

**Office of Public Health Genomics
Centers for Disease Control and Prevention**

**Fiscal Year 2008
Program Review Book**

October 1, 2007 – September 30, 2008

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1.0 CDC's Office of Public Health Genomics

Human genomics is the study of all the genes in a person and the interaction of these genes with each other and a person's environment, behaviors, and lifestyle. Public health genomics is a multidisciplinary field focused on the effective and responsible translation of human genome-based information and applications into health care practices to improve population health. It uses population data on genetic variation and gene-environment interactions to develop evidence-based tools for improving health and preventing disease.

Through the Office of Public Health Genomics (OPHG), the Centers for Disease Control and Prevention (CDC) provides national and international leadership in public health genomics, while building partnerships with other federal agencies, state health departments, public health organizations, professional groups, and the private sector.

1.1 Vision, Mission, and Goals

The vision, mission, and goals of the office focus on the role of public health in translating human genome-based information and applications into population health benefits.

Vision: To use genomic knowledge to improve the lives and health of all people.

Mission: To integrate genomics into public health research, policy, and programs.

Goals: To improve public health interventions for preventing chronic, infectious, environmental, and occupational diseases, through projects focused on population-based genomic research, assessment of the role of family history in determining risk and preventing disease, evaluation of genetic tests, and translation of genome-based information and applications into medical and public health practice.

1.2 Major Projects

Evaluation of Genomics Applications for Practice and Prevention

The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) initiative was launched by OPHG in 2004 to establish and test a systematic, evidence-based process for evaluating genetic tests and other applications of genomic technology that are in transition from research to clinical and public health practice.

Family History Public Health Project

OPHG started the Family History Public Health Project in 2002 to increase awareness of family history as a risk factor for common chronic diseases, such as cancer and diabetes, and to promote its use in programs aimed at reducing the burden of these diseases in populations.

Genomics Translation Projects

In 2008, OPHG awarded five new funding projects to state health departments and academic and research institutions to translate human genome-based information and applications into education, surveillance, and policy interventions. These projects will be part of a new CDC collaborative genomics translation initiative called the Genomic Applications in Practice and Prevention Network (GAPPNet) to be launched in 2009.

Human Genome Epidemiology Network

OPHG established the Human Genome Epidemiology Network (HuGENet™) in 1998 to help translate genetic research findings into opportunities for preventive medicine and public health by advancing the synthesis, interpretation, and dissemination of population-based data on human genetic variation in health and disease.

NHANES III Collaborative Genomics Project

In 2002, OPHG formed a multidisciplinary working group with members from across CDC to develop a proposal to measure the prevalence of selected genetic variants of public health significance in a representative sample of the U.S. population and to examine the associations between the selected genetic variants and disease outcomes available in NHANES III data.

Public Health Genomics Capacity Building

Since 2005, OPHG has funded Centers for Genomics and Public Health within schools of public health at the Universities of Michigan and Washington to provide expertise in translating genomic information into useable public health knowledge, to provide technical assistance to state and community public health agencies, and to integrate genomics into programs and practice.

From July 2003 to June 2008, OPHG supported genomics programs in four state health departments (Michigan, Minnesota, Oregon, and Utah) to integrate genomics knowledge and tools into chronic disease prevention programs and core public health functions.

