



February 2011

## IU Personalized Medicine Institute to develop targeted, individualized treatments

**Institute led by 4 IU Simon Cancer Center members**

Indiana University has announced a major commitment to research in one of health care's most promising fields with the creation of the Indiana Institute for Personalized Medicine.

The institute's members will be drawn from the IU schools of medicine, informatics and nursing, with \$11.25 million in funding provided by the IU School of Medicine, the school's Department of Medicine, IUPUI, the Indiana Physician Scientist Initiative, and the IU Simon Cancer Center. The Indiana Physician Scientist Initiative is funded by a \$60 million grant from the Lilly Endowment.

Building on modern research techniques that have made it possible to decipher the genetic code, detect slight genetic differences between patients and determine how those affect the way the body metabolizes drugs, physicians are beginning to be able to select more appropriate treatments for individual patients. Research to make such tools broadly available remains in the early but promising stages, institute leaders said.

"Much of the future of health care is in personalized medicine, meaning more precise targeting of the right medication to the right patient at the right time," **David Flockhart**, MD, PhD, who has been named director of the institute, said.



Flockhart

"We believe it should lead to cost benefits. It clearly will be better for patients," Dr. Flockhart said.

"The Indiana Institute for Personalized Medicine is a not only a logical extension of our academic mission but is also part of our strategic plan to be a global leader in translational medicine," **David Wilkes**, MD, executive associate dean for research affairs at the IU School of Medicine, said.

Some of the earliest examples of personalized medicine have come in the field of cancer treatment. Oncologists now can test a breast cancer patient's tumor to determine not only whether it is

the type that is stimulated to grow by the hormone estrogen, but whether it is a subtype that can be treated with hormone therapy or another type that requires chemotherapy. Cardiology, pediatrics, and obstetrics also will be important areas of focus for the institute, Dr. Flockhart said.

"To identify more precisely which drugs are likely to be more effective -- or less effective and more toxic -- will have a substantial impact on optimizing health care delivery and rationally curbing costs. In no discipline is this more keenly needed than in cancer care where drugs can be extremely costly and toxic," **Patrick Loehrer** Sr., MD, director of the IU Simon Cancer Center, said.

IU scientists have been working on related research for at least a decade, but creating an institute "allows you to really jump- start research and raise the level participation of an institution in both the laboratory and in the clinic, in a broad range of research interests," Dr. Flockhart said.

For example, **Janet Carpenter**, PhD, RN, a member of the institute, sees personalized medicine playing a key role in improving the treatment of menopause.

"About 6,000 American women enter menopause every day yet personalized medicine has not been well-integrated into their health care," she said. "The institute will play a very important role in ensuring that women receive the most appropriate and effective menopausal symptom management therapies."

Mathew Palakal, PhD, associate dean for graduate studies and research at the School of Informatics noted that "research in personalized medicine spans a broad spectrum from systems biology to nanomedicine to gene therapy. Our research in such areas as systems biology, biological network analysis and proteomics, along with our graduate programs in health informatics and bioinformatics, will enable informatics and the School of Informatics to play a significant role in the success of the institute."

"This science will enable physicians to prescribe the right medicines at the right dosages and intervals to maximize efficacy and prevent unwanted toxicity. It should be a very exciting next 10 years of research," **D. Wade Clapp**, MD, said.

In addition to Flockhart, the institute's leadership will include associate directors **Lang Li**, PhD, associate professor of medical and molecular genetics and associate director of the IU Center for Computational Biology and Bioinformatics; **Jamie Renbarger**, MD, assistant professor of pediatrics, medicine, and obstetrics and gynecology; and **Bryan Schneider**, MD, assistant professor of medicine and of medical and molecular genetics. All are members of the IU Simon Cancer Center.

The new Indiana Institute for Personalized Medicine is headed by four members of the IU Simon Cancer Center:	The institute's mission is to conduct research, train new specialists in personalized medicine, and promote the translation of scientific discoveries into new more precise therapeutics for patient care.
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**David Flockhart**, MD,  
PhD, director

Associate directors are:

**Lang Li**, PhD

**Jamie Renbarger**, MD

**Bryan Schneider**, MD

[Visit the institute's Web  
site.](#)

Training new experts will be supported by the new Brater Scholarship in Personalized Medicine, which will provide funds for research to young physicians in medical fellowship training programs at the school of medicine. The first three fellows to receive Brater scholarships will be selected this summer.

