May 2010

PLCO EEMS Steering Committee accepting request for proposals; deadline is July 15

What is PLCO? The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial is a large randomized controlled trial evaluating screening programs for these cancers. The PLCO Biorepository contains approximately 2.7 million biologic specimens, including blood specimens collected from intervention participants during their six trial screening years and buccal cell specimens collected from control participants.

How can I access PLCO biospecimens and what is 'EEMS'? PLCO biospecimens are available to the entire scientific community. Access to the biospecimens is administered through The Etiologic and Early Marker Studies (EEMS) Program, a component of the PLCO Trial established to facilitate etiologic and early marker research using trial collection biospecimens. EEMS reviews proposal applications twice a year in June and December. More details about PLCO EEMS are available on the PLCO Web site at http://plco.cancer.gov/ or at http://www.plcostars.com/ (you can request an account if you do not already have one).

Does PLCO EEMS have tissue samples in addition to blood and buccal cell specimens? Recent additions to the PLCO Biorepository include tissue microarrays (TMAs) created from formalin-fixed and paraffin-embedded pathology tissues. TMAs are currently available for colon cancer, colorectal adenoma, ovarian cancer, and prostate cancer. Ideally, TMA slides should be cut close to the time of laboratory analysis to preserve antigenicity. To minimize material loss, PLCO seeks multiple proposal applications so that slides can be cut for multiple projects at once. For additional information regarding the PLCO study, PLCO biospecimens, and TMAs, please log-in to the PLCO STaRS Web site at http://www.plcostars.com/.

Is funding provided? PLCO biospecimens and associated data are provided upon approval of the proposal application. However, funding is not provided via the PLCO EEMS review process.

What is the PLCO EEMS application process? Proposals will be accepted for the PLCO EEMS Summer review cycle between June 1, 2010, and July 15, 2010. **Applications will be accepted until July 15, 2010.**

The EEMS application materials (the EEMS application

forms, instructions, NIH biosketch template, confidentiality disclosure agreement (CDA), and the EEMS policy document), as well as general information regarding the EEMS review process can be found on the PLCO STARS home page (http://www.plcostars.com/). Individuals who do not already have access to PLCO STARS can self register by clicking the Login button located on the upper right corner of the page. If you have any questions about registration, or the PLCO STARS Web site you should contact the PAR PLCO Helpdesk at parplcohelpdesk@westate.com or 240-314-2313.

Once your proposal is received, the EEMS Coordinating Center (Westat) will verify that all components are completed and forward the completed proposal packet to the EEMS principal investigators, the PLCO project officer and chief statistician for an initial suitability review. This initial review will be completed by early August 2010; applicants will then be notified of the results of the suitability review. The EEMS Review Panel will then review and provide comments on all suitable proposals based on the study's significance, approach, innovation, compliance to PLCO priorities and policies, proposed statistical approach, proposed laboratory assays and the qualifications of the investigation team. It is anticipated that this review will be completed by mid-September 2010, contingent upon the quantity of proposals received. The EEMS PIs and the PLCO PO will then make the final decision regarding all acceptable proposals based on input from the EEMS Review Panel.

EEMS proposals and additional materials must be submitted electronically through the online application form found on the PLCO STaRS Web site, www.plcostars.com.

Confidentiality Agreements (CDA) should be sent to the following address:

Kevin Brand, JD
Technology Transfer Specialist
Technology Transfer Branch
6120 Executive Blvd., Suite 450
Rockville, MD 20852
Phone: (301) 451-4566
Fax: (301) 402-2117
Email: brandk@mail.nih.gov

What happens after my proposal is approved? If your proposal is approved, you will have up to three years from the date of approval to request the shipment of samples and commence activities on your study; please note that an IRB approval letter, as well as an executed PLCO EEMS Material Transfer Agreement (MTA) will be required in most cases prior to the release of samples. If you are unable to request shipment of samples within this time frame due to lack of funding or other issues, please inform us. Otherwise, your application will be considered withdrawn and these samples will be released, allowing for other investigators to submit proposals to use them. Similarly, you will be required to re-apply should you still wish to use these samples. Additionally, once you receive samples, you have two years to submit

laboratory analysis results to IMS.

If you have any questions, please do not hesitate to contact us (plco-eems@westat.com or 240-314-5896).

May 2010

Core Spotlight

Chemical Genomics, Chemical Synthesis & Organic Drug Lead Development cores

John Turchi, PhD, and his colleagues have long worked to identify small chemicals that would inhibit a protein that had never been targeted before.

