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Fourth annual meeting spotlights transformations in biomedical research and clinical care

Sept. 11, 2012

The position of the Indiana Clinical and Translational Sciences Institute at the center of transformations in the state and national medical research and health care sectors was on display Friday, Aug. 31, during the fourth annual meeting of the Indiana CTSI.

More than 400 registrants turned out at the University Place Conference Center and Hotel for "Transforming Systems, Translating Discoveries" to hear from leaders at the National Institutes of Health, Patient-Centered Outcomes Research Institute, Eli Lilly & Co., Indiana University Health and Indiana University School of Medicine, as well as witness research and poster presentations from investigators across the Indiana CTSI partner institutions of IU, Purdue University and the University of Notre Dame.

"Health care is the biggest driver of our economy in this state, and 'transformation' is the perfect word to describe the changes taking place," said moderator David Johnson, JD, president and CEO of Biocrossroads, noting the morning's speakers put the spotlight on changes in health care policy, delivery, discovery and clinical research.

Among the presenters was Andrew Dahlem, Ph.D., vice president and chief operating officer of Lilly Research Laboratories at Eli Lilly & Co., who emphasized the Indiana CTSI's role in transforming relationships between public and private institutions by pursuing connections with the region's leaders in the pharmaceutical industry.

"The leadership at the Indiana CTSI and Biocrossroads is making the Midwest a very important and interesting place in the transformations that are going on in the pharmaceutical industry," Dr. Dahlem said. "Under [Indiana CTSI Director] Anantha Shekhar, [M.D., Ph.D.] the Indiana CTSI is leading academic researchers to further open the global opportunities of innovation, and find ways to collaborate on new and important disease targets."

David Wilkes, M.D., executive associate dean for research and August M. Watanabe Professor of Medical Research at the IU School of Medicine, also talked about the need to move from a "transactional" model of research to a "transformative" model within the academic sphere, which includes creating stronger institutional mechanisms to reward collaborative research, a key requirement in carrying out effective translational research and one of many challenges currently under review at the IU School of Medicine.

"If we are going to do big team science, how are we going to value the team?" Dr. Wilkes said. "How do you reward the second, third or tenth author on a study? We need to figure out how we are going to value everybody, not just the first and last author."

Nor is the need to encourage collaboration limited to the research arena. Daniel Evans, JD, president and CEO of IU Health addressed the trend toward creating a "medical home" model of health care, a move that requires greater cooperation among divisions within the health care industry.

"As an industry, we're excellent at being a culture of experts, not a culture of community," he said. "The system doesn't see itself as a system of care; it views itself as various silos of care. We need to collaborate with each other for common outcomes focused on the patient."

This sentiment was echoed by Robin Newhouse, Ph.D., chair and professor of organizational systems and adult health at the University of Maryland and a member of the [Patient-Centered Outcomes Research Institute](#), a non-governmental organization established by the Patient Protection and Affordable Care Act to engage patients in the health care process and assist



Anantha

Shekhar, M.D., Ph.D., director of the Indiana CTSI, opens the fourth annual meeting.



David

Wilkes, M.D., executive associate dean for research at the IU School of Medicine, addresses the audience.



Sunil

Badve, M.D., professor of pathology and laboratory medicine and medicine (center), and Yesim Gokmen-Polar, M.D., assistant scientist in medicine (right), both of the IU School of Medicine, present their work on a new diagnostic test for thymoma, a rare cancer of the upper chest.



Shelley

Johns, M.D., assistant professor of medicine at the IU School of

them in making informed health care decisions.

"The real point of PCORI is using people to transform health care processes," Dr. Newhouse said. "This approach is going to change our methods, it's going to change our designs, and it's going to change how we conduct science."

A series of scientific presentations also part of the Aug. 31 program then showcased in precise terms just how the Indiana CTSI works to move new ideas into the clinical sphere – sometimes at a remarkably rapid pace.

Malaz Boustani, M.D., associate professor of medicine at the IU School of Medicine and associate director of the IU Center for Aging Research, spoke about how his work on the [Aging Brain Care model](#) — a new paradigm for providing comprehensive care to patients at risk for dementia — made the jump from a small clinical trial to a highly effective program that has seen more than 1,000 patients in just a few years through strong support from Wishard Hospital and the [Centers for Medicare and Medicaid Services](#). He added the program's earliest funders included the Indiana CTSI.