To help move scientific discoveries to patient bedsides, the institute will have a panel of IU scientists who will advise researchers on steps to

take to move their research beyond the laboratory stages. The advisory panel, with 21 members initially, will be chaired by Dr. Clapp.

The institute also has an external advisory board with five members:

- Caryn Lerman, PhD, Mary W. Calkins Professor of Psychiatry and interim director of the Abramson Cancer Center at the University of Pennsylvania
- Dan Roden, MD, assistant vice chancellor for personalized medicine at Vanderbilt University
- Robert Epstein, MD, MS, president of advanced clinical science and research at Medco Health Solutions Inc.
- Shiew-Mei Huang, PhD, deputy director, Office of Clinical Pharmacology, Center for Drug Evaluation and Research at the U.S. Food and Drug Administration
- Russ Altman, MD, PhD, chairman of the Department of Bioengineering, Stanford University.



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### Antibiotic offers potential for anti-cancer activity

An antibiotic known for its immunosuppressive functions could also point the way to the development of new anti-cancer agents, IU researchers have reported.

The study determined that the compound, tautomycetin, targets an enzyme called SHP2, which plays an important role in cell activities such as proliferation and differentiation. Interestingly, SHP2 mutations are also known to cause several types of leukemia and solid tumors. The findings were reported in the Jan. 28, 2011, issue of the journal *Chemistry and Biology*.

The potential for developing anti-cancer agents grew out of an attempt to determine how tautomycetin exerts its immune suppression activities, **Zhong-Yin Zhang**, PhD, said.



Zhang

The finding is also encouraging because SHP2 is a member of a large family of enzymes called protein tyrosine phosphatases (PTPs), which are important in the signaling processes that control all essential cellular functions. Dysregulation of PTP activity has been linked to several human diseases, including cancer, diabetes, and immune dysfunctions. But their makeup has made it difficult to find potential drugs to act on them, characteristics that have labeled the PTPs as "undruggable," Dr. Zhang said.

"So we have identified a lead -- a natural product produced by the bacteria *Streptomyces* -- that should serve as a foundation for the development of therapeutic agents for a large family of protein tyrosine phosphatase targets. Until now these targets, including SHP2 for leukemia and other cancers, have been deemed undruggable," he said.

Funding for the research was supplied by the National Institutes of Health.



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Core spotlight

Bio-Plex

The Bio-Plex core provides a method that allows investigators to assay cytokines and other proteins in human, mouse, and rat serum, plasma, and cell culture supernatants, as well as nucleic acids and specific phosphorylation states of proteins.

"Almost any biological sample can be adapted for use on the BioPlex, although serum is most common," **Christie Orschell**, PhD, core director, said.

Dr. Orschell pointed out that Bio-Plex offers advantages over Western Blot and ELISA technologies. For example, with Bio-Plex, investigators can perform multiplex analysis of up to 100 different analytes in a single sample of 25uL. Bio-Plex is also faster than the other technologies.

Overall, Dr. Orschell said, "Bio-Plex is best suited for investigators who have a lot of samples to analyze."

**Bio-Plex**

**Christie Orschell**, PhD,  
director.

Questions? Contact Dr.  
Orschell at 278-2485 or e-  
mail [orschlab@iupui.edu](mailto:orschlab@iupui.edu).

The Bio-Plex Core is  
located in Dr. Orschell's  
laboratory, R3-C350  
(Walther Hall).

The Bio-Plex instrument uses a multiplex suspension array based on x-map technology. Microscopic beads, dyed with different ratios of two fluorochromes specific to the bead, are also tagged with an antibody specific for a certain target. The fluorescence of the bead-antibody-target complex is read by a red laser to identify the bead and a green laser to identify beads that have bound to a target. The level of target bound is indicated by the fluorescence intensity.

The core's equipment consists of the Bio-Plex 200 System with High Throughput Fluidics, including the Bio-Plex array reader, Pro II Wash Station automatic plate washer

(accommodating both magnetic- or vacuum-based assays), and Bio-Plex Manager Standard software for analysis.