Public Health Investigations

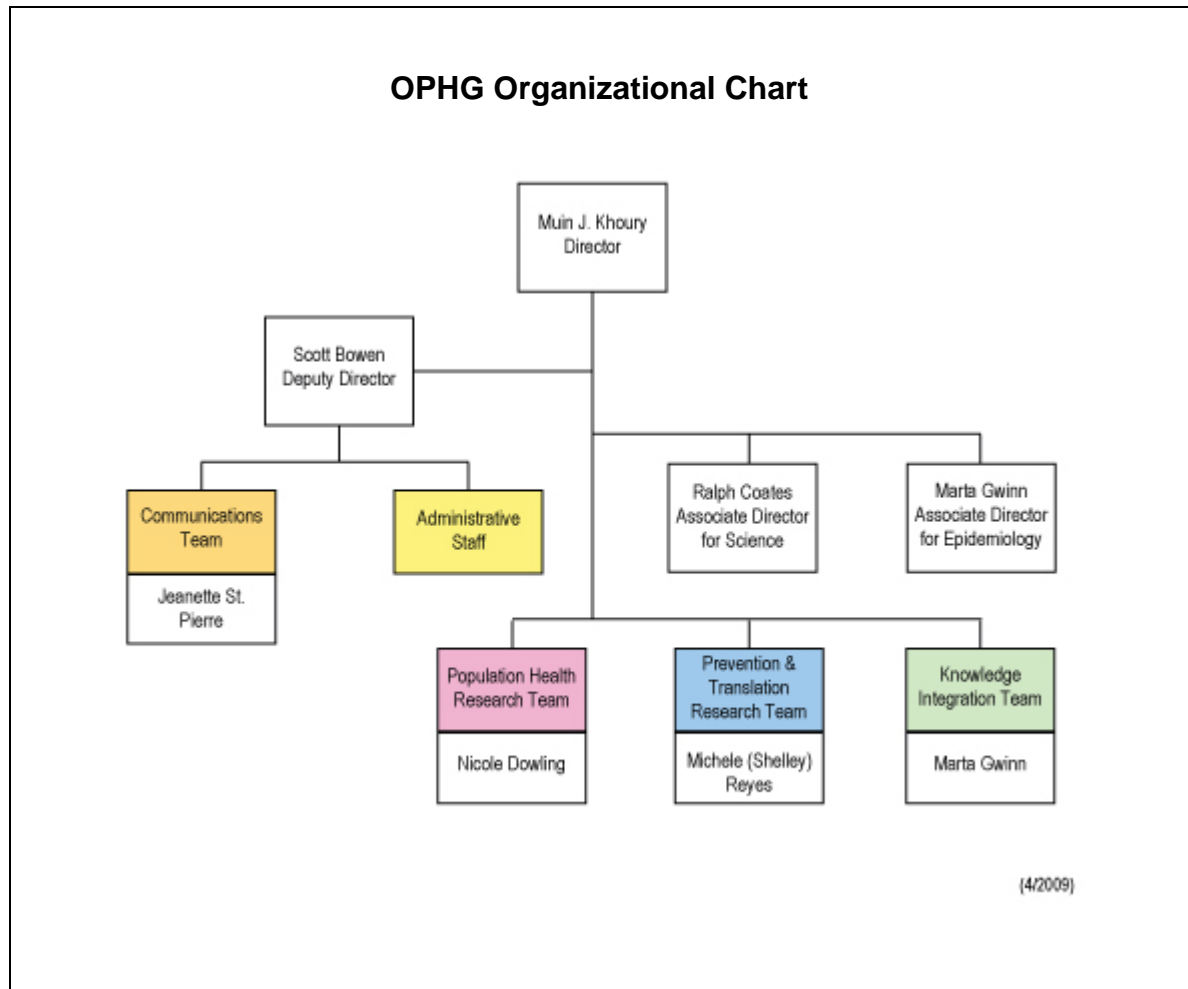
OPHG and the National Center for Influenza and Respiratory Diseases developed the Influenza Public Health Genomics Initiative in 2006 to investigate the role of population genetic variation in the epidemiology of influenza morbidity and mortality and the effectiveness of public health interventions.

Seed Funding for Public Health Genomics Research

Since FY2006, OPHG has funded CDC projects that help build the agency's infrastructure to conduct genomics research and integrate genomics into existing public health research and programs focused on infectious and chronic disease, birth defects, and environmental exposures.

2.0 Organization and Staffing

Dr. Muin J. Khoury, OPHG director, and Scott Bowen, OPHG deputy director, provide strategic leadership for OPHG with support and input from Dr. Marta Gwinn, associate director for epidemiology, Dr. Ralph Coates, associate director for science, and the other senior staff. OPHG has four major teams: the Knowledge Integration Team, the Population Health Research Team, the Prevention and Translation Research Team, and the Communications Team. By the end of FY2008, OPHG supported a total of 45 staff, including 18 federal full-time employees (and four vacancies).



