

**National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)  
Genes, Environment, and Health Initiative:  
Translating Whole Genome Association Data into Clinical Practice**

**Natcher Conference Center, Building 45,  
National Institutes of Health (NIH)  
March 10–11, 2008**

On Monday, March 10, 2008, Dr. Rebekah Rasooly, Deputy Director for the Division of Kidney, Urologic, and Hematologic Diseases, opened the meeting and welcomed the group. Dr. Rasooly thanked chairs, co-chairs, and colleagues for their support in the setup of this conference. Dr. Rasooly introduced Dr. Khoury whom welcomed participants and noted the variety of presentations and case studies.

Dr. Griffin Rodgers, Director of the National Institute of Diabetes and Digestive and Kidney Diseases, presented an overview on the DHHS Secretary's Genes, Environment and Health Initiative (GEI): Research on Complex Diseases. Dr. Rodgers noted that translation is a key part of NIH-funded research, bringing results from the bench to the bedside to the public. He highlighted some new and exciting findings about genetically complex disease that have emerged from Genome-wide Association Studies (GWAS), which have generated important research questions and opportunities for future translation.

Dr. Brenda Weis of the National Institute of Environmental Health Sciences discussed GEI and listed members of the overall Coordinating Committee and the component Exposure Biology and Genetic Subcommittees. Dr. Weis summarized the major questions in exposure assessment and highlighted areas that are the focus of currently funded research in the GEI Exposure Biology Program. The deliverables from this research include environmental sensors and biological response. Dr. Weis outlined the flow of GEI-funded investigation: from GWAS and improved methods of exposure assessment to clinical translation, with eventual integration of the GEI Genetics and Exposure Biology Components. She then reviewed the goals of the conference and introduced Dr. Muin Khoury to chair the first session.

Following Dr. Weis' presentation, experts in the field presented information on the state of research and offered suggestions and commentary on future directions. Copies of slide presentations are available on CD by request. Individuals interested in obtaining copies may e-mail Dr. Rebekah Rasooly at [rrasooly@mail.nih.gov](mailto:rrasooly@mail.nih.gov). Below is a list of sessions, presenters, and the titles of presentations:

**SESSION I – Muin Khoury, chair**

**Keynote talks**

- “From GWA to Health Applications: The Promise”—Francis Collins, National Human Genome Research Institute

- “From Health Applications to Population Health Impact: The Translation Challenge” —Muin Khoury, Centers for Disease Control and Prevention

### **Presentations for Case Study 1: Moving a GWAS Discovery into a Therapeutic Intervention**

- “Inflammatory Bowel Disease Genetics: Crohn’s Disease”—Judy Cho, Yale University
- “Refining and Translating Genomics for Disease Sub Setting and Coordinated Target Discovery for More Effective Therapeutic Clinical Trial Design”—Stephan Targan, Cedars-Sinai Health System
- “Determinants of HIV Response”—David Goldstein, Duke University
- “Predicting Unmodifiable Disease Risks: Emotional and Behavioral Responses”—Theresa Marteau, King’s College London

### **SESSION II – Hakon Hakonarson, chair**

#### **Presentations for Case Study 2: Putting Together a Picture of Risk for a Complex Genetic Trait for Prognostic Testing**

- Thinking Big: Using Genome Wide Association Meta-Analysis to Identify Additional Loci Influencing Type 2 Diabetes, Obesity, and Height—Mark McCarthy, Oxford Centre for Diabetes, Endocrinology, and Metabolism
- “Translating Type 2 Diabetes Whole Genome Association Studies”—Alan Shuldiner, University of Maryland School of Medicine
- “Providing Information on Genetic Risk for Common Disease in the Context of Environmental Risk Factors”—Colleen McBride, National Human Genome Research Institute