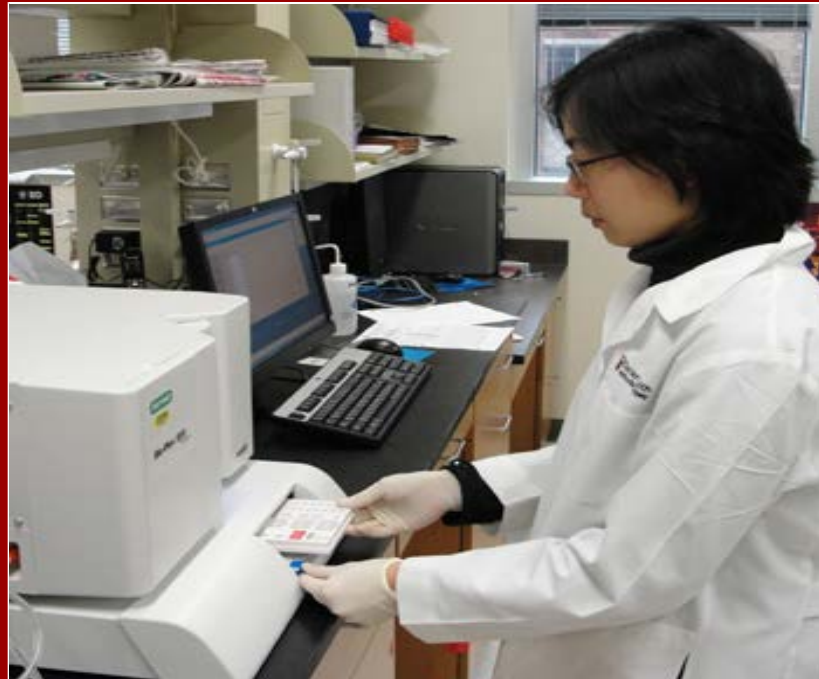
The core's staff offers:

- Communication between user and BioRad regarding kit selection, if needed
- Analysis of samples collected by users
- All reagents and buffers required to run the samples (excluding kits)
- Analysis of raw data and optimization of standard curves using

vendor software

- Delivery of data to user in an excel spreadsheet
- Preparation of report including concentration of target(s) and standard curve fit

Dr. Orschell said discounts are offered to investigators who purchase kits from BioRad, the company that manufactures the Bio-Plex 200 System. The kit includes everything needed to do an assay.



Hui Lin Chua, a post-doc in the Orschell lab, uses the Bio-Plex 200 System.



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## News briefs

### Nakshatri named interim co-program leader of breast program

**Linda Malkas**, PhD, co-program leader of the breast program, has accepted a position at the Beckman Institute at City of Hope Comprehensive Cancer Center as the associate director of basic science. Under the leadership of Dr. Malkas and **George Sledge**, MD, the breast program has grown tremendously, including the award of a Signature Center from IUPUI. **Hari Nakshatri**, BVSc, PhD, will serve as interim co-program leader of the breast program. On a related note, **Robert Hickey**, PhD, (Drs. Malkas and Hickey are married) has been named director of the translational proteomics core facility and co-director of the proteomics core facility at City of Hope.

### Indiana CTSI launches online research volunteer registry

The Indiana Clinical and Translational Sciences Institute (CTSI) - a collaboration between Indiana University, Purdue University and the University of Notre Dame -- recently launched a new Web site to increase enrollment in clinical research studies.

INresearch.org will connect individuals to cutting-edge medical research with a click of a button. Anyone who signs up will be eligible to participate in research studies at the IU School of Medicine.

A significant challenge for many translational researchers is simply finding the people most likely to benefit by trying out a new drug or discovery. INresearch.org registrants are given the opportunity to create and manage an online health profile. Volunteers whose information matches a specific study may be invited by a doctor or project coordinator to participate in a research study.

In addition to community members, faculty, staff physicians, and medical students are encouraged to join, as well as physicians to ask their patients to sign up. INResearch.org is open to everyone, including healthy volunteers and patients looking to be considered for studies focused on specific health conditions.

Volunteers may also explore available research studies prior to registration at [www.indianactsi.org/clinicaltrial](http://www.indianactsi.org/clinicaltrial).

For more information, or to sign up, visit [INresearch.org](http://INresearch.org).