3.0 New Initiatives and Projects in FY2008

3.1 New Prevention and Translation Research Initiative

In FY2008, OPHG formed a new initiative to support translation research and programs to advance knowledge about the validity, utility, utilization and population health impact of genomic applications and family history for improving health and preventing disease in individuals and populations in the United States.

Genomics Translation Projects

In 2008, OPHG awarded five new funding projects to state health departments and academic and research institutions to translate human genome-based information and applications into education, surveillance, practice, and policy interventions based on evidence reviews and recommendations from the U.S. Preventive Services Task Force (USPSTF) and CDC's EGAPP initiative.

- **Family History Education to Improve Genetic Risk Assessment for Cancer**, Principal Investigator: Maren Scheuner, MD, MPH, FACMG, Sepulveda Research Corporation. The goal of this project is to develop, implement, and evaluate a multifaceted education program for health care providers at the Veterans Administration Greater Los Angeles Healthcare System to improve and increase the use of familial risk assessment in clinical practices for early detection of hereditary breast and ovarian cancer and hereditary nonpolyposis colorectal cancer.
- **Pharmacogenomics Education Program: Bridging the Gap between Science and Practice**, Principal Investigator: Grace Kuo, PharmD, MPH, PhD (cand.), University of California, San Diego. The goal of this project is to develop an education program to increase awareness among pharmacists, pharmacy students, and other health care professionals about the validity and utility of pharmacogenomics tests and the potential benefits and harms of using these tests.
- **Promoting Cancer Genomics Best Practices through Surveillance, Education, and Policy**, Principal Investigator: Janice Bach, MS, CGC, Michigan Department of Community Health. The goal of this project is to engage in surveillance/monitoring, health education, and health insurance policy interventions to promote best practices and decrease morbidity and mortality from hereditary cancers in Michigan, particularly among individuals younger than 50 years of age.
- **Oregon Genomics Surveillance Program: Translation of Genomics Applications into Health Practice**, Principal Investigator: Katherine Bradley, PhD, RN, Oregon Department of Human Resources. The goal of this project is to develop, implement, and evaluate a surveillance program to monitor awareness, knowledge, and use among health care providers and the public of cancer-related genomic tests and family history in Oregon. This project will also evaluate disparities associated with accessing cancer-related genetic testing and counseling.
- **Risk-Benefit Framework for Genetic Tests**
Principal Investigator: David L. Veenstra, PhD, PharmD, University of Washington. The goal of this project is to develop and evaluate a quantitative risk-benefit framework for new genetic tests to educate clinicians, policy makers,

and other key decision makers about the potential benefits and harms of genetic testing.

Genomic Applications in Practice and Prevention Network (GAPPNet)

In 2008, OPHG, the National Institutes of Health (NIH), and partner organizations started conceptualizing a new collaborative genomics translation initiative called the Genomic Applications in Practice and Prevention Network (GAPPNet). The goal of GAPPNet is to accelerate and streamline effective and responsible use of validated genomic knowledge and applications, such as genetic tests, technologies, and family history, into medical and public health practice. Key activities of this network will include:

- convening individuals and groups conducting genomics research, programs, and policy activities;
- empowering and sponsoring new research; synthesizing and evaluating research findings; supporting the development of evidence-based recommendations; and
- developing and disseminating validated genomic information and applications for use in medical and public health practice.

The network will involve partners from across the public health field who are working together to realize the promise of genomics in healthcare and disease prevention. The new OPHG-funded projects mentioned above will also become part of this network.

3.2 New CDC Seed-Funded Genomics Projects

In 2008, OPHG awarded seed funding for five new CDC projects to integrate genomics into existing public health research and programs. Priority was given to those projects with potential to demonstrate health impact within a two-year period.

