NIH. The NCI has recently released m.cancer.gov, a mobile version of its website (http://www.cancer.gov). This new app is available in both English and Spanish and features a number of cancer-related resources, including information about cancer types and treatment side effects. The Office of Dietary Supplements (ODS) has also re-released their mobile app, My Dietary Supplements, which allows users to manage their use of vitamins, herbs, and other supplements. The new version now operates on more smartphone platforms, including the iPhone and Android, and is available to download for free from http://ods.od.nih.gov/About/mobile/aboutmyds.aspx.

Several social media accounts also exist with cancer patients, survivors, and their caregivers in mind. For example, the National Library of Medicine has created a Facebook page dedicated solely to caregivers of all illnesses, http://www.facebook.com/NLM4Caregivers. This page provides a wealth of information about to caring for a sick loved one, understanding medical terminology, and the importance of taking care of one’s own health as a caregiver. To obtain health information, two Twitter accounts worth following include @NCIPrevention, the NCI’s Division of Cancer Prevention Twitter feed that discusses early detection, cancer risk, as well as chemoprevention and @medlineplus, Medline Plus’s account that presents daily medical updates on health and wellness.

The NCI’s YouTube channel (http://www.youtube.com/ncigov) is constantly evolving, with new videos posted frequently to the site. These short videos aim to educate the public on the mission of the NCI, the research it supports, clinical trials, and common cancer topics. Several of the posted videos are also available in Spanish.

To view the complete list of new media resources available at the NCI, visit http://www.cancer.gov/global/newmedia or visit each office’s website to learn more about their presence on Facebook, Twitter, and YouTube.

CAM Patient Education Booklet Available from NCI

NCI’s Thinking About Complementary & Alternative Medicine: A Guide for People with Cancer booklet is one of the most popular complementary and alternative medicine (CAM) patient education materials available from the Institute.

It contains information that patients and caregivers can use to understand the types of CAM modalities available to them before, during, and after cancer treatment(s). The booklet also includes 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.

The book is available in hard copy for free from NCI (up to 20 copies) or for a small shipping fee for bulk orders of 20 or more. Ordering instructions are available from the NCI Publications Locator at https://pubs.cancer.gov/ncipl/detail.aspx?prodid=P042 or by calling 1-800-4-CANCER (1-800-422-6237) and mentioning the book title or inventory number (P 042).

This resource is especially useful for hospital patient education departments, private practices, community centers, and any other locations where patients or community members would be interested in learning more about CAM.

Research Highlights

Massage and Cancer: Supporting Patients and Caregivers

A massage can be a relaxing treat after stressful events, or a nice quick rehabilitation for sore or tight muscles. It can also be a hands-on therapy that provides supportive care for cancer patients and their caregivers, relieving more than just stress and tight muscles. Massage can help reduce pain, fatigue, nausea, and other symptoms often suffered by cancer patients and survivors. The benefits are not exclusive to massage recipients – those giving the massage can also feel greater levels of confidence in their ability to help their loved one cope with cancer.

William Collinge, Ph.D., M.P.H., LCSW, is the owner of Collinge and Associates, an independent research and consulting organization funded by research grants from the NIH and other sources. He also runs a private practice focused on cancer survivorship located in Eugene, Oregon.
Dr. Collinge’s work was funded by the Small Business Innovations Research (SBIR) Grant mechanism (R43/R44). SBIR grants are awarded to domestic, for-profit, small businesses to conduct innovative research and development that has potential for commercialization and public benefit. Dr. Collinge was awarded an SBIR grant* to study how touch and massage, used as supportive care and guided by a multimedia instructional program, could affect patient symptoms and side effects, patient quality of life, and caregiver attitudes toward touch as a form of caregiving. Collinge and Associates created the DVD used in the multimedia instruction program titled, Touch, Caring and Cancer: Simple Instruction for Family and Friends. The goal of the DVD was to allow family members to become part of a treatment team for a cancer patient. Using massage and simple touch, both the patients and caregivers could receive benefit. The video provided 78 minutes of instruction by Collinge and two oncology massage therapy researchers and was filmed with live patient-caregiver pairs. A 70-page illustrated manual accompanies the DVD and is designed to teach caregivers techniques for relaxation, acupressure, and simple light touch. The DVD and manual are intended for use at home by patients and caregivers and are available in English, Spanish, and Chinese (Mandarin and Cantonese).