By mid-2006, Dr. Turchi and colleagues made a discovery: They came up with a compound that inhibited a protein-DNA interaction.

Since that initial finding, they have further demonstrated that the inhibition of this particular protein-DNA interaction can kill cancer cells in tissue culture models.

"We can administer the compound effectively to mice without killing them," Dr. Turchi said. "Preliminary analysis shows that it's an effective agent at reducing tumor growth."

To get to that discovery, however, the research moved along slowly in the beginning stages.

What took Turchi and crew nine months to screen 10,000 compounds was drastically cut by a high-throughput library screening done by **Zhong-Yin Zhang**, PhD.

Zhang was able to screen 80,000 compounds in three days for Turchi.

"That was done with a higher degree of sensitivity, a higher degree of reproducibility. That sent us on our way," Turchi said of the high-throughput library screening.

Upon identification of "hits" through high-throughput screening efforts, Turchi turned to the Chemical Synthesis & Organic Drug Lead Development Core for the compounds to be re-synthesized, validated as active agents, and to provide larger quantities for biological testing.

In time, the compounds moved from cellular studies to animal studies thanks to both the Chemical Genomics and Chemical Synthesis cores.

"They (the cores) are almost inextricably connected," Turchi explained. "If you use the Chemical Genomics Core, you're going to get compounds that look like they're doing what you want them to do. At some point, you're going to need more compounds. The Chemical Synthesis Core will get you

more."

What is the Chemical Genomics Core?

Recent advances in genomics, proteomics, systems biology, and chemical biology have resulted in dramatic expansion of our understanding of the molecular underpinnings of living systems. This information enables researchers to develop novel targeted therapies for a variety of intractable diseases.

However, there is a bottleneck currently limiting this type of translational research: the availability of diverse compound collections, chemical synthesis, and other specialized tools for high throughput biology. Academic investigators, who focus on fundamental biological mechanisms, do not have the tools to translate these discoveries into therapeutic agents.

The Chemical Genomics Core was established to facilitate the discovery of small molecule tools for biological pathway analysis and for therapeutic development. Small molecule tools can be very important in the development of therapeutic agents since they can be used to test the effects of altering biological processes in cells, which can lead to the identification of validated targets for drug development. In addition, these novel chemical tools will serve as the starting point for the elaboration of first-in-class targeted therapies.

The mission of the Chemical Genomic Core is to provide IU investigators with cost-effective access to the large-scale screening capacity necessary to identify small molecules that can be optimized as chemical probes to study the functions of genes, cells, and biochemical pathways. The facility also has the capacity for a limited amount of optimization chemistry required to produce useful chemical probes/therapeutic agents from the hits identified in the initial screening.

The Chemical Genomics Core is equipped with automated liquid handling and assay detection instrumentation, structurally-diverse, drug-like small molecule libraries, infrastructure for hit identification and characterization, medicinal chemistry capabilities for targeted chemical synthesis, and a staff experienced in assay development, high throughput screening, and laboratory robotics.

What is the Chemical Synthesis & Organic Drug Lead Development Core?

Faculty from the Department of Chemistry & Chemical Biology, part of the Purdue School of Science, joined forces with the IU Simon Cancer Center in late 2008 to expedite the translational research and drug development efforts of cancer researchers, establishing the Chemical Synthesis & Organic Drug Lead Development Core.

"The Department of Chemistry & Chemical Biology experienced a dramatic increase in the number of calls from the School of Medicine for collaborations involving chemical synthesis as translational research efforts increased on campus from 2005 onward," Eric Long, PhD, core director, said.

The synthesis core, housed within the School of Science, consists of a fully functional synthetic organic chemistry laboratory with ready access to routine analytical instrumentation, located in the chemistry department, which includes LCMS, NMR, UV, and GCMS.

Key contacts

Chemical Genomics Core

Director: Zhong-Yin Zhang, PhD, 274-8025 or zyzhang@iupui.edu

Chemical Synthesis & Organic Drug Lead Development Core

Director: Eric Long, PhD, eclong@iupui.edu

Tax Georgiadis, PhD, director of synthesis, tgeorgia@iupui.edu

For more information on the Chemical Synthesis Core, call 274-6804.

In addition, Tax Georgiadis, PhD, the core's synthesis director, brings more than 20 years of academic and industrial experience in synthetic/medicinal chemistry, allowing him to handle the wide variety of requests from biomedical researchers. Dr. Georgiadis also has practical experience in patent examination, which enables him to further assist clients interested in protecting any IP that may result from their discoveries.

