The American Physiological Society selects University of Toledo's Dr. Bina Joe as the new Editor-in-Chief

Congratulations to Dr. Bina Joe, who will be the incoming Editor-in-Chief of one of the journals of the American Physiological Society, Physiological Genomics. Dr. Joe’s appointment begins officially on July 1, 2015. Physiological Genomics publishes the results of a wide variety of experimental and computational studies from human and model systems to link genes and pathways to physiological functions (http://physiolgenomics.physiology.org/).

Dr. Bina Joe is a Professor of Physiology and Pharmacology and the founding Director of the Center for Hypertension and Personalized Medicine at the University of Toledo College of Medicine. She is also a Fellow of the American Heart Association. She received her Ph.D. from the University of Mysore in India. After a brief postdoctoral fellowship at the Indian Institute of Science in Bangalore, she worked briefly in AstraZeneca India before moving to the United States as an International Fogarty Scholar to conduct Molecular Genetics research on Arthritis in the Intramural Research Division of the National Institutes of Health, Bethesda, MD. For the past 15 years, she has been instrumental in leading the Research Program on the Physiological Genomics at the University of Toledo. Her research centers on the Genetics of Hypertension, which is continually funded through multiple grants from the NHLBI/NIH. She is the recipient of several Research Awards including the Young Scholar Award from the American Society of Hypertension and the Lewis K. Dahl Memorial Lecture Award from the American Heart Association Council on Hypertension. Her research work is published in several top tier journals including PNAS, Cell and Nature Communications. Dr. Joe has mentored several Research Assistant Professors, postdoctoral fellows and graduate students, many of whom have won various accolades in their careers. She continues to serve on multiple NIH and other International review panels, is the Scientific Organizer of several International Conferences in USA and in UK and is currently engaged in various leadership activities to promote Research in her Institution. Besides being an internationally recognized Researcher, she has taken on multiple leadership positions within the American Physiological Society and the American Heart Association. Notably, she has contributed substantially to the development of the Physiological Genomics group of the American Physiological Society and was recognized with a Distinguished Service Award. Bina has been a member of the APS for over a decade, has served on the Editorial Board of Hypertension and been the Associate Editor for Physiological Genomics.
Where are you from? What are your ancestral roots?
Your DNA has the answers

Ahmed Al-Khudhair

Human DNA or, as we call it, "The book of life" (also called "the human genome") is key to revealing more about human ancestral and ethnic roots. The genomes of 1092 individuals, from 14 groups of people with different ethnic and geographical profiles, was carefully examined in the bioinformatics lab at the University of Toledo Health Science Campus. As reported in a recent project publication (Inference Of Distant Genetic Relations In Humans Using "1000 Genomes"; www.ncbi.nlm.nih.gov/pubmed/?term=25573959), our lab successfully developed new computational tools to explore the whole human genome to characterize the patterns of genetic differences, and also to precisely infer genetic relationships that go back as far as nine generations (your great-great-great-great-great-great-great grandparents).

The main challenge in carrying out this research project was that each human DNA profile includes over 3 billion lines of information, which equates to terabytes of data. This amount of data could easily overwhelm and paralyze any typical desktop operating system, but our bioinformatics tools and programming languages allowed us to handle this massive amount of data. We successfully compared nearly 100,000 pairs of individuals, and determined the patterns of these differences. We found that any two individuals of Asian origin have about 3.5 million differences between their genomes. More differences were found between any two persons of European origin (about 3.8 million). But the highest number of differences was between individuals of African origin (over 5 million). This tends to support other evidence that humans originated in Africa, with smaller groups emigrating to populate the other continents. The study also found a wider range of genetic differences among individuals of American origin (about 4 million), which can be attributed to the recent mixing of populations in the New World. Any person interested in discovering his or her continental origin can simply compare their DNA to the other 1092 individuals in the project.

The project also introduced a new approach that precisely infers familial relationship. This approach was based on the total number of rare variants shared between any two individuals. Rare variants were most likely acquired in recent generations. For any two individuals, the closer the familial relationship, the larger the number of rare variants shared between them. Our investigation precisely confirmed 40 known familial relationships. Furthermore, 271 pairs of individuals were predicted to be relatives as far back as nine generations. The amount of data, the number of individuals involved in this project, and the bioinformatics approach we used, significantly increased the prediction sensitivity, which created a base for useful molecular genetics techniques in criminal investigations, civil familial searching, as well as for population, clinical, and association studies.

Ahmed Al-Khudhair completed a MSBS degree in the Bioinformatics & Proteomics/Genomics program at the University of Toledo College of Medicine and Life Sciences. He is currently pursuing a PhD degree in the Cardiovascular and Metabolic Diseases track in the Biomedical Sciences Graduate Education program at the UT College of Medicine on the Health Science Campus. For more information, contact Ahmed.Alkhudhair@rockets.utoledo.edu
Clinical Research Snippets

Anand B. Mutgi, MD
Sadik A. Khuder, PhD

This month we bring to your attention another article with a preventive medicine theme.

Diabetes treatment guidelines emphasize good glycemic control. A target level of 6.9% or lower (glycated hemoglobin level ≤52 mmol per mole) is recommended and is considered to be associated with a lower risk of diabetic complications. This study investigated the excess risks of death according to the level of glycemic control in a Swedish population of patients with type 1 diabetes. The investigators utilized the Swedish National Diabetes Register, which includes information on risk factors, complications of diabetes, and medications in patients 18 years of age or older. Patients with at least one listing between January 1, 1998, and December 31, 2011, were included in the study. For the first registration of each patient with type 1 diabetes, five unregistered controls matched with the patient for age, sex, and county were randomly selected from the general population in Sweden. The study included 33,915 patients with type 1 diabetes and 169,249 controls matched for age and sex.

