Workforce Development

Two Clinical Investigation PhDs Granted Fall 2015

Karla Esbona and Michael Repplinger join five other students who have earned a PhD in the ICTR Graduate Program in Clinical Investigation (GPCI).

Discovery Science with Translational Implications

Karla Esbona, MS, earned the PhD after presenting her dissertation titled, *Cyclooxygenase 2 Overexpression and the Collagen-Dense Breast Tumor Microenvironment*. Patricia Keely, PhD, professor of cell and regenerative biology, and Lee Wilke, MD, professor of surgery, were her primary advisers. Esbona’s ultimate goal for this research is to develop Cox-2 inhibitors as therapies for breast cancer.

Keely comments, "Breast cancer is the most common type of cancer in American women, excluding skin cancers, with 200,000 diagnosed cases and 40,000 deaths yearly. Findings from Karla's dissertation research support a new therapeutic approach for breast cancer."

She continues, "Cox-2 inhibitors may be able to act as treatments for certain breast cancer subtypes or as preventative agents for patients with specific risk profiles, in particular tumors arising in dense breast tissue. Karla's research has great translational potential."

Esbona benefited from numerous NIH grants to Keely and to UW research centers in addition to her support from the CTSA award that funds UW ICTR and the Clinical Investigation program. Her research project received services from the UW Translational Research Initiatives in Pathology laboratory, which is supported by the UW Department of Pathology and Laboratory Medicine and UW Carbone Cancer Center.

Esbona is continuing her research in the UWCCC where she will be conducting a clinical trial based on her doctoral research. She previously earned an MS in Microbiology at UW-Madison in 2008.

Diagnostic Methods in the Emergency Department

Emergency Medicine physician Michael Repplinger, MD, MS, earned the PhD in Clinical Investigation in Fall 2015 with a dissertation titled, *Diagnosing Acute Appendicitis: Historical Trends and Future Paradigms*. Scott Reeder, MD, PhD, professor of radiology, served as his primary mentor. The ultimate purpose of Repplinger’s research was to evaluate the efficacy of magnetic resonance imaging (MRI) to diagnose appendicitis in the general population.

Reeder comments, “Although appendicitis is a commonly observed cause for abdominal pain for patients evaluated in the emergency department, the utility of various imaging modalities had never been evaluated either against each other, or versus direct clinical evaluation by physicians.”

"Michael conducted a series of four studies for his dissertation work. His goal was to demonstrate that MRI, an imaging method that requires no ionizing radiation, was equivalent in efficacy to commonly ordered computed tomography (CT) scans that use X-rays to evaluate the abdomen. Reducing medical radiation exposure, where possible, is an important public health goal,” Reeder adds.

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Changes Coming for the KL2 Scholar Application Process

The upcoming application for the 2017 KL2 Scholars will have different deadlines than in prior years. UW ICTR is changing competition due dates to allow scholars to apply for an independent K in February. K Award applicants should hear back from NIH in time for them to subsequently apply to the ICTR KL2 Scholars Program. This change is designed to assist junior investigators hampered by the NIH ban on applying for two K awards simultaneously.

Chairs and deans must still nominate candidates by Aug 1, but full applications will not be due until Oct. Both the application and the nomination process are being revised, so potential applicants and departments should stay tuned for notices describing these changes in future ICTR newsletters and on the web portal (ictr.wisc.edu/KL2Scholars).

Appointments in 2017 will not start until July, and are dependent upon a successful renewal of the NIH Clinical and Translational Science Award that supports ICTR. Questions about the program can be directed to Tisha Kawahara, program coordinator, tnkawahara@wisc.edu.

Introducing New ICTR KL2 Leader

Manish Shah, MD, MPH, has been named leader of the UW ICTR KL2 Scholars Program. Shah is an associate professor of Emergency Medicine, where he is the John and Tashia Morgridge Vice Chair for Research and Academic Affairs. Shah is a health services researcher, emergency physician, and EMS physician focusing on improving the delivery of EMS and ED care to older adults. Read more online (www.emed.wisc.edu/manish-n-shah-md-mp).
Kimberly Shoenbill, MD, MS, a dissertator in the Clinical Investigation PhD program and researcher in the Department of Biostatistics and Medical Informatics, recently earned board certification in Clinical Informatics. Clinical Informatics is a subspecialty certification offered through the American Board of Preventive Medicine and the American Board of Pathology since 2013.