Additional scientific presenters included Ahmed Amin, Ph.D., of Purdue University, and Mayland Chang, Ph.D., of the University of Notre Dame. Dr. Amin, co-founder and CEO of [Microfluidic Innovations](#), a start-up corporation that develops [programmable "labs-on-a-chip"](#) that can be modified to carry out a wide range of clinical tests, noted his work began as research supported in part by the Indiana CTSI. Dr. Chang, a professional specialist in chemistry and biochemistry at the University of Notre Dame, also credited the Indiana CTSI for providing pilot funds and support for a lab assistant on her work toward a compound with potential to accelerate wound healing in patients with diabetes.

The tremendous potential and pitfalls of transforming lab research such as Dr. Chang's into new compounds for clinical use is a key challenge being tackled by the National Center for Accelerating Translational Science -- the new home of the Clinical and Translational Science Award that supports the Indiana CTSI and 60 similar centers across the United States -- added Christopher Austin, M.D., scientific director of the Center for Translational Therapeutics at NIH, during the afternoon session.

"From the very beginning, NCATS was designed as a collaborative instrument," Dr. Austin said, pointing out that the pharmaceutical industry's failure rate of 99 percent of new compounds for each new drug can only be improved through systematic study and innovation, including the sort of team science and public-private partnerships encouraged by the CTSA's.

In Indiana, Dr. Shekhar said this means acting as a central force pulling together [partnerships](#) from across IU, Purdue and Notre Dame, as well as with key health care players such as IU Health, Wishard Health Services and Eli Lilly — not to mention other CTSA centers across the Midwest.

"The Indiana CTSI is leading the charge in transforming the ways in which research gets done across large organizations," he said. "This doesn't just include working with industrial partners to improve the success rate of discovering new compounds, but also academic, research and public groups to encourage preclinical innovation, education for the next generation of translational researchers and relationships in the community."

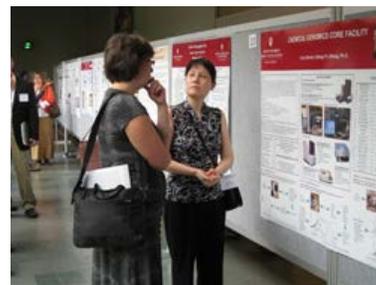
Added Dr. Austin: "This is truly a remarkable consortium. In my view, the CTSA is one of the crown jewels of NIH."

Additional information and slides from this year's annual meeting will be posted to the Indiana CTSI HUB in the coming weeks. Check back at www.indianactsi.org/news under the drop down menu labeled "Meetings" for continuing coverage.

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Medicine, discusses her research at the poster session.



Researchers discuss their work at the poster session.



Tim Ratliff, Ph.D., of Purdue; Zhong-Yin Zhang, Ph.D., of IUSM; Christopher Austin, M.D., of NIH; and Paul Helquist, Ph.D., of Notre Dame, participate in a panel discussion on therapeutics and drug discovery.



Tim Ratliff, Ph.D., director of the Cancer Research Center at Purdue, presents.

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Nanoparticles engineered at Notre Dame promise to improve blood cancer treatment

Sept. 11, 2012

With support from the Indiana Clinical and Translational Sciences Institute, University of Notre Dame researchers have engineered nanoparticles that show great promise for the treatment of multiple myeloma, an incurable cancer of the plasma cells in bone marrow. The research is described in a recent edition of [Nature's Blood Cancer Journal](#).

One of the difficulties doctors face in treating multiple myeloma comes from the fact that cancer cells of this type start to develop resistance to the leading chemotherapeutic treatment, doxorubicin, when they adhere to tissue in bone marrow.

"The nanoparticles we have designed accomplish many things at once," says [Başar Bilgiçer](#), assistant professor of [chemical and biomolecular engineering](#) and [chemistry and biochemistry](#), and an investigator in Notre Dame's [Advanced Diagnostics and Therapeutics \(AD&T\)](#) initiative.

"First, they reduce the development of resistance to doxorubicin. Second, they actually get the cancer cells to actively consume the drug-loaded nanoparticles. Third, they reduce the toxic effect the drug has on healthy organs."

The nanoparticles are coated with a special peptide that targets a specific receptor on the outside of multiple myeloma cells. These receptors cause the cells to adhere to bone marrow tissue and turn on the drug resistance mechanisms. But through the use of the newly developed peptide, the nanoparticles are able to bind to the receptors instead and prevent the cancer cells from adhering to the bone marrow in the first place.