1. Effects of Preconceptional Folic Acid Supplementation on Epigenetic Patterns of DNA Methylation. Investigators: Krista Crider, PhD (CCHP/NCBDDD), Craig Hooper, PhD (CCHP/NCBDDD)
2. Autism Spectrum Disorder: High-throughput Screening for Potential Candidate Genes and Etiologic Hazardous Agents of Environmental Origin. Investigators: Eugene Demchuk, PhD (ATSDR/DTEM/OD), Michael Schwartz, MD, MS (CCEHIP/NCEH/OTPER), Patricia Ruiz, PhD (ATSDR/DTEM/OD), Hugh Hansen, PhD (ATSDR/DTEM/OD)
3. Evaluation of the Modifying Effect of Apolipoprotein E (APOE) Genotype on the Association of Prenatal Blood Lead Levels and Auditory Brainstem Response Among Infants Born in Two New York City Hospitals. Investigator: Timothy A. Dignam, MPH (CCEHIP/NCEH)
4. Genetic Modulation of Worker Susceptibility to Noise-induced Hearing Loss. Investigators: Rickie R. Davis, PhD (CDC/NIOSH/DART) and Mary Ann Butler, PhD (NIOSH/DART)
5. Integrative Genomic Approach in Prediction of Chronic Beryllium Disease (CBD). Investigators: Erin McCanlies, PhD (NIOSH/HELD), Petia Simeonova, MD, PhD (NIOSH/HELD/TMBB) and Berran Yucesoy, PhD (NIOSH/HELD/TMBB)

Descriptions of these projects can be found at:

<http://www.cdc.gov/genomics/activities/fund2008.htm>.

4.0 Scientific Highlights in FY2008

4.1 Evaluation of Genomic Applications in Practice and Prevention (EGAPP)

EGAPP Recommendation Statements

In December 2007, the CDC-supported independent EGAPP Working Group released its first recommendation statement, which addresses the use of cytochrome P450 (CYP450) testing in adults with depression beginning treatment with a widely prescribed class of antidepressants. The EGAPP Working Group did not find sufficient evidence to support the use of CYP450 testing in adults beginning treatment with selective serotonin reuptake inhibitors (SSRI) in patients with non-psychotic depression. EGAPP discourages the use of CYP450 testing for patients beginning SSRI treatment until more research is completed. This recommendation statement was published in *Genetics in Medicine* and can be accessed free of charge at:

www.geneticsinmedicine.org/pt/re/gim/fulltext.00125817-200712000-00004.htm. OPHG is conducting an evaluation to assess awareness and use of this EGAPP recommendation among health care providers, health plans and payers, policy makers, and consumer groups.

EGAPP efforts in FY2008 were primarily focused on the development of evidence-based products that address the following:

- the use of *UGT1A1* genotyping in metastatic colorectal cancer patients treated with irinotecan
- identifying DNA testing strategies that can reduce morbidity and mortality from Lynch Syndrome
- the use of tumor gene expression profiling in breast cancer patients

Another important paper that appeared in the January 2009 issue of *Genetics in Medicine*, entitled The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) initiative: methods of the EGAPP Working Group, was originally published in an online ahead of print format in 2008. The paper is important in that it provides in-depth coverage and detailed descriptions of EGAPP methods and processes, while promoting transparency and dissemination of knowledge. This paper, as well as the three most recent EGAPP recommendation statements can be accessed free of charge at: <http://www.geneticsinmedicine.org/pt/re/gim/toc.00125817-200901000-00000.htm>.

EGAPP Evidence Reports

In FY2008, OPHG funded an evidence-based practice center, through an interagency agreement with the Agency for Healthcare Research and Quality, to develop the following evidence-based report: *Impact of Gene Expression Profiling Tests on Breast Cancer Outcomes*. This report is available free of charge at: www.ahrq.gov/clinic/tp/brcgenetp.htm.

EGAPP Stakeholders Group

In January 2008, the CDC-supported EGAPP Stakeholders Group (ESG) held its first meeting in Houston, Texas. Of the 35 stakeholders, 32 attended this meeting as well as an EGAPP Working Group member, CDC staff, and EGAPP consultants. The meeting focused on understanding EGAPP; understanding challenges associated with evaluating genetic tests and how the EGAPP Working Group functions and develops recommendations; developing approaches for communicating to key audiences and other stakeholders and ways to interface with EGAPP; and defining plans to move forward.

In July 2008, the ESG held its second meeting in Seattle, Washington. The meeting was sponsored and hosted by the Center for Genomics and Public Health at the University of Washington. More than 30 participants attended the meeting, including 24 stakeholders, CDC staff, and EGAPP consultants. The meeting focused on further clarifying how the ESG and the EGAPP Working Group would interact, defining the work of the ESG subcommittees for Topics, Communication, and Information Technology, and outlining how the ESG could increase awareness of EGAPP and facilitate dissemination of EGAPP reports and recommendations.

