

GEMS Spring Meeting Monday, April 27th, 2015 EPA, room C111 (RTP Main Campus)

Understanding How Genetic Variation Modifies Responses to Environmental Exposures

Program

| 8:30 - 8:45 | Registration |
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| 8:45 - 9:00 | Welcome Channa Keshava, Ph.D., GEMS President, EPA Stephanie L. Smith-Roe, GEMS President-Elect, DNTP/NIEHS |
| 9:00 - 10:00 | Using Diversity Outbred Mice to Identify the Genetic Basis for Toxicity Thresholds and Susceptibility John E. French, Ph.D., Special Volunteer at DNTP/NIEHS, Adjunct Professor, UNC-Chapel Hill |
| 10:00 - 10:15 | Coffee Break |
| 10:15 - 11:15 | Genetics of Environmentally-Induced Airway Disease in the Collaborative Cross Mouse Population Samir N. Kelada, Ph.D., M.P.H., Assistant Professor, Department of Genetics, UNC-Chapel Hill |
| 11:15 - 11:30 | A Tribute for Fredrick J. de Serres, Ph.D. Michael Shelby, Ph.D. , Special Volunteer at DNTP/NIEHS |
| 11:30 - 1:00 | Lunch at EPA Cafeteria |
| 1:00 - 1:15 | Announcements |
| 1:15 - 2:15 | Genetic Architecture of Environmental Sensitivity: Lessons from Drosophila Trudy F.C. Mackay, Ph.D., William Neal Reynolds Distinguished University Professor of Biological Sciences, NCSU |
| 2:15 - 3:15 | Smoking and the Epigenome Across the Lifecourse Stephanie J. London, M.D., Dr.P.H., Deputy Chief, Epidemiology Branch and Principle Investigator, NIEHS |
| 3:15 - 3:30 | Closing Remarks |

GEMS Spring Meeting 2015 Speaker Biographies

John E. (Jef) French, Ph.D. Adjunct Professor, UNC-Chapel Hill DNTP/NIEHS Special Volunteer GEMS Past President

At the Center for Pharmacogenomics and Individualized Therapy in the Eshelman School of Pharmacy and the Department of Nutrition in the Gillings School of Global Public Health, Dr. French continues his focus on the development of new population based mouse models to investigate inter-individual variation in toxic response to drugs and xenobiotics to better understand the basis for susceptibility and to identify genetic and epigenetic variants associated with toxicity and disease.

Dr. French earned his Ph.D. at North Carolina State University and recently retired after 40 years of service to the USPHS while serving at the US Food and Drug Administration, National Toxicology Program/NIEHS, and the Intramural Research Program at the NIEHS. He has organized and participated in a number of national and international meetings and published more than 120 peer-reviewed papers. During his tenure at NTP/NIEHS, Dr. French received NIH Merit Awards for his leadership and research as Group Leader, Transgenic Carcinogenesis Group from 1994-2006 and the NTP Host Susceptibility Initiative from 2007-2013. The NTP Host Susceptibility Initiative is a multidisciplinary research and testing program created to increase understanding of the genetic basis for population-level differences for both toxicants and/or disease susceptibility. The initiative has aided understanding of how and why substances in our environment are hazardous to some individuals and not to others. He continues to be involved in the Initiative as a Special Volunteer working on data mining from completed projects and consulting on the use of population based mouse models in toxicology and environmental health.

Samir N. Kelada, Ph.D., M.P.H. Assistant Professor Department of Genetics, UNC-Chapel Hill Curriculum in Toxicology, UNC-Chapel Hill

Dr. Kelada is an Assistant Professor in the Department of Genetics at the University of North Carolina at Chapel Hill (UNC). Broadly speaking, his interests are in gene-environment interactions in respiratory diseases including asthma and acute lung injury. Along with colleagues at UNC and the Jackson Laboratory, Dr. Kelada utilized incipient lines of the Collaborative Cross to identify genetic loci that regulate allergen-induced airway gene and protein expression, and ultimately inflammation phenotypes.

Dr. Kelada received a MPH in Environmental Health from the University of Michigan School of Public Health, followed by a PhD in Toxicology from University of Washington, and finally post-doctoral training in Genetics & Genomics in the lab of Dr. Francis S. Collins at NIH. Dr. Kelada is member of the Society of Toxicology and American Thoracic Society, and the International Mammalian Genome Society, and is an active member of the Curricula in Toxicology and Genetics & Molecular Biology at UNC.

