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Recommended Citation
Washington University in St. Louis Institute of Clinical and Translational Sciences.
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Human Genetics and Genomics Core of the ICTS

The ICTS Human Genetics and Genomics (HGG) core is directed by Michael Province, PhD (Professor and Director of the Division of Statistical Genomics) and co-directed by Jeffrey I. Gordon, MD (Dr. Robert J. Glaser Distinguished University Professor and Director, Center for Genome Sciences). This core relies on existing Washington University infrastructure: the Genome Center (GC), the Center for Genome Sciences (CGS) and the Division of Statistical Genomics (DSG). The HGG provides an easy entry point to the appropriate resources from these areas that can provide the services needed to support genetics research.

HGG was established through the CTSA grant to assist investigators by providing statistical genetics input in experimental design, analysis and interpretation. Just as the ICTS Research Design and Biostatistics Group assists investigators with protocol design, database development and statistical analytics in general, the additional expertise required for genetics research is readily available through the HGG. The HGG core staff also provides significant expertise in managing the unique problems of manipulating large datasets for genetic studies on a recently-upgraded computer cluster.

HGG efforts include:

- Providing study design, power and sample size calculations, and pilot data analysis for ICTS clinical investigators preparing to submit grant applications involving genetic epidemiological or translational genetics studies.
- Reaching out to clinical researchers and advertising the availability of statistical genomics collaborative opportunities through the Division of Statistical Genomics website (https://dsgweb.wustl.edu)
- Conducting a bi-weekly Statistical Genetics Methods Forum seminar to provide a forum for investigators to keep abreast of the latest methodologies. In fall 08 the focus was statistical methods for the analysis of Genome-Wide Association Scan (GWAS) and in spring 09 the focus was on methods for analyzing the microbiome. (The forum is currently on summer break and will resume in fall 09).

Message from the Director: Kenneth S. Polonsky, MD

I recently had the pleasure of speaking to an audience of enthusiastic pre and postdoctoral trainees and scholars during the Career Development Retreat hosted by the ICTS Clinical Research Training Center. Using diabetes as the example, I reviewed many opportunities that span the range from basic T1 investigations into insulin secretion and insulin action to the need for proof-of-concept experiments that explore novel approaches to this disease in the clinic to the role of large scale populations studies aimed at prevention and early detection and treatment. Similar opportunities exist for exciting research in many different human diseases.

My suggestion to these young scientists exploring research as a career was first to determine where their interests and skills lie and then to try and identify appropriate mentors who can help them acquire the skills necessary to be successful in their research. I believe that the ICTS has established an outstanding infrastructure to help trainees launch successful careers in clinical and translational research.

In this issue of the ICTS News we have included the names of the new KL2 scholars recently accepted into the ICTS Clinical and Translational Research Training programs. As these new investigators grow in experience, we are hopeful that the resources supported by the ICTS and the evolving CTSA consortium can facilitate their impact on the health of our communities.
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- Constructing a Statistical Genetics Analysis Results database with GWAS results from the NHLBI Family Heart Study, the Framingham Heart Study, the Johns Hopkins Family Heart Study and the Tumor Sequencing Project. These databases currently contain GWAS analysis results for over 1 million SNPs on over 10,000 subjects on hundreds of complex traits and diseases, mostly in heart disease and cancer domains. Keeping in mind the considerable human subjects/IRB issues that must be addressed, the HGG is attempting to find the best way to make these data available to all ICTS investigators.

HGG is also involved in a number of cross-CTSA projects. For example, HGG created the Genetic Analysis Workshop 16 semi-simulated dataset (a Genome-Wide Association project) and loaded this into NCBI's public warehouse dbGaP. This was a semi-simulated dataset, based upon GWAS SNPs from the Framingham Heart Study, in which a complex pathway of longitudinal phenotypes was simulated, based upon the lipid pathway and its effect on atherosclerosis/heart disease.