4.2 Family History Public Health Project

Evaluation Study of the Family Healthware™

In October 2007, three OPHG-sponsored research centers at the University of Michigan School of Medicine, Evanston Northwestern Healthcare Research Institute, and Case Western Reserve University School of Medicine completed data collection for an evaluation study of the Family Healthware tool. This Web-based tool provides users with a familial risk assessment for six chronic conditions (breast, colorectal, and ovarian cancer, coronary heart disease, diabetes, and stroke) and a “prevention plan” containing personalized recommendations for lifestyle changes and screening recommendations.

Approximately 3,600 participants and 190 clinicians from 13 states participated in this study. Approximately 82% of the participants showed a moderate to high familial risk for at least one of the six diseases included in the tool.

Awareness and Behavior Change Preliminary Findings:

- Most study participants were aware of their familial risk and were also accurate in evaluating their risk level. However, participants in the high risk category tended to underestimate their familial risk.
- Participants who were aware of their elevated familial risk for specific diseases were not more likely to undertake screening tests for the diseases involved.
- Participants who were informed of their familial risk and advised to take measures according to their risk were more likely to talk to their primary care physician about this risk in their next appointment. They were also more likely to collect additional family history information from their relatives.

The Family History Impact Trial (FHITr) working group, which was formed to evaluate the study results, will be publishing a series of papers throughout FY2009 based on these investigations. This study appeared to indicate that, among people with access to primary healthcare and preventive services, it might be possible to induce some positive changes using family history. It also appeared to indicate that family history could be an essential component of public health prevention strategies for the six chronic conditions studied, as it can help identify groups at risk for these conditions and could also help health providers make decisions about screening and early testing for some diseases, which can lead to detection of early signs of disease among those with high familial risk.

New U.S. Surgeon General's My Family Health Portrait Tool

OPHG is a member of the HHS American Health Information Community (AHIC) Family History working group, which is part of the HHS Initiative on Personalized Health Care. This working group helps to set the standards for collecting family history and is working to update and improve the U.S. Surgeon General's My Family Health Portrait tool (<https://familyhistory.hhs.gov/fhh-web/home.action>). OPHG is helping to develop a plan to enable consumers to share their family health history information electronically and securely with family members and healthcare providers, and ultimately, to allow this information to become part of the consumer's electronic health record (EHR).

OPHG is also working with the National Institute of Genomic Medicine of Mexico, in order to create a Spanish version of the new My Family Health Portrait tool that will be linked to electronic medical records. Other collaborative activities focus on integrating English versions of the new My Family Health Portrait tool into the electronic medical records system of the Veterans Administration (VA) and the Indian Health Service (IHS).

Family Matters Workshop

In June 2008, OPHG held the *Family Matters Workshop: Developing a Portrait of Your Family Health History*. This workshop provided an opportunity for CDC staff to learn about what family health history is and why it is important for health, how to collect their family health history and check for signs of elevated health risks, and resources available for collecting family health history. A total of 23 participants attended the event, and numerous individuals participated remotely from Alaska, Massachusetts, Pennsylvania, New Jersey, Washington DC, West Virginia, and Colorado.