The core's goal is to support the synthetic and medicinal chemistry needs of IU Simon Cancer Center investigators as well as other academic entities within IUPUI and throughout the state. Prior to the establishment of the Synthesis Core, biomedical researchers on the IUPUI campus and throughout Indiana had nowhere to turn within the state to obtain cost-effective, custom syntheses of needed compounds. The core also is available to the broader life sciences community of central Indiana and elsewhere on a fee-for-service basis.

The synthetic efforts of the core include the synthesis of:

- Literature-cited compounds (including patented agents)
- Compounds discovered through high-throughput screening such as occurs in the Chemical Genomics Core
- Experimental agents
- Focused libraries

In addition to synthesis, the core can provide:

- Improved ADMET (adsorption, distribution, metabolism, excretion, toxicity) properties of lead compounds to improve biological activity
- Lead optimization (SAR analysis)
- Database searching and data mining of drug discovery targets
- Insight on the patentability of chemical matter
- Chemical informatics

May 2010

News briefs

CEUs available during June 4 event at Fairbanks Hall

The IU Simon Cancer Center is partnering with Cancer Support Community of Central Indiana, formerly the Wellness Community, to present A Celebration of Wellness: Honoring the Spirit of Survivorship Friday, June 4 in Fairbanks Hall, 340 W. 10th St., Room 1112. This free educational symposium is for people with cancer and their loved ones. For health care professionals, there is a $20 fee, which includes CEUs. The symposium includes opening remarks by **Larry Cripe**, MD, clinical director and interim director of the IU School of Medicine's Division of Hematology/Oncology and founder of the cancer center's CompleteLife program. Deanna Dewberry of WISH-TV, Sherman Burdette of Fox 59, and Lorene Burkhart -- a central Indiana author, entrepreneur, philanthropist and cancer survivor -- are guest speakers during the event. The symposium includes lunch, a butterfly release, and an afternoon Q&A session with IU Simon Cancer Center physicians. Registration begins at 9:30 a.m.; closing remarks begin at 2:15 p.m. To RSVP, call 257-1505 or e-mail events@cancersupportindy.org. Free parking is available.

Vaughn places 23rd in virtual bike ride

LaTrice Vaughn, RN, who was honored by Lance Armstrong while he completed the Tour of California earlier this month, finished in 23rd place in the "I Ride For" virtual game. Because of that, her name will be entered into a drawing in which her dedication sticker, if selected, will be on the Team RadioShack bikes during this year's Tour de France. Vaughn, who was Armstrong's nurse while he was treated here, dedicated her virtual ride to IU Simon Cancer Center patients. Watch a Fox 59 news clip. See a photo.

CS-Keys named a success story

CS-Keys Inc., a biotechnology company focusing on the discovery and development of third generation cancer-associated biomarkers using proteomics, was named one of 100 "success stories" that were fueled by federally-funded research, according to the

Science Coalition's "Sparking Economic Growth: How Federally Funded University Research Creates Innovation, New Companies and Jobs." **Linda Malkas**, PhD, and **Robert Hickey**, PhD, are among the company's founders.

Radiation oncology earns accreditation

The radiation oncology services at Indiana University Hospital/Clarian Health Radiation Oncology have been awarded a three-year accreditation following a recent survey by the American College of Radiology (ACR).

The ACR, headquartered in Reston, Va., awards accreditation to facilities for the achievement of high practice standards after a peer-review evaluation. Evaluations are conducted by board-certified physicians and medical physicists who are experts in the field. They assess the qualifications of the personnel and the adequacy of the facility equipment. The surveyors report their findings to the ACR's Committee on Accreditation, which subsequently provides the practice with a comprehensive report.

The ACR is a national organization serving more than 32,000 diagnostic and interventional radiologists, radiation oncologists, and nuclear medicine and medical physicists with programs focusing on the practice of medical imaging and radiation oncology and the delivery of comprehensive health care services.

IUSCC awards Wright Scholarships to med students

Three IUSM students have been awarded William J. Wright Scholarships by the IU Simon Cancer Center. They are:

- Theodore T. Brown, fourth-year medical student in pathology
- Neil C. Estabrook, fourth-year medical student in radiation oncology
- Adam Golas, third-year medical student in hematology/oncology

This scholarship is awarded to third- and fourth-year medical students, physicians in cancer-related postdoctoral programs, and/or medical doctors employed by IUSM and pursuing cancer-related fellowship training who demonstrate

commitment to, or potential for, conducting cancer research as well as outstanding character and well-defined professional goals.

