



September 2009

## **IU researchers boost research and jobs with stimulus legislation grants**

Indiana University School of Medicine scientists, including members of the IU Simon Cancer Center, have received more than \$12 million in grants funded by the federal economic stimulus legislation, funding that has bolstered both research initiatives and research employment on the medical center campus.

More than 40 researchers have received American Recovery and Reinvestment Act awards, ranging from a \$1.4 million National Science Foundation grant supporting innovative research on proteins to smaller awards enabling investigators to hire lab assistants for summer jobs. Approximately 75 research-related jobs have been created or saved on the IUPUI campus as a result of the grants to IUSM scientists. Other than the National Science Foundation award, all of the grants are from the National Institutes of Health.

The grants are supporting a variety of research initiatives seeking to better understand and find improved treatments for a broad range of diseases, including Alzheimer's and other neurodegenerative diseases, attention deficit/hyperactivity disorder, cardiovascular disease, osteoporosis, and others.

IU has created a Web site -- [www.stimulus.iu.edu](http://www.stimulus.iu.edu) -- to provide information about all federal grants the university has received through the economic stimulus legislation. As of Aug. 31, the university had received \$16,980,925 through 57 projects.

The following cancer center members received the following grants:

A \$1.4 million National Science Foundation grant, awarded to **Keith Dunker**, PhD, and colleagues will enable the researchers to expand a database of protein information used by scientists around the world.

The work by Dunker and his colleagues challenges the traditional view that proteins' three dimensional structures are key to determining their function. They have identified many proteins that perform crucial tasks without specific structures and in the process are opening new potential avenues to treat such diseases as cancer, heart disease,

diabetes, Parkinson's, Alzheimer's, and others.

With a \$1.5 million grant from the National Institutes of Health, a team of scientists will investigate how the vaccinia virus, which is related to the smallpox virus, alters the function of immune cells to avoid being detected by the body's immune system. Vaccinia is the virus used to create vaccines against smallpox infection, and improving the vaccine capabilities of this virus will be useful in preventing smallpox infection as well as in the design of new vaccines against cancer and other diseases. The research team includes **Janice Blum**, PhD; **Randy Brutkiewicz**, PhD; **Mark Kaplan**, PhD; and **David Wilkes**, MD. The grant will create at least six new research positions and retain the jobs of three more.

A grant of nearly \$419,000 will enable **Reuben Kapur**, PhD, to continue studying how vital cells in the bone marrow -- called hematopoietic stem cells -- renew themselves. These adult stem cells are responsible for the creation of all the body's red and white blood cells and are the key component in bone marrow and cord blood transplants used to treat leukemia, lymphomas, and other diseases. In particular, Kapur and his team will evaluate a compound that could make it easier to grow the cells in the laboratory, which could improve the availability and effectiveness of the cord blood and bone marrow transplants.

Without the grant, Dr. Kapur said, it would have been necessary to reduce his laboratory staff by three full-time positions, including two post-doctoral researchers and a laboratory technician.

Dr. **Kaplan** also received \$385,000 to continue research in the body's immune system to better understand the genetic and cellular processes that produced inflammation in such diseases as Type 1 diabetes, arthritis, and colitis. The grant, which continues work in an area Dr. Kaplan has been studying for 11 years, saved three jobs in his laboratory.

As part of the project, Dr. Kaplan and colleagues will be studying children with ulcerative colitis and Crohn's disease to determine whether the presence of different forms of a particular protein -- STAT4 -- can be used to develop a blood test for those and other immune diseases.

**Mark Kelley**, PhD, was awarded \$358,757 to research how DNA repair mechanisms are involved in neurotoxicity during cancer treatments commonly referred to as "chemobrain." The studies funded by this stimulus money will continue work he has been doing with his collaborator, **Michael Vasko**, PhD, to understand and prevent the neurotoxic side effects of chemotherapy and radiation on both central and peripheral nervous system functions.