Family History Publications in FY2008

- Scheuner MT and Yoon PW. The use of family history in clinical medicine and public health. In: Handbook of Genomic Medicine. Willard H, Ginsburg G, eds. New York: *ELSEVIER* (in press).
- Robitaille J, Yoon PW, Irizarry-Delacruz M, Liu T, Moore CA, Looker AC, Khoury MJ. Prevalence, Family History, and Prevention of Reported Osteoporosis in U.S. Women. *Am J Prev Med*. July 2008; 35(1):47-54
- Ghosh A, Liu T, Khoury MJ, Valdez R. Family History of Diabetes and Prevalence of the Metabolic Syndrome in U.S. Adults without Diabetes: 6-year results from the National Health and Nutrition Examination Survey (1999-2004). [in clearance]
- Liu T, Valdez R, Yoon P, Crocker D, Moonesinghe R, Khoury MJ. The association between family history of asthma and the prevalence of asthma among US adults: National Health and Nutrition Examination Survey, 1999–2004. [in press]
- Kim C, Liu T, Valdez R, Beckles G. Family history among parous women with histories of gestational diabetes mellitus only and diagnosed diabetes mellitus in the Third National Health and Nutrition Examination Survey. [draft]
- Mvundura M, Henraya McGruder, Muin J. Khoury, Rodolfo Valdez, Paula W. Yoon. Family History as a Risk Factor for Early-Onset Stroke / Transient Ischemic Attack Among U.S. Adults. [Public Health Genomics](#). 2009 Mar 23. [Epub ahead of print]
- Epidemiologic approaches to the use of family history in public health practice. Authors: Rodolfo Valdez, Muin J. Khoury, Paula W. Yoon [draft of book chapter]

4.3 Human Genome Epidemiology Network (HuGENet™)

HuGE Navigator

In September 2007, OPHG launched HuGE Navigator (<http://www.hugenavigator.net>), which is an up-to-date knowledge base in human genome epidemiology, with information on population prevalence of genetic variants, gene-disease associations, gene-gene and gene-environment interactions, and evaluation of genetic tests. In FY2008, OPHG added approximately 8,000 scientific articles on human genome epidemiology were added to the HuGE Navigator. By the end of December 2008, the HuGE Navigator contained about 40,000 scientific articles (>80% genetic association studies), indexed by gene, study type, category and MeSH terms from PubMed.

HuGE Reviews

HuGE Reviews are systematic reviews of research findings on particular gene-disease associations, which are published in partnership with 10 scientific journals. These reviews typically point to gaps in existing epidemiologic and clinical knowledge, thus stimulating further research in these areas. In FY2008, 10 HuGE reviews were published. Thirteen HuGE reviews are anticipated in 2009 on genetic risk factors and pregnancy and childbirth, mental disorders and epilepsy, lung cancer, and general cancer risk.

- [Angiotensin II type 1 receptor polymorphisms and susceptibility to hypertension: a HuGE review.](#) Genet Med. 2008 Aug.
- [Meta-analysis and pooled analysis of GSTM1 and CYP1A1 polymorphisms and oral and pharyngeal cancers: a HuGE-GSEC review.](#) Genet Med. 2008 Jun
- [Association study between interleukin 1 beta gene and epileptic disorders: a HuGe review and meta-analysis.](#) Genet Med. 2008 Feb
- [Genetic risk factors for placental abruption: a HuGE review and meta-analysis.](#) Epidemiology. 2008 Mar.
- [Glutathione S-transferase M1 \(GSTM1\) polymorphisms and lung cancer: a literature-based systematic HuGE review and meta-analysis.](#) Am J Epidemiol. 2008 Apr
- [Meta- and pooled analyses of the methylenetetrahydrofolate reductase C677T and A1298C polymorphisms and gastric cancer risk: a huge-GSEC review.](#) Am J Epidemiol. 2008 Mar.
- [Genetic variants of glutathione S-transferase as possible risk factors for hepatocellular carcinoma: a HuGE systematic review and meta-analysis.](#) Am J Epidemiol. 2008 Feb.
- [Meta-analysis of the association of the Taq1A polymorphism with the risk of alcohol dependency: a HuGE gene-disease association review.](#) Am J Epidemiol. 2008 Jan.
- [The E-cadherin gene polymorphism 160C->A and cancer risk: A HuGE review and meta-analysis of 26 case-control studies.](#) Am J Epidemiol. 2008 Jan.
- [Joint effects of the N-acetyltransferase 1 and 2 \(NAT1 and NAT2\) genes and smoking on bladder carcinogenesis: a literature-based systematic HuGE review and evidence synthesis.](#) Am J Epidemiol. 2007 Oct.

HuGE Workshops

In August and September 2008, OPHG conducted two CDC workshops entitled “HuGE Navigator – Human Genome Epidemiology and Public Health Research.” These workshops provided an opportunity for CDC researchers and health professionals to learn basic concepts of human genome epidemiology and how to use the HuGE

Navigator for conducting scientific literature searches about gene, disease, and environment interactions. A total of 33 attendees participated in each workshop. Attendees were from the following CDC divisions and offices: COTPER, NCCDPHP, NCBDDD, NCZVED, NCPDCID, OSI, NCHHSTP, NCIRD, NCEH, CHAPS, DHAP, ATSDR, and NCPHI.