Shoenbill, who took the exam in 2015, comments, “I am very excited to go forward and use the skills I have gained during my graduate work in Clinical Investigation and Biomedical Informatics. Having this board certification will increase my ability to find a position where I can use my knowledge of clinical medicine, information systems, research methods, and analytical tools to improve patient outcomes and healthcare delivery.”

“This is a wonderful achievement by an ICTR student,” says Shoenbill’s primary adviser, Eneida Mendonça, MD, PhD, associate professor of Biostatistics and Medical Informatics, and an ICTR assistant director for clinical informatics. “It reinforces both the high quality and the value of the ICTR graduate program in Clinical Investigation.”

Shoenbill’s doctoral research centers on hypertension, and uses informatics methods to analyze patients’ data from the electronic health record and associated administrative data, to better understand predictors of delays in hypertension management. This information can help health care providers tailor treatment to individuals, increase adherence to guidelines, and decrease morbidity and mortality associated with untreated disease. The American Heart Association estimates hypertension will affect 41.4% of adults in the US by 2030.

Since Clinical Informatics is a new subspecialty certification, interested individuals should carefully investigate current requirements, as eligibility standards are being phased in.

Hypertension management is the focus of Shoenbill’s clinical informatics research.

ICTR Biomedical Informatics Services

Investigators who are interested in working with electronic health records (EHR) have access to a wide array of services, ranging from simple data queries using i2b2 for cohort discovery and complex data pulls using the Clinical Research Data Service (CRDS) to obtain EHR data, to text analysis utilizing natural language processing (NLP) and machine learning.

Ongoing studies working with the ICTR Biomedical Informatics (BMI) group include research into hypertension management (see Shoenbill research description), trauma survivor outcomes, and surveillance of hospital acquired infections using NLP, among many other topics.

In addition to Clinical Informatics, ICTR BMI offers a broad array of other services to provide support to investigators in the field of bioinformatics and clinical/health research. BMI personnel provide ICTR investigators with secure and efficient information technology solutions, implementing existing tools whenever available, and developing novel methods and solutions as needed.

More information about available services is available online (ictr.wisc.edu/BMI) or by emailing ICTR BMI (bmi-ictr@hslc.wisc.edu).

Two Clinical Investigation PhDs... Continued from page 1

Repplinger’s studies culminated in a direct comparison of the accuracy of MRI versus CT to diagnose appendicitis in a prospective cohort of over 200 patients at UW Hospital.

These studies were funded by Department of Radiology Research and Development funds, an NIH K24 mid-career mentoring award to Reeder, and three competitive ICTR awards to Repplinger; a KL2 Scholar Award (2013-present), a Clinical and Translational Research Pilot (2011), and a Translational Basic and Clinical Research Pilot (2015).

Repplinger previously earned the MS in Clinical Investigation in 2012. He continues his appointment as an Assistant Professor in the UW Department of Emergency Medicine.

ICTR Graduate Program in Clinical Investigation

More information about the program is available online (ictr.wisc.edu/GraduateProgram) or by contacting Sally Wedde, Education Programs Administrator, sewedde@wisc.edu. The yearly application deadline is Feb 1.
The Morgridge Institute for Research, as part of its Metabolism Initiative, is working with UW-Madison investigators to greatly expand the scope of “mass spec” applications on campus. A new resource housed in the UW-Madison Biotechnology Center brings together a multi-million dollar investment in mass spectrometry tools from multiple sources to form a central repository to tackle large-scale investigations.

Mass spectrometers were made available from three different places: The laboratory of Josha Coon, PhD, professor of chemistry and biomolecular chemistry; Dave Pagliarini, PhD, director of the new Morgridge Metabolism Initiative; and the Great Lakes Bioenergy Research Center. The Morgridge Institute and the Department of Biochemistry provided additional funding to purchase three new mass spectrometers, as well.

Clinical and translational research increasingly uses assays based on mass spectrometry to identify molecules or groups of molecules associated with disease states. As an example, the Wisconsin Registry for Alzheimer’s Prevention, is using mass spectrometry to identify risk factors associated with Alzheimer’s disease, before clinical symptoms arise.

Did you know?