Dr. Collinge conducted a randomized controlled trial of a multi-ethnic sample of 97 adult caregiver-patient pairs. Pairs were randomized to either the treatment or control group. Pairs in the treatment group met with other subjects, viewed the instructional DVD together, and were then given a copy of the DVD plus data collection materials. The participants were encouraged to view the materials of both the DVD and manual as often as they liked and practice the techniques of their choice three times per week, with a suggested duration of 20 minutes. However, pairs were told that as little as 5 minutes could be beneficial.

The control group acted as an attention control which required caregivers to read to the patients at least three times per week with a suggested duration of 20 minutes, but were told as little as 5 minutes would be beneficial. Reading material could be of any type of literature of the patient’s choice. Control group participants were allowed to join the intervention after 4 weeks and all subjects were followed for another 16 weeks.

Both the treatment and control groups were to report on session effects for one session each week as they related to the pre-and post-session severity levels for pain, fatigue, stress/anxiety, nausea, and depression, and an optional other category. The caregivers in each group also filled out surveys to assess their stress levels and feelings toward caregiving.

Results showed significant reductions for all symptoms after both the treatment and control group activities. Pain reduced 18% in the control group and 34% in the massage treatment group. Fatigue was reduced 20% vs. 32% (reading vs. massage); stress/anxiety, 28% vs. 44%; nausea, 12% vs. 29%; depression 22% vs. 31%; and other symptoms 17% vs. 42%. Massage was shown to be significantly superior to reading for stress/anxiety, pain, fatigue, and other symptoms. Both groups of caregivers had significant increases over the 4 weeks in satisfaction with their ability to help their partners feel better, and they had reduced concern about causing distress. Results have been published in *Journal of the Society for Integrative Oncology***, *Seminars in Oncology Nursing***, and another article about the research is currently under review.

Dr. Collinge notes that he wanted to pursue this area of research because he “saw a need for caregivers to be able to offer something tangible to benefit the well-being of their loved ones with cancer. Caregivers experience distress from a perceived inability to reduce suffering in a loved one. This intervention benefits the patient, makes caregiving more satisfying for the giver, and strengthens the quality of their relationship, all at the same time.” He was pleased with the results because “informal caregivers using the techniques were able to achieve results approaching those of professionals. Caregivers can easily learn safe and simple techniques from a very low-cost multimedia intervention. Patients can experience the benefits of touch and massage far more frequently than they would ever be able to if relying on professionals. This has huge potential for overcoming disparities in palliative care for low-income and underserved populations.”

This study is currently being adapted for use in Vietnam. “The Vietnamese version is being used at National Cancer Hospital in Hanoi to train caregivers. We are collecting data from sample families in Hanoi, and it will be interesting to see how the program might help meet palliative care needs in an under-resourced country like Vietnam,” notes Dr. Collinge.

In summary, this research shows that supportive care at home can offer benefits

*Project Number: R44CA103606
to both patients and caregivers at relatively low cost and effort. Caregivers’ self-efficacy about their caregiving can be increased and patients can see improvements in their quality of life.

Connie Dresser, RDPh, LN, Program Director for Dr. Collinge’s grant, noted that the project was significant because “the study results indicate there is a good possibility that similar outcomes could be achieved by caregivers of patients with other chronic diseases or depression. Today, technology has completely taken over how we live and the art of tangible communication (such as face-to-face and writing) has decreased from the previous norms. Dr. Collinge’s work offers a meaningful and healthy way of reengaging with family, friends, and patients.”

Dr. Collinge is also busy working on a current R43 grant**** from NCI titled “Palliative care provider online education in evidence-based complementary therapies.” This current research aims to develop the first online continuing education program for palliative care personnel who teach evidence-based applications of complementary therapies in the palliative care setting. Dr. Collinge stresses that palliative care is one of the most rapidly expanding sectors in health care and complementary therapies offer significant benefits for reducing suffering and improving quality of life. However, there are currently no systematic educational offerings to help health care professionals learn how to use complementary therapies with diverse patient groups in the palliative care setting. Through the R43 grant, Dr. Collinge is working to create an interactive website delivering educational curricula to health care professionals about complementary therapies and palliative care. This is a large undertaking that will consist of multiple reviews of the literature, working with a team of professionals in palliative care, and creating and reviewing course content and the best methods of delivery.