## Indiana CTSI accepting proposals

The Indiana Clinical and Translational Sciences Institute (CTSI) is now accepting applications for its spring [Core Pilot Funding Program](#). The program will provide up to \$10,000 in core services from a CTSI Designated Core. Applications are due April 11. Indiana CTSI is also seeking proposals from IUSM CTSI-designated cores to support the purchase of equipment that will enhance the research environment and contribute to the research mission of IUSM and the Indiana CTSI. Up to \$100,000 is available and may be used with matching funds for larger purchases. Applications are due March 30. [Learn more](#).



## 2 cores move into space at Walther

The [Therapeutic Validation Core](#) and the [Angiogenesis, Endothelial & Pro-Angiogenic Cell Core](#) have both moved to Walther Hall, Room C343. To reach the Angio Core, call 278-7232. Call 278-6608 for Therapeutic Validation.

## Reminders

- **Membership criteria changes**

IU Simon Cancer Center membership criteria, benefits, and responsibilities have been updated. Membership in the IU Simon Cancer Center is open to full-time faculty of Indiana University or IUPUI who contribute on some level to the overall mission of the cancer center in areas of research, education, patient care, or community outreach. [Learn more](#).

- **Miss a Combined Seminar Series?**

Did you miss a Combined Seminar Series? You can now watch it online. A full listing of past Seminar Series events is [here](#). Also, speakers for the 2010-11 academic year have been announced. You can find the schedule [here](#).

- **Grants available to researchers**

For the latest grant opportunities, visit the [Funding Opportunities](#) page on the IUSCC Web site.



Tony and Andrea Pedregon (left) present a \$40,000 gift to the IU Simon Cancer Center's melanoma research program.

Andrea, wife of NHRA two-time Funny Car champion Tony Pedregon, organized the creation and sale of a wall calendar featuring the wives of NHRA drivers and the husband of female driver Ashley Force Hood. The fund-raising project was in memory of Andrea's friend, Angi Austin, who died of melanoma in 2010. **Christopher Touloukian, MD**, (third from left) and **Patrick Loehrer MD**, director of the cancer center, accept the gift. [See other photo.](#)

**Cancer center members in the news**

- In the Jan. 25 issue of [Nucleic Acids Research](#), **Jinyi Shao, MD**, **Mircea Ivan, MD, PhD**, **Daniela Matei, MD**, and colleagues propose that platelet derived growth factor (PDGF)-regulated gene transcription involves alterations in non-coding RNAs and provides evidence for a miR-dependent feedback mechanism balancing growth factor receptor signaling in cancer cells.
- **Larry Cripe, MD**, and colleagues reported in the journal [Blood](#) that lestaurtinib treatment following chemotherapy did not increase response rates or prolong survival of patients with FLT3 mutant AML in first relapse.
- **Khalid Mohammad, MD, PhD**, **Theresa Guise, MD**, and colleagues wrote: "Our results demonstrate that therapeutic targeting of TGF- $\beta$  may prevent the development of melanoma bone metastases and decrease the progression of established osteolytic lesions," in [Cancer Research](#).
- **G. Marie Swanson, PhD, MPH**, and Victoria Rakowski, RN, BS, chief operating officer of the American Cancer Society, Great Lakes Division, have released [Cancer Disparities in Indiana: An Epidemiologic Profile](#).
- **George Sledge, MD**, has been named a finalist in this year's *Indiana Business Journal's* Health Care Heroes. He is one of three finalists in the Advancements in Health Care category. The winner will be announced during an awards program March 4.



Cripe



Swanson

**New members**

- [Helmut Hanenberg, MD](#)  
*Department of Pediatrics*  
Full member, Hematopoiesis, Microenvironment, and Immunology
- [Susan Hickman, PhD](#)  
*IU School of Nursing*  
Associate member, Cancer Prevention and Control
- [Yan Liu, PhD](#)  
*Department of Pediatrics*

Associate member, Hematopoiesis, Microenvironment, and Immunology

[Brenna McDonald](#), PsyD

*Department of Radiology*

Associate member, Cancer Prevention and Control

[Kevin Rand](#), PhD

*Department of Psychology*

Full member, Cancer Prevention and Control

[Nathan Stupiansky](#), PhD

*Department of Pediatrics*

Associate member, Cancer Prevention and Control