Dr. Kelada received a University of North Carolina Junior Faculty Development Award in 2013 and the

Joy Cappel Young Investigator Award from Rockland Immunochemicals in 2014. In 2015, Dr. Kelada received an Outstanding New Environmental Scientists (ONES) Award from the National Institute of Environmental Health Sciences (NIEHS), a competitive grant given to promising new environmental health scientists. His grant award will be used to identify genes and pathways that mediate the effect of air pollution on the development of allergic airway disease through studies using the Collaborative Cross mouse genetics reference population.

Trudy F.C. Mackay, Ph.D., FRS William Neal Reynolds Distinguished University Professor of Biological Sciences and Associate Member of Entomology North Carolina State University

Dr. Mackay earned her Ph.D. from the University of Edinburgh and performed her postdoctoral studies at Dalhousie University, Nova Scotia, Canada. Dr. Mackay has been the recipient of numerous distinguished awards, including the Genetics Society of America Medal, and she was elected to the National Academy of the Sciences in 2010. She is also a Fellow of AAAS, the Royal Society, and the American Academy of Arts and Sciences, and a Member of the New York Academy of Sciences. Dr. Mackay has authored or co-authored over 170 refereed publications and several books and book chapters. She is on the editorial boards of *PLoS Genetics, OpenBiology* and *Genes, Brain and Behavior*. She also served as associate editor of *Genetics* for 12 years. She is a member of AAAS, the Genetics Society of America, Sigma Xi, and the Society for the Study of Evolution. She has served as the treasurer of the Genetics Society of America and is a past president of the American Genetics Association.

Research in Dr. Mackay's laboratory focuses on understanding the genetic and environmental factors affecting variation in quantitative traits – traits for which phenotypic variation is continuously distributed in natural populations, with population variation often approximating a statistical normal distribution on an appropriate scale. The continuous variation arises from genetic complexity and environmental sensitivity. Quantitative genetic variation is the substrate for phenotypic evolution in natural populations and for selective breeding of domestic crop and animal species, and underlies susceptibility to common complex diseases and behavioral disorders in humans, as well as responses to pharmacological therapies. Dr. Mackay's goal for understanding the genetic architecture of any quantitative trait is to peer within the black bell curve to elucidate the rules for translating genetic variation among individuals to phenotypic variation for the trait, at the level of primary variation in DNA sequence and intermediate phenotypes of transcript, protein and metabolite abundance, and in a range of relevant environments. In pursuit of these and other goals, Dr. Mackay has created a *Drosophila* Genetic Reference Panel of 205 sequenced inbred lines.

Stephanie J. London, M.D., Dr.Ph.H Deputy Chief, Epidemiology Branch and Principle Investigator Immunity, Inflammation, and Disease Laboratory NIEHS

Dr. London earned her AB, MPH, DrPH and MD from Harvard University. She is Board Certified in Internal Medicine and Preventive Medicine with Specialty in Occupational and Environmental Medicine.

Dr. London was Assistant Professor in the Department of Preventive Medicine at the University of Southern California School of Medicine before coming to NIEHS in 1995. Dr. London's Genetics, Environment, and Respiratory Disease Group focuses on genetic susceptibility and interactions between genetics and the environment in relation to respiratory endpoints, including asthma, pulmonary function, and chronic obstructive pulmonary disease.

Dr. London has initiated and collaborated in national and international epidemiological studies on the impact of environmental exposures, nutrition, genetics and epigenetics on respiratory health. Since 2008, her genetic and genomic work has focused on genome-wide association approaches. She formed and leads the CHARGE pulmonary group, which has published several genome wide association study meta-analyses of pulmonary phenotypes and has several ongoing projects in collaboration with the SpiroMeta consortium in the UK and other collaborators in Europe, Latin America and Asia. The group has identified over 33 novel loci related to pulmonary function and the related trait of airflow obstruction (Hancock et al., Nat Genet 2010; Soler-Artigas et al., Nat Genet 2011; Wilk et al., AJRCCM 2012) and has employed genome-wide approaches to studying interaction with an environmental exposure, namely cigarette smoking, to identify novel findings that would have been missed by studying genetic main effects alone (Hancock et al., PLoS Genet 2012). The CHARGE pulmonary group is pursuing analyses of rare variants using exome chip, 1,000 genome imputation and sequencing data. Her talk today will focus on her work in identifying novel epigenetic effects of tobacco smoke.