Dr. Collinge notes that he wanted to do this work because “complementary therapies are underutilized in palliative care environments. They have a lot to offer in terms of comfort and symptom reduction, but practitioners need help making evidence-based decisions. We aim to help them sort through the strengths and limitations of complementary therapies in palliative care.”

Compound Found in Green Tea May Help Improve Pancreatic Cancer Treatments

Pancreatic cancers tend to be very aggressive, with a very small percentage of patients surviving 5 years after diagnosis. Results of a new, NCI-supported* study suggest there may be a new weapon in the fight against pancreatic cancer — one found in a very popular beverage. Epigallocatechin gallate (EGCG) is a component in green tea that has anti-tumor activity in the laboratory. Numerous studies, in a number of different cancer types, have shown that EGCG may decrease tumor cell growth, increase apoptosis (programmed cell death), and prevent formation of new blood vessels around tumor cells.

In the current study**, researchers investigated the effects of EGCG on pancreatic cells. Treatment of pancreatic cells with EGCG resulted in decreased cell migration and increased apoptosis. The researchers also treated cells with a combination of EGCG and gemcitabine, a chemotherapy drug used by pancreatic cancer patients. The results indicated that while EGCG and gemcitabine alone were effective in increasing cell death and apoptosis, the effects were greater when the two agents were used in combination. EGCG also enhanced the effects of CP690550, an immunosuppressant drug that has been shown to have anticancer activity.

While the exact mechanisms of EGCG’s actions on pancreatic cancer cells are unknown, results of this study suggest that EGCG may be interfering with a protein — STAT3 — involved with cancer progression. STAT3 is a member of the signal transduction and activators of transcription (STAT) family of proteins, which are important for normal cell growth. When STAT3 is activated, a number of genes necessary for tumor cell growth and survival are turned on. In this study, treatment of pancreatic cancer cells with EGCG resulted in lower levels of STAT3 in the cells. In addition, levels of certain genes that are turned on in cancer and controlled by STAT3 were inhibited following EGCG treatment.

While this initial study used an in vitro model only, the authors noted that their results “provide a new application method, in which the use of EGCG can enhance the therapeutic effects of anticancer drugs while possibly reducing their side effects.”

To read more about this study, go to http://www.ncbi.nlm.nih.gov/pubmed/22348037.

* Project Number: R01CA125262
A New Report Offers Review of Research on Exercise in Cancer Survivors

An increasing amount of research suggests that exercise may help cancer patients feel better during treatment. But what about when the chemo and radiation are finally over — does exercise help or hinder survival? A systematic review* by Rachel Ballard-Barbash (Associate Director of the Applied Research Program in the Division of Cancer Control and Population Sciences at NCI) and her colleagues, published in the Journal of the National Cancer Institute, examined recent studies that investigated the effects of physical activity on mortality and/or cancer biomarkers in cancer survivors.

The majority of studies included in this review were published after 2009 and focused on breast cancer survivors. Other types of cancers included in the review were colorectal, prostate, ovarian, and brain.

Almost all of the breast cancer studies reviewed indicated that physical activity (before or after breast cancer diagnosis) may be related with greater survival. In addition, about half of the breast cancer studies suggested a dose-response effect — greater amounts of exercise were associated with larger decreases in mortality risk. There were also a number of studies that revealed physical activity may increase survival in colorectal cancer survivors. There was not enough evidence in the reviewed studies to support a relationship between physical activity and mortality risk for survivors of other types of cancer.

This review also identified studies that reported links between physical activity and biomarkers in cancer survivors. Among breast cancer survivors, results of randomized controlled trials have suggested that physical activity may result in beneficial changes in circulating insulin levels and insulin-related pathways. Results of randomized controlled studies of survivors of other cancer types indicated that exercise may lead to beneficial changes in biomarkers related to inflammation and immunity.

Although the outcomes of physical activity seem promising, the authors of the review note there are some caveats that prevent them from making specific recommendations for cancer survivors. The studies included in this review assessed physical activity in different ways and reported various types of exercise. For example, among observational studies, the questionnaires that were used examined participants’ physical activity over various time points (exercise in the past year versus exercise in the past 6 months). Among randomized control studies, there were a variety of exercise interventions used, including aerobic exercise, walking, and strength training.