These data were used in the Genetic Analysis Workshop 16, hosted by the DSG in St. Louis in the fall of 2008, and attended by 350 statistical geneticists world-wide. It provided a mechanism by which to test and compare the performance of the newest statistical genetics analysis methods for Genome-Wide Association, epistasis, and the cumulative impact of rare and small effect genetic variants on complex phenotypes.

The HGG core is most interested in assisting ICTS investigators in developing new projects and in forming new long term collaborations in dissecting the genetics of complex traits and defining the role of genetics in personalized medicine. For assistance with genomics research involving patient populations, contact Human Genetics & Genomics at 314-362-1096 or ictsgenetics@dsgmail.wustl.edu.

Animal Resource Centers Funded by NIH

The NIH National Center for Research Resources (NCRR) has funded three animal resource centers: (1) the Mutant Mouse Regional Resource Center (MMRRC; http://www.mmrrc.org), (2) the National Rat Resource and Research Center (RRRC; http://www.nrrrc.missouri.edu/), and (3) the National Swine Resource and Research Center (NSRRC; http://www.nsrrc.missouri.edu/). These centers provide mouse, rat and pig models for biomedical research.

These animal resource centers will collaborate with CTSAs to use existing or create new animal models for preclinical trials of newly developed drugs and attempts to increase the speed of drug screening and enable faster identification of drugs that would fail in human trials. See the websites for further information.

In the News

The NIH's National Center for Research Resources (NCRR) announced on July 14 that 7 new institutions were awarded clinical and translations science awards (CTSAs) and would join the national consortium. Institutions to receive funding are the Medical University of South Carolina, Mount Sinai School of Medicine, New York University School of Medicine, University of Arkansas for Medical Sciences, University of Florida, University of Illinois at Chicago, and University of Texas Medical Branch. To see descriptions about the awardees, visit the website (www.ncrr.nih.gov/ctsa2009).

The NCRR also released its CTSA program progress report for 2006-2008. To learn more about CTSA institutions or read about Washington University's activities, visit the website (www.ctsaweb.org).

Mario Castro, MD, MPH, Associate Professor of Medicine and Pediatrics at WU, and Co-Investigator for the ICTS Community Engagement program, has been featured in local and international publications as the PI of a clinical study for treating asthma by bronchial thermoplasty via the Alair® System from Asthmatx. Trials of 297 patients in six countries showed that the treatment worked in 79% of the patients and cut emergency room visits. Reuters picked up the story on May 18, "Device helps ease severe asthma without drugs," and since then both international (ABC Science, May 19, Australian Broadcast System) and local publications (The St. Louis American, May 27) have featured the research, as well as a July 15 media segment on KTVI-Fox 2.

Terry Murray, PhD, Associate Professor and Dean of the ICTS partner institution, the Saint Louis University School of Nursing, was featured in the St. Louis American (“SLU dean lays out workforce development plan at MFH conference,” June 4, 2009). The article explored her innovative hands-on model for nursing education, a Dedicated Education Unit at St. John's Mercy Medical Center. Murray spoke about her model at the Missouri Foundation for Health Summit in June.
First National Predoctoral Clinical Research Training Meeting Held at Washington University in St. Louis

There has never been a venue for predoctoral clinical and translational research trainees to come together to share research findings, experiences, and networking opportunities. That changed this spring when the ICTS Clinical Research Training Center (CRTC) hosted the first National Predoctoral Clinical Research Training Program Meeting on May 4-5, 2009 at Washington University in St. Louis. Even when the NIH became unable to fund the conference due to budgetary constraints, that did not deter the Predoctoral Program director, Dr. Jay F. Piccirillo, co-directors Drs. Evan Kharasch and Michael DeBaun, or coordinator Dan Detlefsen and project assistant Joe Wilson from making the meeting a reality. They picked up the phone, sent emails, and found sponsors at WU who were willing to support the inaugural meeting. The Office of the Dean at the School of Medicine, the ICTS, Barnes-Jewish Hospital Foundation, and the WU Departments of Internal Medicine and Pediatrics became the meeting’s sponsors.