The particles also carry the chemotherapeutic drug with them. When a particle attaches itself to an MM cell, the cell rapidly takes up the nanoparticle, and only then is the drug released, causing the DNA of cancer cell to break apart and the cell to die.

"Our research on mice shows that the nanoparticle formulation reduces the toxic effect doxorubicin has on other tissues, such as the kidneys and liver," adds [Tanyel Kiziltepe](#), a research assistant professor with the Department of Chemical and Biomolecular Engineering and AD&T.

"We believe further research will show that the heart is less affected as well. This could greatly reduce the harmful side-effects of this chemotherapy."

The group had to tackle three important problems associated with all nanoparticle-based therapies, said [Jonathan Ashley](#), one of the leading researchers of the project.

"There was some complex bioengineering involved in developing the particles. We were able to precisely control the number of drug and targeting elements on each nanoparticle, achieve homogeneous nanoparticle size distribution and eliminate the batch-to-batch variability in particle production."

Before advancing to human clinical trials, the team plans further research and testing to improve the design of the nanoparticles and to find the optimum amount and combination of chemotherapy drugs for this new treatment.

It was supported by funding from the Indiana Clinical and Translational Sciences Institute.

Courtesy the University of Notre Dame

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Başar Bilgiçer,
assistant professor of chemical and biomolecular engineering and
chemistry and biochemistry at the University of Notre Dame.

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Indiana CTSI sends first cohort of translational scholars to Australia

Sept. 11, 2012

Medical researchers and researchers-in-training from Indiana University and Purdue University traveled to Australia from June 29 to July 7 to participate in the second international exchange program between the Indiana Clinical and Translational Sciences Institute and the John Curtin School of Medical Research at the Australian National University in Canberra, Australia.

Established in 2011, the Indiana CTSI-ANU exchange program aims at creating international scholars with expertise in translational science. The program sprang from a partnership between ANU, a prestigious public teaching and research university located in the governing capital of Australia, and the Indiana CTSI, a collaborative research institute between IU, Purdue and the University of Notre Dame. The first scholars to participate in the program were selected from among several scholarship and degree programs established by the Indiana CTSI in its first four years.

"Simply the opportunity to meet our fellow faculty and learn more about how they approach translational research is very valuable," said Jon Story, Ph.D., director of the predoctoral training program at the Indiana CTSI. "Many presentations were on topics different from what we're normally exposed to."

Investigators selected to participate in the trip included two junior faculty supported by the Indiana CTSI Young Investigator (K Scholar) Award; two graduate student researchers supported by Indiana CTSI Training (T Trainee) Award; and two M.D. students from the Indiana CTSI [translational science master's degree program](#). The primary educational experience was the opportunity to participate in the Third Annual Bootes Course on Translational Medicine, "The Pathway from Discovery to Healthcare," a four-day course structured around the four phases of translational medicine – preclinical research, clinical research, translation of new discoveries into health care and policy, and global health.

"It was very inspiring to experience the whole translational research process laid out — from the pre-clinical phase to the public health phase — over the course of four days," said Melissa Kacena, Ph.D., assistant professor of orthopaedic surgery at the IU School of Medicine, noting each presenter leveraged their personal experiences as translational researchers to illustrate each stage in the process.

"Everyone knows there are certain fundamental steps to translating research; however, I also feel there are some important differences in their approach in Australia. There are certain ways they get things done that aren't the same as how we get things done. Interacting with people from different countries truly broadens your knowledge."

The other Indiana CTSI Young Investigator to participate in the trip was John P. Breinholt III, M.D., assistant professor of clinical pediatrics at the IU School of Medicine. Additional exchange participants were Rikki Enzor, an M.D./Ph.D. student in microbiology and immunology at the IU School of Medicine, and Andrew Koivuniemi, an M.D./Ph.D. student in biomedical engineering at Purdue University, and Aisha N. Davis and Renecia Watkins, both IU School of Medicine students enrolled in the translational science master's program.

"Beyond being my first chance to travel to the eastern and southern hemispheres, it was fantastic to be able to sit and meditate and listen to experts on the topic of translational medicine and policy," Koivuniemi said. "I felt this opportunity really helped me hone my perspective and purpose and will serve me very well in my career."