In addition, more cancer types should be investigated, along with more racial and ethnic groups. The authors of this review concluded that while exercise may be safe for cancer survivors and help improve survival, “additional research is warranted before clear conclusions can be reached on the effects of physical activity on disease outcomes among many groups of cancer survivors.”

To read more about these findings, go to: http://www.ncbi.nlm.nih.gov/pubmed/22570317.

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NCI’s CAM FY 2010 Annual Report Released

The National Cancer Institute’s Office of Cancer Complementary and Alternative Medicine (OCCAM) announces the release of the sixth NCI CAM Annual Report. NCI’s Annual Report on Complementary and Alternative Medicine: Fiscal Year 2010 includes an in-depth analysis of NCI’s CAM research portfolio, summaries of CAM research projects, a list of NCI funded peer-reviewed scientific publications, and details on NCI’s CAM training, conferences, and communications activities.

Highlights of articles in the report include:

- Scientists Study Biomarkers of High-Fiber Diets to Lower Risk of Colorectal Cancer
- Compound in Cruciferous Vegetables Studied Against Pancreatic Cancer
- Soy Bread Studied in Men with Prostate Cancer
- Yoga Studied to Relieve Fatigue and Stress in Breast Cancer Patients

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NCI’s Annual Report on Complementary and Alternative Medicine: Fiscal Year 2010 is available for viewing on the OCCAM Website at http://www.cancer.gov/cam/cam_annual_report_fy10.pdf. Past reports are also available for viewing at http://www.cancer.gov/cam/cam_annual_report.html. In February 2012, OCCAM Cancer Research Training Award (CRTA) Fellow Jeans Santana presented a poster at the Latino Medical Student Association (LMSA) Joint 7th Annual National and 39th Annual Northeast Conference at Harvard Medical School in Boston, Massachusetts. The LMSA was founded in 1987 as the National Network of Latin American Medical Students to help support, educate, and unify Latino(a) medical students in the United States. The network is composed of members from five regions across the United States: Midwest, Northeast, Southeast, Southwest, and West. This year’s conference was open to participants at all stages of their medical (and pre-medical) careers — attendees ranged from high school students with a dream of pursuing medicine to physicians seeking to mentor young students. Mr. Santana presented research that examined the prevalence of complementary and alternative medicine (CAM) use and the effect of acculturation among U.S.- and foreign-born Hispanic adults diagnosed with cancer. The data were obtained from two large surveys: the 2001 California Health Interview Survey and the 2007 National Health Interview Survey. A portion of the data is still being analyzed, but so far, the findings have suggested that CAM use among the patients surveyed was high. The most commonly reported CAM modalities used were physical activity and manipulative and body-based therapies. Mr. Santana concluded that future studies should oversample Hispanic cancer patients and investigate health-seeking behavior in the Hispanic population and the safety and efficacy of CAM therapies. Attending the LMSA Conference was a positive experience for Mr. Santana, who is attending medical school in the fall. “Aside from the opportunity to present my research and represent OCCAM, I was able to attend a number of extremely useful workshops. Through these workshops, I learned about conducting clinical and basic science research after medical school, how to prepare for the United States Medical Licensing Exam Steps 1 and 2, and how to manage finances throughout medical school,” he noted. Mr. Santana was also impressed by the keynote speaker, Dr. Raul Ruiz, who “talked about achieving big in the medical field and also the responsibility we should carry for those voices not commonly heard in public health policy meetings, such as minority and underserved populations.” With the pressures of deadlines, projects, and meetings, de-stressing during the workday is often hard for many people to do. However, on April 30th, 2012, more than seventy researchers, clinicians, and members of the general public were one step closer to reducing their stress thanks in part to Yang Yang, Ph.D. Dr. Yang presented a lecture titled “Taiji and Qigong: A Multidimensional Approach to Wellness” during which audience members participated in meditation activities, learned basic taiji movements (also known as t’ai chi), and even danced together. The lecture was hosted by the National Cancer Institute’s Office of Cancer Complementary and Alternative Medicine (OCCAM). Dr. Yang’s lecture provided an overview of the traditional practices of taiji and qigong, showcased his prior research, and explored potential avenues for use of taiji and qigong among cancer patients, survivors, and caregivers. “We invited Dr. Yang to visit for two reasons: first, he is interested in doing research with cancer patients and wanted to learn about NCI’s relevant programs and second, to give the NCI staff who manage research portfolios with taiji projects an opportunity to learn more about this practice,” said Dr. Jeffrey D. White, OCCAM’s Director. A common misconception of taiji is that it is a practice of only slow and choreographed movements. Traditional taiji is more than just slow, deliberate movements; it is composed of static qigong meditations, dynamic movements, and “push hands,” a technique involving a partner that improves balance, reaction time, and strength. Taiji, a form of Chinese...
martial arts, is rooted in Daoist philosophy, which strives to balance the complementary forces of the yin with the yang. Dr. Yang, a world renowned Taiji and Qigong Master with over 25 years of teaching experience, explained an important component of taiji is the concept of qigong. Qigong describes the interaction of the energy, qi, with the practice or foundation, gong. It is through this interaction that the mental, spiritual, and physical benefits of practicing taiji are obtained.