The results show that for patients with type 1 diabetes, who had on-target glycemic control, the excess risk of death from any cause or from cardiovascular disease did not decrease over time and the risks were still more than twice the risks in the general population. For patients with diabetes who had very poor glycemic control, the risks of death from any cause and of death from cardiovascular causes were 8 and 10 times as high, respectively, as those in the general population.

The authors noted that patients with type 1 diabetes generally do not have excess rates of obesity, hypertension, or hypercholesterolemia1 and the increased risks of death among patients with type 1 diabetes who have good glycemic control is unexplained. In discussing the limitations of the study, the investigators...
acknowledged that the history of glycated hemoglobin levels was not complete for many patients. Therefore, the finding of this study may not be applicable to patients who have consistently good glycemic control from the time of diagnosis onward. It is possible that a history of poor glycemic control is associated with increased cardiovascular risk. Second, patients with type 2 diabetes were not excluded from the control group. Third, investigators could have underestimated diabetic coma as a cause of death, since the majority of unspecified diabetes-related deaths occurred outside the hospital. As noted, hypoglycemia is difficult to document in real-life studies, since patients with hypoglycemic symptoms do not always measure glucose levels.

The results of this study contrast with those of earlier published studies in that the risk of death was greater among patients with type 1 diabetes and normal albuminuria than among controls. The author noted that an increased glycated hemoglobin level remained a powerful risk factor for death after adjustment for renal complications, indicating the presence of a substantial residual risk associated with poor glycemic control.

**New clinical trials**

**PROSPER** - Patient-centered Research into Outcomes Stroke patients Prefer and Effectiveness Research  
Dr. Tietjen - Neurology

Extension Study to Evaluate the Long-Term Safety and Efficacy of Elagolix in Subjects with Moderate to Severe Endometriosis Associated Pain  
Dr. Neuhoff - Obstetrics and Gynecology

Connect® MDS/AML: The Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML) Disease Registry  
Dr. Verghese - Medicine

**UT DHRP-IRB Workload & Statistics**

Carolyn Pinkston, MPH, RN, CIP

The Department for Human Research Protections (DHRP) and Institutional Review Boards (IRBs) are charged with the responsibility of reviewing all human research conducted at The University of Toledo. This task includes all student-driven, education related research; undergraduate, graduate and post-graduate, all faculty initiated (unfunded) research and all industry sponsored studies. The research is reviewed by the appropriate IRB; Social, Behavioral and Educational IRB or Biomedical IRB. Research submitted to one of the two internal IRBs is reviewed per federal regulation and institutional policies in one of the following categories:

**Not Human Subject Research** - research involving de-identified human data or specimens is considered Not Human Subject’s research. The IRB provides a determination and documentation for the researcher in those situations

**Exempt** - The IRB is responsible for making a determination whether research is Exempt under one of the six categories in 45 CFR 46.101(b). If the research is determined to be exempt, the regulatory provisions in the remainder of 45 CFR part 46 do not apply and further review is not necessary. However, when research is exempt from regulatory requirements under the Common Rule, institutions and investigators still have a responsibility to adhere to the underlying ethical principles for research involving human subjects.

**Expedited** - Research in this category involves activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the eight categories defined by regulation. This category of research activity may be reviewed by the IRB via the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110.

**Convened** - All research conducted by faculty, staff, or students that does not meet Exempt or Expedited criteria, (> than minimal risk), must be reviewed by a Convened IRB in accordance with DHHS regulations 45
CFR Part 46 and FDA regulations CFR Title 21 Part 56. In order for the research application to be approved, the majority of those members present at the meeting must agree to approve the research.

**Board Administrative Actions** – This area of activity involves the processing of study closures, final reports, reminder notices, Chair responses, Not Human Subject Research determinations, the review of Adverse Events and other items or issues requiring documentation, consultation and signature of the IRB Chair for inclusion in the research file.

**Additional protections required for vulnerable populations under 45 CFR 46.** Beyond the basic elements for the protection of human research subjects described in **Subpart A**, research involving vulnerable populations must meet additional stipulations prior to initiation.

**Subpart B** - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
**Subpart C** - Additional Protections Pertaining to Research Involving Prisoners as Subjects
**Subpart D** - Additional Protections for Children Involved as Subjects in Research

**External Research and CIRBs**
The University is engaged in numerous IRB Agreements with external entities. These collaborative and cooperative research agreements require additional time and effort to remain compliant with federal requirements and institutional policies.

In addition to the internal IRBs, some industry sponsored research may also be reviewed by one of the two Central IRBs with whom the University has an agreement, the Western IRB (WIRB) or Schulman and Associates IRB (SAIRB).

The following diagrams provide an overview of the volume of research reviewed by the UT IRBs:
Kuali Coeus “KC” Electronic IRB Application Trainings

Training for the KC research application process has begun! Research and Sponsored Programs in collaboration with the Department of Human Research Protections are beginning to roll out the new electronic IRB application system. The new submission process will allow Principal Investigators to initiate new human subject research protocol applications, amend, modify and request renewals for existing protocols and view exactly where their study resides in the approval process via direct computer access.

Attendance is on a first come first served basis, please reserve your seat in advance of the training date as access permissions must be arranged.

Classes are scheduled on the Main Campus as follows:

**Memorial Field House Computer Lab, Room 1240.** Please email IRB.SBE@utoledo.edu with your seat reservation request.
Classes are scheduled on the Health Science Campus as follows:

**Collier Building, Room 1210.** Please email Jamie.VanNatta@utoledo.edu or call 383-6651 with your seat reservation request.

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**Contact Us**

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