--Eric Schoch



## *iuscc research news*

September 2009

### **Cancer research takes turn, offers potential treatment for macular degeneration**

---

IU School of Medicine research and a federal small business grant have set an Indianapolis startup company on a path to develop potential new treatments for age-related macular degeneration.

The National Institutes of Health has awarded a \$225,000 Small Business Technology Transfer (STTR) grant to ApeX Therapeutics and **Mark Kelley**, PhD., its co-founder.

The age-related macular degeneration project represents a new direction for Kelley's research, which has focused on the mechanisms cells use to repair damaged DNA and how those mechanisms can be manipulated when developing cancer treatments. In particular, Kelley's work has examined a protein called APE1 and its activities in tumor development.

A new drug to treat age-related macular degeneration would be welcome -- it is the leading cause of severe vision loss in people over age 60 and more than seven million older Americans have or are at high risk to develop advanced macular degeneration.

The type of age-related macular degeneration that causes most of the vision loss is caused by abnormal blood vessel growth in the eye, which has led to treatments using drugs designed to block blood vessel growth in cancer -- known as anti-angiogenesis drugs. No more than a third of patients get significant benefits from those drugs, however.

The pursuit of a treatment for macular degeneration came about because "we were studying the effects of an APE1 inhibitor in cancer, and we saw that it had anti-angiogenesis effects," Kelley said.

"The grant and research will provide a new dimension to the work of ApeX Therapeutics, which was founded to develop oncology related products," Martin Haslinger, PhD, chief executive officer, said.

"We're not changing the direction of the company, we're adding on."

Haslinger said the company, which has offices and laboratory space in the IU Emerging Technology Center in Indianapolis, hopes to have a compound worthy of taking to

clinical testing in about six months.

Kelley's research received support from the Indiana Clinical and Translational Sciences Institute, IU Medical Group, and ITRAC.

"This STTR grant is a culmination of how the translational research process can work -- laboratory research developments progress with CTSI assistance and are developed commercially by a local company built on school of medicine research," Kelley said.



September 2009

**Core Spotlight**

---

**Center for Computational Biology and Bioinformatics**

The Center for Computational Biology and Bioinformatics, part of the IU School of Medicine for the past two years, is a new core available to IU Simon Cancer Center members.

It brings world-class, cutting-edge research in computational biology and bioinformatics with a special emphasis on the problems of identifying the functions and structures of various protein entities in a manner that stimulates both academic and commercial collaborations.

"We're all focusing on the use of computer logarithms to help us solve problems in biology," **Keith Dunker**, PhD, director of the Center for Computational Biology and Bioinformatics, said. "That's the whole idea of the center."

The multi-disciplinary core provides a variety of consulting and collaborative research. It offers:

- Genetic association study data analysis
- Microarray gene expression
- SELDI / MALDI proteomics
- LC-MS/MS and GC-MS/MS proteomics data analysis
- Next generation sequencing
- Pharmacokinetics/pharmacodynamics modeling and trial simulations
- Protein disorder and structure prediction

The core also provides genome annotations and browsing, cross-platform analysis, database integration and management, and hourly consulting services.

Located in the HITS building, the core's director is **Lang Li**, PhD. He can be reached at 274-4332. **Dunker** can be reached at 278-9220.



September 2009

## News Briefs

### ITRAC marks its third anniversary

ITRAC (Indiana University Melvin and Bren Simon Cancer Center Translational Research Acceleration Collaboration) marks its third anniversary in October.

Emphasizing the success of this initiative and the blueprint it provides for experimental project design, ITRAC recently served as the template for the newly-created Indiana Clinical and Translational Sciences Institute (CTSI), a medical research initiative that combines the strengths of IU and Purdue universities, business, and government to swiftly transform discoveries into better patient care and business opportunities.