Traditional taiji practice emphasizes a sequence of static qigong meditations before dynamic, mindful movements are practiced. The sequences of qigong meditations occur while sitting, lying, and standing, although the order does not matter. During his lecture, Dr. Yang described the spiritual and mental benefits of seated meditations as well as the physical benefits, such as increased core strength, before encouraging members of the audience to join him in a seated meditation. He then described the physical benefits of standing meditation, such as improved posture, balance, strength, and sleep. Using a slow cadence, Dr. Yang led the audience through a series of standing meditations and breathing exercises. Finally, with the help of four volunteers, Dr. Yang explained how lying meditations could be used to help combat insomnia, pain, and increase range of motion.

Regardless of the type of meditation practiced, Dr. Yang stressed the ultimate goal of the static qigong meditation is to obtain tranquility within one’s daily life. He also highlighted several other benefits of practicing taiji and qigong including increasing the quality of one’s life, increasing muscle strength, gaining a positive outlook, increasing confidence, and improving one’s sleep.

As both a practitioner and researcher, Dr. Yang is dedicated to using evidence-based research in the use of taiji and qigong as complementary therapies. Dr. Yang earned his Ph.D. in Kinesiology from the University of Illinois, Urbana-Champaign and has used his doctorate to enhance his mastery of taiji practice and to better understand the mechanisms of taiji practice from a biomedical perspective. Dr. Yang is the author of the highly acclaimed book, *Taijiquan: The Art of Nurturing, The Science of Power*, and has published several biomedical articles. To date, Dr. Yang’s research has focused on the use of taiji and qigong among older adults. More specifically, he has conducted several longitudinal controlled trials to investigate how taiji and qigong improve balance, gait, force control, and lower body strength among older adults and how the use of taiji and qigong influence antibody response to the influenza vaccine.

As the founder and director of the Center for Taiji and Qigong Studies and part-time teacher at Memorial Sloan Kettering Cancer Center, Dr. Yang’s current research interest involves the use of taiji and qigong among cancer patients, survivors, and caregivers. Due to the holistic, mind-body nature of the practice of taiji, Dr. Yang hopes to investigate the role it may play in reducing cancer-related symptoms such as stress, anxiety, insomnia, pain, and fatigue. According to Dr. Yang, “Taiji/qigong combines the benefits of physical exercise and meditation, and I believe there is great potential for this mind/body/spirit integrative exercise to help cancer patients, survivors, and caregivers. Past research has provided a solid framework, but there is much work to be done. To improve trial design and continue to build a solid body of evidence, researchers should recognize that the basic model of therapeutic benefit from mind/body/spirit integrative exercise is systemic, and therefore quite different from cellular pathology which is the foundational paradigm of pharmaceutical research. The dosage of taiji/qigong therapy delivered to subjects, though central to clinical research, is largely unknown, yet certainly variable, both between and within existing studies. The dosage of any mind/body therapy is a function of both quantity and quality of practice. Though a challenging task, we need to develop methods to characterize and measure dosage in future taiji/qigong trials.”

For inquiries on cancer and CAM, please contact 1-800-4-CANCER (1-800-422-6237)