**MICHR Joins MARCH Consortium**

The Michigan Institute for Clinical and Health Research (MICHR) has joined the Midwest Area Research Consortium for Health (MARCH) ([www.marchhealth.org](http://www.marchhealth.org)). MICHR will partner with six other institutions that hold NIH Clinical and Translational Science Awards (CTSA) to facilitate multi-site research studies and cross-CTSA collaborations, promoting efficient, effective, and demographically-balanced research.

“MICHR is proud to be part of MARCH and strengthen collaborative partnerships with other CTSA in the Great Lakes area,” said George Mashour, MD, PhD, Associate Dean for Clinical and Translational Research, and MICHR Executive Director. “We anticipate accelerating additional discoveries toward better health by sharing research and expertise with one another.”

MARCH members include: Indiana University, Mayo Clinic, Medical College of Wisconsin, The Ohio State University, University of Michigan, University of Minnesota, and UW-Madison. The central administrative office is at UW ICTR.

Jennifer Bufford, MS, MARCH administrative director, notes, “We welcome our colleagues at MICHR to the MARCH consortium. Their inclusion increases MARCH resources for multi-site research with the addition of [UMClinicalStudies.org](http://UMClinicalStudies.org), a clinical research registry of 23,000 participants, and EMERSE, an electronic medical record search engine developed at MICHR.”

“Research focused on either rare diseases or demographically small populations will benefit by the expanded range of the MARCH consortium afforded by Michigan’s participation,” she notes.

Learn more about MARCH ([www.marchhealth.org](http://www.marchhealth.org)) and MICHR ([www.michr.umich.edu/](http://www.michr.umich.edu/)) online.

**New Campus Mass Spectrometry Resource Unveiled**

The Morgridge Institute for Research, as part of its Metabolism Initiative, is working with UW-Madison investigators to greatly expand the scope of “mass spec” applications on campus. A new resource housed in the UW-Madison Biotechnology Center brings together a multi-million dollar investment in mass spectrometry tools from multiple sources to form a central repository to tackle large-scale investigations.

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More information about the new resource and participating partners, is available on the Morgridge web site ([morgridge.org/newsarticle/morgridge-campus-partner-to-power-up-mass-spec-potential/](http://morgridge.org/newsarticle/morgridge-campus-partner-to-power-up-mass-spec-potential/)).

Interested investigators can contact Jason Russell, PhD, Associate Director, Laboratory for Biomolecular Mass Spectrometry, jrussell@morgridge.org.
Five New Scholars Join ICTR KL2 Program

Two openings in the UW ICTR KL2 program were filled in January by Kara Goss, MD, and Amy Fowler, MD, PhD. They will be joined in June by Sarah Panzer, MD, Robert Redfield, MD, and Olayinka Shiyanbola, PhD. Goss and Fowler’s mid-year appointments were made possible by the early departure of scholars who received grants from NIH that made them ineligible for the NIH-funded KL2 program.

Christine Sorkness, PharmD, ICTR senior associate executive director, comments, “The KL2 program is treasured by all of ICTR’s engaged faculty and staff. Every year we have the privilege of mentoring a group of extremely talented scholars in clinical and translational research.” “With each cohort, a few scholars depart the program early when their professional success makes them ineligible for continued support. It is a delightful problem to have!” Sorkness continues.

The departing scholars were Lee Eckhardt, MD (Medicine) and Federico Rey, PhD (Bacteriology), both of whom received an R01 award from NIH; Rey also received a USDA Agricultural Research Service award.

The KL2 program is a key part of the ICTR commitment to training the future biomedical workforce and provides career development, mentoring, and protected time for research to promising young investigators in clinical and translational research. Applicants hold a faculty appointment at UW or the equivalent at MCRF.