Since its inception, ITRAC has evolved into a philosophy to drive the IUSCC's format and programmatic integration toward achieving comprehensive cancer status. Overall, it has provided assistance to 113 cancer-focused projects, awarding more than \$1 million to therapeutic projects, biomarker projects, model development/target validation projects, and projects focusing on cancer prevention and control.

But ITRAC's success is based on more than just funding pilot projects. The ITRAC platform performs many other critical roles to help promote research at IUSCC, including:

- Assisting in the experimental design strategy & identifying bottlenecks
- Facilitating new partnerships, collaborations, working groups (such as Small Molecule Working Group; Brain Tumor Working Group and others), and project teams to develop larger clinically focused initiatives to bring research from the bench to the clinic and the clinic to the bench
- Locating needed resources (internal and external) & linking PIs with shared resources
- Identifying intellectual property
- Facilitating external research funding, including partial funding from industry

The return on investment measures prove that the resources ITRAC pulls together help move the projects from

concept to external funding. Metrics show that for every \$1 invested using internal pilot funding, the IUSCC received almost \$5 in return from external funding.

**What is ITRAC?**

ITRAC is a planning and funding process which can facilitate the development of new cancer diagnostics and therapies from the laboratory to the bedside and back. Overall, ITRAC aims to support development of innovative and improved treatments to better detect, treat and, ultimately, cure cancer.

**Contacts**

Mary Murray  
278-4956

Crystal Banks  
278-3312

In addition to assisting individual scientists, however, ITRAC benefits the overall mission of the IUSCC and its members. For example, ITRAC has assisted in the identification and formation of two cores -- In Vivo Pharmacology Core and the Chemical Synthesis & Organic Drug Lead Development Core -- since 2006.

Additionally, the Clinical Pharmacology Analytical Core (CPAC) also expanded its services to include preclinical pharmacokinetics. With the formation of these cores, investigators can use internal resources for their project needs, reducing the cost of the project and possible time delays often seen in outsourcing. Following ITRAC's project design model,

core faculty members have also formed a working group, Resource Cores Consortium, to coordinate and strength efforts across campus.

ITRAC complements a growing emphasis by the National Institutes of Health on accelerating the development and testing processes that basic science laboratory discoveries go through to become new patient treatments. The result is that the cancer center's basic and clinical scientific components are more synergistically integrated.

**Dr. Nakshatri named associate director for education**

Harikrishna Nakshatri, BVSc, PhD, has been named associate director for education at the IU Simon Cancer

Center. Nakshatri will be responsible for overseeing faculty development and training programs at the cancer center. He will also be responsible for scholarship programs, seminars, and other education events. Nakshatri also becomes a senior leader at the cancer center in which he will play a key role in setting the strategic direction, policies, and priorities of all educational and outreach activities.



Nakshatri

Nakshatri's research interests are on the mechanisms of anti-estrogen resistance and metastasis in breast cancer.



His ongoing research includes elucidating the mechanisms by which the serine/threonine kinase AKT alters estrogen signaling and confers anti-estrogen resistance.

His laboratory identified and commercialized biomarkers that may predict response to anti-estrogen therapy. His laboratory demonstrated constitutive activation of the nuclear factor kappaB in a subset of breast cancer. Activated nuclear factor kappaB confers chemotherapy resistance and enhances metastasis. An inhibitor of nuclear factor kappaB developed by his lab in collaboration with other institutions is currently in a phase I clinical trial for cancer. National Institutes of Health, Department of Defense, Susan G. Komen for Cure, and other private foundations have funded his research. He is the author or co-author of more than 80 publications.

Nakshatri earned his bachelor's degree in veterinary sciences from the University of Agricultural Sciences in Bangalore, India, and his doctorate from Memorial University of Newfoundland in St. John's, Canada. He completed his post-doctoral fellowship at the University of Louis Pasteur in Strasbourg, France.