Outrun the Sun is June 5

The annual Outrun the Sun Race Against Melanoma is Saturday, June 5 at Fort Benjamin Harrison State Park. The race begins at 7 p.m. and includes a 5-mile timed run, a 5K run/walk, and a one-mile fun walk. For full details, visit http://www.outrunthesun.org/.

Cancer center members in the news

- **Mark Kelley**, PhD, has been appointed to the NCI's Subcommitte F - Manpower & Training, which provides advice and recommendations to the NCI director on the scientific and technical merit of applications for grants-in-aid of research training in broad areas relevant to basic and clinical cancer research. Also, ApeX Therapeutics, of which Kelley is the scientific founder, recently launched a new Web site. Visit http://apextherapeutics.com/.


Kelley

- **Indra Das**, PhD, will participate in the FDA's "Device Improvements to Reduce the Number of Under-Doses, Over-doses, and Misaligned Exposures from Therapeutic Radiation" public meeting June 9-10 in Washington, D.C.
- **Thomas Hurley, PhD,** and **Anna McDaniel**, DNS, RN, FAAN, have been named Chancellor's Professors, the most distinguished appointment an individual faculty member can attain at IUPUI. It recognizes senior faculty who display a record of extensive accomplishment and leadership in teaching, research, and campus service.


McDaniel

- **Dave Ingram**, MD, director of neonatal-perinatal medicine, has been elected the 2011-12 vice president of the Society for Pediatric Research (SPR). Following his term as vice-president, he will serve as president from 2012 to 2013. SPR is the largest international society for the encouragement of young investigators engaged in research to benefit children. Through co-sponsorship with the Pediatric Academic Societies annual meeting, SPR provides a forum for the interchange of ideas and opportunities and for the presentation of innovative pediatric research. SPR also actively supports the development of future pediatric scientists through sponsorship of student research training programs and awards. Dr.

Ingram currently serves as a representative on the SPR Council of Pediatric Subspecialties and the PAS Program Planning Committee.

- **Sunil Badve**, MBBS, has been appointed to the Susan G. Komen for the Cure Scientific Advisory Council. The Scientific Advisory Council is focused on the organization's research program and the research with the best chance of providing effective treatments within 10 years.


Badve

- **Lawrence Einhorn**, MD, presented "Lance Armstrong and the Tour de Cancer" in early May at Moffitt Cancer Center. Also, during the Medical Alumni Reunion Weekend (May 22-23), the IUSM presented Dr. Einhorn with a Distinguished Alumni Award.

- LaTrice Vaughn, RN; **Kathy Miller**, MD; **Sunil Badve**, MD; **Noah Hahn**, MD; **Daniela Matei**, MD; and **Gabi Chiorean**, MD, are presenting abstracts at ASCO June 4-8 in Chicago.

- **Richard Foster**, MD, and colleagues report in *Molecular Cancer Therapeutics*: "The biological effects of celecoxib treatment (increased apoptosis) justify further study of the antitumor effects of Cox-2 inhibitors in invasive transitional cell carcinoma."

Grants available to researchers

For the latest grant opportunities, visit the Funding Opportunities page on the IUSCC Web site.

New grants

Janice Blum, PhD
"Class II Antigen Presentation Via Chaperone Mediated Autophagy"
NIH-NIAID

Alexander Dent, PhD
"Control of Autoimmunity by Follicular Helper T Cells and BCL6"
NIH-NIAID

Brittney-Shea Herbert, PhD
"Targeting Telomerase for the Treatment of Refractory Breast Cancers"
Komen Cancer Foundation

Kurt Kroenke, MD
"Burdette Kunkel Mindfulness-Based Stress Reduction for Patients with Persistent Cancer Related

Linda Malkas, PhD
"A Peptide Antibody Directed Against Cancer-associated PCNA Expressed in Breast Cancer Has Therapeutic Potential"
U.S. Army

Andrew Saykin, PsyD
"Effect of Manganese Exposure on GABA and Glutamate in Human Brains by MRS"
Purdue University

Michael Vasko, PhD
"An Intracellular Signaling Switch for Maintaining Peripheral Sensitization"
NIH-NINDS

Fatigue"
Walther Cancer Foundation