As the program directors and staff planned the meeting they found they had a much larger task of identifying predoctoral training programs across the country and building a network for communication. “The prep was extensive,” says Dan Detlefsen, “but we never lost sight of our goal to bring trainees together so they could interact and share their research. This meeting was not about the administrators, it was about the trainees.” The predoctoral trainees appreciated that their research was the focus. There were 132 trainees and program directors, from 25 institutions, in attendance. “I was surprised by how enthusiastically the trainees interacted with one another,” says Dr. Piccirillo. “Their research was being recognized by their peers, as well as directors and mentors, so they engaged at a high level.”

Chancellor Mark S. Wrighton opened the meeting with a discussion of the importance of multidisciplinary clinical and translational research to the improvement of the nation’s health. Keynote speakers continued to set that same tone each morning. George Macones, MD, MSCE, the Mitchell and Elaine Yanow Professor and Chair of the WU Department of Obstetrics and Gynecology, spoke on “How to Succeed in Science.” David B. Wilde, MD, PhD, the Medical Director for the Division of Clinical Research Resources at the NCRR, spoke on “Effective Mentoring.”

The meeting’s format engaged the scholars in both formal and informal ways. Formally, students presented their research in poster sessions and oral presentations. Program directors chose their top three trainees to present their work orally for ten minutes in faculty-moderated sessions. The poster session was held in the Farrell Learning and Teaching Center on the first afternoon and a panel of past trainees spoke about “Life After the Predoctoral Program” on the second day. Participants commented in the evaluation that it was an “opportunity to see the work of the students both in their oral presentations and their posters” and both helped create connections for potential collaborations. Another attendee commented: “After speaking with several trainees I was surprised by the similarities in our research. I plan on contacting a few fellows to see how their project develops over the next several months.” Informally, the trainees got to have fun while at dinner at the City Museum in downtown St. Louis the first evening. The museum, known for its unique, innovative, and participatory setting promoted interaction during dinner, where students and program directors from different institutions were seated together. In addition, tours of the various hospitals, labs and clinical cores at the WU Medical Center provided views of the state-of-the art facilities.
The ICTS welcomes 7 new clinical research scholars to the ICTS KL2 2009 cohort. The ICTS KL2 Career Development Awards are aimed at fellows, post-doctoral scholars, and junior faculty who are committed to multidisciplinary careers in clinical and translational research. Scholars must have support from their department to devote 75% of their time to clinical research training over the course of 2 to 3 years. Scholars work toward degrees in clinical investigation (MSCI), public health (MPH or MSPH) or coursework that furthers their research. Scholars have two mentors, a primary and secondary, from different disciplines to advise them and oversee their progress. The program is funded by the NIH CTSA grant KL2 RR024994, the Institute of Clinical and Translational Sciences, Barnes Jewish Hospital Foundation, and St. Louis Children’s Hospital. The new KL2s join a cohort of 11 continuing scholars. Scholars selected to the program as of July 2009 are:

**Li-Shiun Chen, MD**  
Instructor, WU Department of Psychiatry  
**Mentors:** Laura J. Bierut, MD, and John P. Rice, PhD, both Professors of Psychiatry  
**Research:** The Interplay of Genetic and Environmental Risks in Nicotine Dependence

**Andria L. Ford, MD**  
Instructor, WU Department of Neurology  
**Mentors:** Jin-Moo Lee, MD, PhD, Associate Professor of Neurology and Colin P. Derdeyn, MD, Associate Professor of Radiology  
**Research:** MR-Derived Cerebral Oxygen Metabolism as a Predictor of Infarction

**Erin R. Foster, OTD**  
Instructor, WU Program in Occupational Therapy  
**Mentors:** Tamara Hershey, PhD, Associate Professor of Psychiatry, and Joel Perlmutter, MD, Professor of Neurology  
**Research:** Relevance of Cognitive Impairment in Parkinson Disease to Function in Daily Life