He joined the IU School of Medicine in 1996. He has served and continues to serve on scientific review committees of the NIH, Department of Defense, and Susan G. Komen for Cure. He is also on the editorial boards of scientific journals. He is actively involved in training post-doctoral fellows, surgical residents, and medical students.

**Guise heads developing Tumor Biology and Microenvironment program**

**Theresa Guise**, MD, is a new cancer center member and co-leader of the new and developing program Tumor Biology and Microenvironment. **Wade Clapp**, MD, is the program's other co-leader.

In the program, investigators will work to understand how different environments are unique and how they provide signals to tumor cells or how tumor cells signal to those environments, according to Guise.

Guise's clinical focus is bone/soft tissue, bone marrow, breast cancer, melanoma, and urologic cancer. She has received funding for TGFbeta signaling and bone metastases, role of hypoxia in bone metastases, adrenomedullin in bone metastases, endothelins in pathological, and normal bone remodeling.

Most recently a professor at the University of Virginia, in Charlottesville, Va., Guise graduated magna cum laude from Gannon University and received her medical degree from the University of Pittsburgh School of Medicine. She completed her internship and residency in internal medicine at the University of Pittsburgh Health Center and was a fellow in endocrinology and metabolism at the University of Texas Health Science Center.



She is the recipient of many honors and awards, including a National Research Service Award and Clinical Investigator Award, both presented by the National Institutes of Health; the American Society for Bone and Mineral Research's Fuller Albright Award; and the U.S. Army's New Investigator Award.

Guise's office is located in Walther Hall, Room C-104; she can be reached at 278-6012.

### **Walther Hall dedication set for Oct. 8**

Leaders of Indiana University and the city of Indianapolis will gather on Oct. 8 to dedicate Joseph E. Walther Hall, the university's newest and largest research facility.

The 238,371-square-foot structure links the two



Walther Hall at night

research buildings at its east and west ends -- Research II and the Cancer Research Institute -- to form a three-building, 500,000-square-foot interconnected research complex on the IU School of Medicine campus. Although the building houses scientists in a broad range of disciplines, the focus of much of the research is on cancer and many of the investigators are members of the IU Simon Cancer Center.

The new building is named after the founder of the Walther Cancer Foundation, which significantly contributed to research at IU, in particular through long-term funding of such initiatives as the Walther Oncology Center at the IU School of Medicine and the Mary Margaret Walther Program for Cancer Care Research at the IU School of Nursing.

Speakers at the ceremony, which will begin at 11 a.m. in the second floor atrium of Walther Hall, will include IU President Michael McRobbie, Indianapolis Mayor Gregory Ballard, Charles Bantz, chancellor of IUPUI, D. Craig Brater, dean of the IU School of Medicine, **David Wilkes**, executive associate dean for research affairs at the IU School of Medicine, Distinguished Professor **Lawrence Einhorn**, and Ora Pescovitz, executive vice president for medical affairs at the University of Michigan, formerly executive associate dean for research affairs at the IU School of Medicine.

### **Huge Evansville response for tissue bank**

The Susan G. Komen for the Cure Tissue Bank at the IU

Simon Cancer Center collected an astonishing 1,362 blood samples in Evansville Sept. 19, breaking all previous records for number of samples collected in a day. The tissue bank now has samples from 6,642 donors, including 698 tissue donors.

### IT support specialist, research operations manager join IUSCC

- [Elizabeth Henderson](#) recently joined the IU Simon Cancer Center as a computer support specialist. You can reach her at 278-7474. With Henderson now on the IT team, Josh Nichols' focus will be Web development and server administration. His new phone number is 278-3521.
- [Kim Burrows](#) has been named the cancer center's research operations manager in Walther Hall. In this position, Burrows is responsible for oversight of all facilities-related matters, proper operation and maintenance of infrastructure systems and equipment directly tied to the operations of research laboratories. She will train staff on shared equipment, assist and/or arrange for maintenance, repair, and troubleshooting of equipment, and advise investigators and lab personnel on specialized lab operations and provisions. Burrows serves as the primary contact for building maintenance, safety, and custodial services among others. Burrows' office is C-350; her phone number is 278-9530. She holds a bachelor's degree in biology from Purdue University.