#### **Presentations for Case Study 3: Cancer Genetics and Genomics: Evidence-Based Guidelines for Gene-Based Testing**

- “Evaluation of Genomic Applications in Practice and Prevention, BRCA1 Testing”—Al Berg, University of Washington
- “Implications of Germline Variation for Breast Cancer Treatment”—Mark Robson, Memorial Sloan-Kettering Cancer Center
- “Genetic Counseling Challenges with Genetic Risk for Cancer”—Jill Stopfer, University of Pennsylvania
- “Molecular Diagnosis of Kidney Failure”—Matthias Kretzler, University of Michigan
- “Application of Molecular Information to Primary Diagnosis of Breast Cancer for Targeted Treatment Decisions and Improved Patient Outcome”—John Sninsky, Celera

### **SESSION III – Joan Scott, chair**

#### **Keynote talks**

- “Incorporating Genetic Information into Clinical Practice”—Wylie Burke, University of Washington

- “Commercial Development of Genetic Tests”—Brad Popovich, Sirius Genomics

#### **Presentations for Case Study 4: Pharmacogenetics and Translations in General Practice**

- “Pharmacogenetics and GWAS”—Hakon Hakonarson, Children’s Hospital of Philadelphia
- “Pharmacogenetic Clinical Trials”—Nik Schork, Scripps Research Institute
- “Warfarin Dosing and Genetic Variation”—Allan Rettie, University of Washington
- “Economic Considerations in the Use of Pharmacogenomics”—David Veenstra, University of Washington

#### **SESSION IV – Paul Kimmel, chair**

After the formal presentations, Dr. Paul Kimmel of the National Institute of Diabetes and Digestive and Kidney Diseases chaired Session IV: Setting a Translation Research Agenda. During this moderated discussion, participants considered emerging themes and questions about translating genetic data from GWAS of common disease into clinical research and applications and identify key questions for future research. Dr. Kimmel noted the list of important potential areas for further work in translation of genetic findings related to common disease included: elucidation of biologic pathways; genetic diagnostics; clues for therapeutic development; clinical trials to test the use of genetic information; behavioral responses, adoptive and maladaptive, to information about genetics; and dissemination of accurate information about the use of genetic data to the public and practitioners. Participants provided feedback on a variety of discussion questions.

Some of the points raised included:

- One of the major benefits of GWAS is important new leads for basic research on disease etiology and potential therapeutics, and resources should be dedicated to this type of translation as well as to patient-oriented studies.
- More genetic variation studies are needed. Currently, most studies to date have focused on individuals of European ancestry.
- Whole genome sequencing will be emerging in the foreseeable future and may overtake research on the use of variants identified in GWAS.
- Randomized Clinical Trials using genetic information about common disease may be premature; it might be better to direct resources to observational studies at this point
- There is a need to prioritize translational efforts to focus on those most likely to produce a significant effect on health, and those with the most favorable balance of potential benefits and harms
- There is a need for methods to evaluate and assure the accuracy of existing commercial genetic testing providers and the legitimacy of results provided to individuals, as well as the need for studies to assess the impact of such testing on both individuals and populations.
- Collaborative research between companies providing genetic tests and the public sector might enhance the value, utility and reliability of such tests

- It is important to evaluate how the use of validated genetic tests may impact lifestyle and behavioral modifications
- Concerns remain about the use of genetic testing results and the individual's ability to receive health care coverage.
- Much of the information about interpreting genetic testing is provided to patients by general practitioners and research on the impact of these tests will need to be carried out in that setting.
- The paradigm is shifting in that consumers are increasingly requesting and obtaining genetic test results on their own, rather than having them provided by a medical practitioner, which raises new kinds of issues about the use and impact of these tests.
- There is a need for a neutral place providing information to educate consumers, such as SNPedia. One database managed and curated by professionals with a host of comprehensive resources would be helpful.
- Physician education should focus on test quality issues ('what can the test tell us/what remains unknown') to impart information about the potential value of available tests, since there is considerable patient demand for information about the use of relatively uninformative genetic tests. Research on how to improve physician education should be integrated with ongoing efforts to enhance the efficacy of Continuing Medical Education programs.

For more information about this topic, individuals may refer to the following article, which provides more details about this field of research: Genetic risk. With new disease genes, a bounty of questions. *Science*. 2008 Mar 28; 319(5871): 1754-5.

Dr. Rasooly thanked participants and adjourned the meeting.