Other participants noted that the course provided specific examples related to the translational research process -- such as the importance of public-private partnerships to advancing scientific discoveries into the health care sphere --



Indiana

CTSI-ANU exchange scholars outside the John Curtin School of Medical Research. Front row (left to right): John Breinholt, III, M.D.; Aisha Davis; Carrie Hansel; Linda DiMeglio, M.D., MPH; Melissa Kacena, Ph.D. Back row (left to right): Bobbie Enzor; Rikki Enzor; Andrew Koivuniemi and Renecia Watkins.



The

exchange scholars listen to Paul Gatenby, MBBM, Ph.D., professor of immunology at the Australian National University.



Indiana

CTSI scholars enjoy a "power breakfast" at the Australian National University.

that have traditionally been under-emphasized in biomedical research education.

"I particularly enjoyed hearing about the process of developing a novel therapeutic and working with industry to see it reach first proof of concept in humans and clinical trials, as these are issues not often addressed in the academic setting," Enzor said. "I also appreciated the participation by people involved in the policy making process—from both academia and government."

Additional trip highlights included the opportunity to tour the Australian Phenomics Facility at JCSMR and the clinical trials unit at Canberra Hospital.

The next step in the Indiana CTSI-ANU partnership will be to welcome its first cohort of international scholars from Australia in order to create a true two-way exchange program, said R. Mark Payne, M.D., director of the Master of Science program in Translational Sciences for the CTSI, which oversees the exchange program with ANU. Next summer, the Indiana CTSI will launch a new, five-day course for this group, "Biotech: Bench to Business" which will complement the Bootes Course at ANU. The program will focus on technology transfer, seen by many as one of the Indiana CTSI's greatest strengths, whereas ANU will continue to place the greatest emphasis on their strength of adapting translational research into clinical care and public health in their course.

Other participants in the trip to Australia included Dr. Story, professor of nutritional science and associate dean of the graduate school at Purdue; Dr. Payne, professor of pediatrics and medicine and molecular genetics at the IU School of Medicine ; Linda DiMeglio, M.D., MPH, director of career development in the Indiana CTSI Research Education, Training and Career Development Program and associate professor of pediatrics at the IU School of Medicine; and Carrie Hansel, program coordinator for the Translational Science Degree Program at the Indiana CTSI. Drs. Story, Payne, DiMeglio, Kacena and Breinholt each presented a lecture at the Bootes Course in addition to participating as scholars.

The 2012 Indiana CTSI-ANU exchange program received \$50,000 in support from the Indiana CTSI and a \$10,000 International Development Fund Grant from the Office of the Vice Chancellor for Research at IUPUI.

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Indiana CTSI and West Virginia CTSI award inaugural partnerships grants

Sept. 11, 2012

The Indiana Clinical and Translational Sciences Institute and West Virginia Clinical and Translational Science Institute have granted \$100,000 to support cross-institutional research projects focused on developing treatments for alcoholism and dental anxiety.

These awards are the first granted through a new joint pilot funding program that supports research to address health and health care issues at the Indiana CTSI and West Virginia CTSI. The Indiana CTSI is one of 60 centers established by the Clinical and Translational Science Award of the National Institutes of Health to accelerate research that translations laboratory research into new treatments and therapies. The West Virginia CTSI is supported by an NIH Institutional Development Award Program Infrastructure for Clinical and Translational Research.

"The Indiana CTSI is pleased to work with our partners at the West Virginia CTSI to help usher these two promising projects into the next phase of their development," said Anantha Shekhar, M.D., Ph.D., director of the Indiana CTSI and associate dean for translational research and Raymond E. Houk Professor of Psychiatry at the IU School of Medicine. "Alcoholism and anxiety, including the fears which prevent some from accessing adequate dental care, are serious problems that require novel solutions."

Nicholas J. Grahame, Ph.D., associate professor of psychology at Indiana University Purdue University Indianapolis, and Han-Ting (Hunter) Zhang, M.D., Ph.D., assistant professor of behavioral medicine and psychiatry and physiology and pharmacology at West Virginia University, will receive \$50,000 to support their investigation into an enzyme with potential as a treatment for the treatment of alcoholism. The title of this project is "Effects of the selective PDE4B inhibitor TDP-003 on ethanol consumption and seeking behavior."

Specifically, the funds will support continued research into an enzyme that appears to be a potential drug target for reducing "alcohol-seeking behavior" in problem drinkers. Dr. Grahame will closely advise Dr. Zhang's lab on developing conditioned taste aversion procedures, while Dr. Zhang will work with Dr. Grahame on this novel and promising target for alcoholism. The combination of their expertise and facilities at IU and WVU is expected to accelerate this work. It's estimated that about 18 million Americans are affected by alcoholism.