### Cancer center members in the news

- **David A. Flockhart**, MD, PhD, is the recipient of the American College of Clinical Pharmacology's 2009 Nathaniel T. Kwit Memorial Distinguished Service Award. This award acknowledges contributions in evaluating and communicating the value of pharmacogenetic testing to physicians and pharmacists in clinical practice.
- "Solving the Cancer Puzzle," in the October issue of *Men's Health*, features **Larry Einhorn**, MD, and **Bryan Schneider**, MD. [Read the story.](#)  *Men's Health* is the largest men's lifestyle magazine brand in the world, with a readership of more than 20 million, according to its publisher.
- **Rafat Abonour**, MD, sets out for his fifth consecutive [Miles for Myeloma](#), traveling 207 miles by bike from

Evansville to Indianapolis, on Friday, Oct. 2. Dubbed Trek for Treatment, this year's Miles for Myeloma concludes with a finish-line celebration at 4:15 p.m. Saturday, Oct. 3 on Vermont Street on the south side of the IUPUI Campus Center. All are invited. To date, Dr. Abonour has biked or run nearly 700 miles across Indiana and raised \$1 million for multiple myeloma research. All of the funds are used for research at the IU Simon Cancer Center. [Read news release.](#)

- **Lindsey Mayo**, PhD, recently presented at two international workshops. Mayo presented "TGFbeta1-SMAD3/4 Signaling Induces Mdm2 Expression and Correlates with Late Stage Metastatic Breast Cancer" at the International Mdm2 Workshop V held at Ghent University (Belgium). The conference focused on the emerging topics in Mdm2 and Mdmx-regulation of the p19ART-Mdm2-p53 signaling pathway during cell growth, embryonic, and cancer development. Mdm2 and key modifiers of p53 are considered promising targets for cancer treatment. Mayo presented "PTEN/p53/MASPIN Network to Suppress Angiogenesis" at the 14th International p53 Workshop held at the Crown Plaza Hotel, Fudan University in Shanghai, China.



Cindi Hart, a champion cyclist and speed skater and a two-time breast cancer survivor, chats with **Patrick Loehrer**, MD, moments before kicking off Spokes of Hope from the IU Simon Cancer Center. Cindi organized Spokes of Hope which involved a group of

people from Cyclists Combating Cancer who biked to Washington, D.C., to tell lawmakers about the importance of funding cancer research. Cindi biked more than 400 miles from Sept. 10-16. **Robert Goulet**, MD, and **Rafat Abonour**, MD, biked with Cindi to Richmond, Ind., after the kickoff.

**New grants**

- **A. Keith Dunker**,  
PhD  
"DisProt Database: A  
Central Repository of  
Information on  
Intrinsically  
Disordered Proteins"  
NSF
- **Brenda Grimes**,  
PhD  
"Disruption of  
Centromeric  
Chromatin as a  
Cause of  
Chromosome  
Instability in Breast  
Cancer"  
U.S. DOD
- **Mervin Yoder**, MD  
"Engineering  
Collagen Matrices  
that Modulate in vivo  
Vessel Formation  
NIH-NHLBI"

**New members**

- **John Chirgwin**, PhD  
*Department of  
Medicine  
Division of  
Endocrinology*  
Member, Tumor  
Biology and  
Microenvironment
- **Theresa Guise**, MD  
*Department of  
Medicine  
Division of  
Endocrinology*  
Member, Tumor  
Biology and

Microenvironment

- **Cary Mariash, MD**  
*Methodist Research  
Institute  
Affiliate*
- **Beth Pflug, PhD**  
*Department of  
Medicine  
Division of Clinical  
Pharmacology  
Member, Tumor  
Biology and  
Microenvironment*