**Raksha Jain, MD**  
Instructor, WU Department of Medicine, Division of Pulmonary and Critical Care  
**Mentors:** Steven L. Brody, MD, Associate Professor, Medicine, and Mario Castro, MD, MPH, Professor of Medicine and Pediatrics, both in the Division of Pulmonary and Critical Care  
**Research:** Hormonal Influences on Mucociliary Clearance in Airway Diseases

**Jonas Marschall, MD**  
Instructor, WU Department of Medicine, Division of Infectious Diseases  
**Mentors:** Jeffrey Henderson, MD, PhD, Instructor, and David K. Warren, MD, MPH, Assistant Professor, both in the Department of Medicine, Division of Infectious Diseases  
**Research:** Host and Microbial Factors Associated with E. Coli Urinary Source Bacteremia

**Shelby Sullivan, MD**  
Instructor, WU Department of Medicine, Division of Gastroenterology  
**Mentors:** Samuel Klein, MD, William H. Danforth Professor of Medicine and Nutritional Science, Chief, Division of Geriatrics and Nutritional Science, and John O. Holloszy, MD, Professor and Director, Section of Applied Physiology, Department of Medicine, Division of Geriatrics and Nutritional Science  
**Research:** Exercise Dose and Nonalcoholic Fatty Liver Disease

**Allison Wright Willis, MD**  
Assistant Professor, WU Department of Neurology  
**Mentors:** Brad A. Racette, MD, Professor, WU Department of Neurology, Vice Chairman, Clinical Affairs and Mario Schootman, PhD, Associate Professor of Epidemiology and Medicine; Chief, Division of Health Behavior Research  
**Research:** Parkinson’s Disease and Heavy Metal Exposure: A Community Spatial Epidemiology Study
Was the meeting a success? Of those who filled out evaluations, 97% thought the meeting was personally useful and 98% said they would recommend the meeting to next year’s trainees. New predoctoral students throughout the country will have that opportunity as the CRTC staff is already planning the Second National Predoctoral Clinical Research Training Meeting to be held again at WU on May 3-4, 2010.

The ICTS Clinical Research Training Center TL1 predoctoral program provides training in patient-oriented research to predoctoral students in medical and other allied health professions through didactic coursework, mentored training, work-in-progress research discussions, and journal clubs and conferences. The program offers two tracks: a short-term (summer) research core and an intensive (one-year) research core. Trainees represent a wide variety of clinical disciplines including neurology, surgery, pediatrics, infectious diseases, pulmonary and critical care, emergency medicine, speech pathology, physical therapy, occupational therapy, hematology, oncology, OB/GYN, and anesthesiology. ICTS partner institutions, Saint Louis University, Southern Illinois University Edwardsville and the St. Louis College of Pharmacy, have had trainees accepted into the program. Funding for this predoctoral program is provided by the NIH CTSA grant TL1 RR024995, the Institute of Clinical and Translational Sciences, the Office of the Dean at the School of Medicine, and the St. Louis College of Pharmacy.

For more information visit the conference website and for information about the ICTS Center for Clinical Research Training Predoctoral Program visit the CRTC website or contact Dan Detlefsen at ddetlefs@dom.wustl.edu.

ICTS Administrative Data Core: SEER Medicare Database

The recently established ICTS Administrative Data Core (funded in June, 2009 through the BJHF/ICTS RFA) is committed to helping ICTS members use the SEER Medicare databases for health services and outcomes research. The individual cancer databases are robust resources with administrative data and detailed information on cancer stage, diagnosis and treatment. Individual databases are available through the National Cancer Institute (NCI) for a variety of malignancies, including head and neck, colorectal, pancreas, lung, breast, uterus, ovary, prostate, kidney/renal, lymphoma, bladder, liver, and other cancers.

The Core currently has SEER-Medicare data for the breast cancer population from 1999-2004, with permission to link the data to information about the facility where surgery was performed. These data can be used by other ICTS researchers after NCI approval of the protocol, data use agreement, and request form for release of restricted hospital variables. The ICTS Administrative Data Core will assist investigators in obtaining NCI approval and in management of the data. The Core will assist with writing code to identify relevant populations, recoding variables, identification of comorbidities, and other data management issues.