### Mid-Year Appointments

**Amy Fowler, MD, PhD**

Assistant Professor, SMPH  
Department of Radiology  
**FFNP-PET Imaging of Progesterone Receptor as a Biomarker of Endocrine Sensitivity in Patients with Breast Cancer**  
**Mentors:**  
Wendy DeMartini, MD, SMPH (Radiology)  
Robert Jeraj, PhD, SMPH (Medical Physics & Human Oncology)  
John Katzenellenbogen, PhD, U Illinois - Champaign (Chemistry)

**Kara Goss, MD**

Assistant Professor, SMPH  
Department of Medicine (Allergy, Pulmonary, & Critical Care)  
**Long Term Cardiopulmonary Adaptations After Postnatal Hyperoxia Exposure**  
**Mentors:**  
Marlowe Eldridge, MD, SMPH (Pediatrics)  
Tim Lahm, MD, Indiana University (Medicine)  
J Carter Ralphe, MD, SMPH, (Pediatrics)

### June 2016 Appointments

**Sarah Panzer, MD**

Assistant Professor, SMPH  
Department of Medicine (Nephrology)  
**Preventing Failure of Kidney Transplants: Identifying Novel Immunologic Mechanisms**  
**Mentors:**  
Arjang Djamali, MD, SMPH (Medicine)  
William Burlingham, PhD, SMPH (Surgery)  
Andreas Friedl, MD, SMPH (Pathology and Laboratory Medicine)

**Robert Redfield, MD**

Assistant Professor, SMPH  
Department of Surgery (Transplantation)  
**Characterizing Novel Therapeutic Strategies for the Prevention and Reduction of Donor Specific Antibody in Kidney Transplantation**  
**Mentors:**  
Arjang Djamali, MD, SMPH (Medicine)  
William Burlingham, PhD, SMPH (Surgery)  
Dixon Kaufman, MD, PhD, SMPH (Surgery)

**Olayinka Shiyanbola, PhD**

Assistant Professor, School of Pharmacy  
Social and Administrative Sciences Division  
**Development of a Culturally-Appropriate Medication Adherence Intervention for African Americans with Type 2 Diabetes**  
**Mentors:**  
Earlise Ward, PhD, (School of Nursing)  
Daniel Bolt, PhD, School of Education (Educational Psychology)  
Carolyn Brown, PhD, University of Texas-Austin (College of Pharmacy)
RFA for this program will be released in late 2016. The next computational tools to guide clinical trials, gather/analyze electronic health records data, or guide diagnosis. The next

Three Marshfield-UW Research Pilot Awards were awarded in Dec 2015. Projects required investigator collaboration between Marshfield Clinic/Marshfield Clinic Research Foundation and UW-Madison and use of population-based clinical data for therapeutic or basic targets or for the development of computational tools to guide clinical trials, gather/analyze electronic health records data, or guide diagnosis. The next RFA for this program will be released in late 2016.

- Tonia Carter, PhD, Project Scientist, MCRF Personalized Medicine Project
- Karen Hansen, MD, MS, Associate Professor, UW Department of Medicine
- Do Polymorphisms in the ECE1 Isoform b Promoter Associate with Osteoporosis?

The goal of this project is to identify patients and their kindred at high risk of osteoporosis, permitting early intervention. Peak bone mineral density is a critical factor determining one’s lifetime risk of osteoporosis. Despite the significant influence of genetic variability on peak bone mass and subsequent risk of osteoporosis, researchers have only identified two genes, the vitamin D receptor gene and the estrogen receptor gene, as contributing to osteoporosis. This study will test the association of the ECE1 genotype with greater risk of osteoporosis in postmenopausal women.

- Scott Hebbring, PhD, Associate Research Scientist, MCRF Center for Human Genetics
- David C Page, PhD, Professor, UW Department of Biostatistics and Medical Informatics
- Application of Pedigree Data in an Electronic Health Record for Precision Medicine

The goal is to identify clinically relevant diseases that can be predicted with EHR-linked familial data. Family history is one of the strongest predictors of a wide spectrum of diseases and may be the result of shared genetic and/or environmental factors. This project applies standard logistic regression and machine learning techniques to predict disease risk; variables that will be considered in the predictive algorithms may include age, sex, diagnoses, cohabitation, and genetic relatedness.

- Peggy L Peissig, PhD, MBA, Associate Research Scientist, MCRF Biomedical Informatics Research Center
- Yirong Wu, PhD, Associate Scientist, UW Department of Radiology
- Breast Cancer Phenotyping and Prediction using the Electronic Health Record

The aim of this project is to increase the overall efficacy of breast cancer management by targeting more intense screening and preventive measures to those women at the highest risk. These investigators will develop an innovative Breast Cancer Machine-learned Advice-based Phenotyping (BMAP) model to integrate physician expertise and machine-learned logic rules, for identifying subjects with the most harmful breast cancers from the EHR via risk prediction models.