Andrew W. Goddard, M.D., professor of psychiatry and professor of radiology and imaging sciences at the IU School of Medicine, and Daniel W. McNeil, Ph.D., Eberly Professor of Public Service and psychology and clinical processor of dental practice and rural health at West Virginia University, will receive \$50,000 to support their research on easing symptoms related to dental anxiety.

These funds will support the design of a clinical trial focused on using a combination of a skin patch designed to deliver anti-anxiety mediation and exposure therapy to reduce or eliminate the fear experienced by some patients when visiting the dentist. The title of this project is "Enhancing Exposure for Dental Phobia using D-Cycloserine." Dental fear and phobia is a common problem that prevents many patient from receiving adequate dental care and treatment.

"We would like to congratulate all the four investigators at our two institutions," said Uma Sundaram, M.D., director of the West Virginia CTSI, professor of medicine, microbiology, immunology and cell biology at West Virginia University and assistant vice president of the WVU Health Robert C. Byrd Health Sciences Center. "These projects will create significant new synergies amongst our institutions in clinical and translational research and further our



Anantha Shekhar, M.D., Ph.D., director of the Indiana Clinical and Translational Sciences Institute.



Uma Sundaram, M.D., director of the West Virginia Clinical and Translational Science Institute

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Indiana CTSI Opportunities — September 2012

Indiana CTSI fall core pilot grants — request for applications

The Indiana Clinical and Translational Sciences Institute is seeking applications from faculty whose research may benefit from technologies and expertise offered by core facilities at Indiana University, Purdue University and the University of Notre Dame.

The Indiana Fall Core Pilot grant program provides up to \$10,000 in core services. A complete list of core facilities is online; only cores denoted with a CTSI seal are eligible. The primary goal of this program is funding projects with outstanding scientific merit that can be linked to generating extramural funding or novel intellectual property.

To access complete grant guidelines and application forms, log into the Indiana CTSI [grants management system](#) using your university ID and select "Pilot Funding for Research Use of Core Facilities - 2012.10."

The application deadline is **5 p.m. Monday, Oct. 15**. This grant is available to Indiana University (IUSM, IUPUI, IU Bloomington) Purdue and Notre Dame faculty.

For more information, email Lisa Dinsmore at ictsi@iupui.edu.

Alzheimer Research Pilot Grant Program — applications open

The Indiana Clinical and Translational Sciences Institute in conjunction with the Indiana Alzheimer Disease Center is offering pilot funding to investigators developing translational research projects focused on Alzheimer disease, frontotemporal dementia or diffuse Lewy body disease, as well as other neurodegenerative or vascular dementias.

Applications related to basic mechanisms of memory, learning and cognition, or the delivery of health care services, are also welcome.

This pilot grant mechanism aims to provide funding that will allow investigators to obtain preliminary data that will likely lead to extramural funding or generate novel intellectual property. Applications are limited to \$25,000.

To access complete grant guidelines and application forms, log into the Indiana CTSI [grants management system](#) using your university ID and select "Alzheimer Research Pilot Grant Program (ARP)."

Application deadline is **5 p.m. Monday, Nov. 5**. This grant is available to Indiana University (IUSM, IUPUI, IU Bloomington) Purdue and Notre Dame faculty.

For more information, email Lisa Dinsmore at ictsi@iupui.edu.

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On the Horizon — September 2012

Second Annual Disease and Therapeutic Response Modeling Symposium

The Indiana Clinical and Translational Sciences Institute will host the Second Annual Indiana CTSI Symposium on Disease and Therapeutic Response Modeling on Nov. 13 and 14 in Indianapolis.

This two-day program will include speakers from academia, industry and regulatory agencies as well as poster presentations that will cover diverse disease areas and modeling approaches.

Speakers include Jamie Dananberg, M.D., executive vice president at Takeda Pharmaceuticals; Peter Bonate, Ph.D., senior director at Astellas Pharmaceuticals; Marc Gastonguay, Ph.D., chief scientific officer at Metrum Institute; Nick Holford, Ph.D., professor of pharmacology and clinical pharmacology at the University of Auckland; and Goñi Joaquín, a postdoctoral researcher at IU Bloomington.

Registration details will be announced soon. For more information, contact Christine McDonald at chrimcdo@iupui.edu.

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