The National Cancer Institute is offering a training course on November 16 and 17 in Bethesda, Maryland. This training program provides valuable insights into the data tables, variables and best approaches for data management and analysis for researchers interested in using these data. The course has already sold out but we will keep you informed when they may offer another.

For more information on the ICTS Administrative Data core, contact Margaret Olsen, MPH, PhD (molseg@wustl.edu) or Victoria Fraser, MD (vfraser@wustl.edu).
May 28: Site visit by The UCSF Clinical and Translational Science Institute. The University of California at San Francisco's CTSI Co-Director, Deborah Grady, MD, MPH, and Executive Director, Susan Autry, MBA, spent the day visiting WU's ICTS to learn more about the Recruitment Enhancement Core (REC) and other components of the ICTS Center for Applied Research Sciences (CARS). They met with CARS Director, Sam Klein, MD, and its Co-Director, John Newcomer, MD, who also handles regulatory support services, and discussed training and other infrastructure topics with ICTS's leaders -- Director Kenneth S. Polonsky, MD, and Co-Director Bradley Evanoff, MD, MPH.

June 25: Center for Applied Research Sciences: Brown Bag Seminar featured two ICTS core directors, Rakesh Nagarajan, MD, PhD, from the Center for Biomedical Informatics (CBMI) and Ken Schechtman, PhD, from the Research Design & Biostatistics Group (RDBG).

June 26: ICTS Clinical Research Training Center: The CRTC hosted the 3rd Annual Career Development Retreat. Speakers from WU included Kenneth S. Polonsky, MD, Aldolphus Busch Professor and Chairman, Department of Medicine, and Director, WU ICTS; Jeffrey F. Peipert, MD, PhD, Robert J. Terry Professor and Vice Chair of Research, Department of Obstetrics and Gynecology, and Thomas M. De Fer, MD, FACP, Associate Professor of Medicine, Director, Internal Medicine Clerkship and the ACES Program.

Have you Met? from Page 4

The KL2 Career Development Awards program is now seeking applications for awards beginning July 2010. The program encourages applications from a variety of disciplines as well as junior researchers from ICTS partner institutions. Scholars receive 75% salary support (up to $75,000/per year) for a minimum of two consecutive years, tuition for graduate coursework, and $25,000 per year for research related expenses. For more information contact Alison Ebers, Program Coordinator, at 314-454-8255 or aebers@dom.wustl.edu.

KL2 Information Session. Clinical Research Training Center, 2nd Floor, Wohl Clinic. Sessions to learn about the program and how to apply will be held on Tuesday, August 11: 3:30-4:30 p.m. and Wednesday, August 19: 10:00-11:00 a.m. The deadline for applications is September 30. RSVP requested but not required to 314-454-8224 or mfavazza@dom.wustl.edu

Save the Date—September 30 (4:00–6:00) Clinical Research Training Center, 2nd Floor, Wohl Clinic. A reception for the Career Development Awards, Post-doctoral, Predoctoral and Doris Duke Programs. RSVP requested, but not required, by September 23 to mfavazza@dom.wustl.edu or 314-454-8224.

Call for Papers—Science Translational Medicine. A new journal by the publishers of Science will post their first issue in October 2009. Elias A. Zerhouni, former Director of the NIH, will serve as its Chief Scientific Adviser, along with a distinguished interdisciplinary advisory board, including Jeffrey I. Gordon, MD, ICTS Executive Committee member. Visit their website to learn more about submitting your research.

Publishing Partnerships for the Society for Clinical and Translational Science (SCTS). The SCTS has entered into an agreement with the journal Clinical and Translational Science (CTS), published by Wiley-Blackwell, as its official peer-review publication. WU is a founding member in the SCTS, a national society which supports the CTSA consortium and its researchers. SCTS has also become a partner in CTSciNET, a social networking software system for junior investigators.