HuGENet™ Meeting

In January 2008, OPHG conducted a two-day meeting entitled “Networks, Genome-Wide Association Studies, and the Knowledge Base on Genetic Variation and Human Health.” Fifty five participants from a variety of research organizations and universities in the United States and globally, including 29 members of the HuGE Working Group attended this meeting. The participants discussed approaches for developing the knowledge base on genetic variation and human health, focusing on “field synopses” that summarize genetic associations with specific diseases and a proposal for an online encyclopedia. Key themes and discussion topics included:

- interim cumulative evidence on genetic associations: applying interim “Venice criteria”;
- field synopses: reviewing results of pilot studies;
- genome-wide association studies: integrating evidence into field synopses;
- distributed online knowledge base: connecting the dots; and
- linking field synopses with data collections through networks and biobanks.

The participants agreed to collaborate on a second edition of *Human Genome Epidemiology*, which is due to be published as a hardcover text book by Oxford University Press, and also online as part of a new Public Health and Epidemiology module in *Oxford Scholarship Online (OSO)*, a cross-searchable electronic library of key Oxford academic titles, in Fall 2009.

HuGE Publications in FY2008

- Janssens AC, Gwinn M, Bradley LA, Oostra BA, van Duijn CM, Khoury MJ. A critical appraisal of the scientific basis of commercial genomic profiles used to assess health risks and personalize health interventions. *Am J Hum Genet* 2008 Mar;82(3):593-9.
- Janssens AC, Moonesinghe R, Yang Q, Steyerberg EW, van Duijn CM, Khoury MJ. The impact of genotype frequencies on the clinical validity of genomic profiling for predicting common chronic diseases. *Genet Med.* 2007;9(8):528-35.
- Moonesinghe R, Khoury MJ, Liu T, Ioannidis JP. Required sample size and nonreplicability thresholds for heterogeneous genetic associations. *Proc Natl Acad Sci U S A.* 2008 Jan 15;105(2):617-22. Epub 2008 Jan 3.
- Yu W, Gwinn M, Clyne M, Yesupriya A, Khoury MJ. A navigator for human genome epidemiology. *Nat Genet.* 2008 Feb;40(2):124-5.
- Yu W, Clyne M, Dolan SM, Yesupriya A, Wulf A, Liu T, et al. GAPscreeener: An automatic tool for screening human genetic association literature in PubMed using the support vector machine technique. *BMC Bioinformatics* 2008, 9:205 (22 April 2008)
- Yesupriya A, Evangelou E, Kavvoura FK, Patsopoulos NA, Clyne M, Walsh MC, et al. Reporting of Human Genome Epidemiology (HuGE) association studies: an empirical assessment. *BMC Med Res Methodol.* 2008 May 20;8(1):31. [Epub ahead of print] PMID: 18492284 [PubMed - as supplied by publisher]

- Yesupriya A, Yu W, Clyne M, Gwinn M, Khoury MJ. The continued need to synthesize the results of genetic associations across multiple studies. *Genet Med* 2008;10:633-5.
- Yu W, Wulf A, Yesupriya A, Clyne M, Khoury MJ, Gwinn M. HuGE Watch: tracking trends and patterns of published studies of genetic association and human genome epidemiology in near-real time. *Eur J Hum Genet*. 2008 May 14. [Epub ahead of print] PMID: 18478035 [PubMed - as supplied by publisher]
- Yu W, Yesupriya A, Wulf A, Qu J, Gwinn M, Khoury MJ. An automatic method to generate domain-specific investigator networks using PubMed abstracts. *BMC Med Inform Decis Mak* 2007; 20:7:17.
- Yu W, Yesupriya A, Wulf A, Qu J, Khoury MJ, Gwinn M. An open source infrastructure for managing knowledge and finding potential collaborators in a domain-specific subset of PubMed, with an example from human genome epidemiology. *BMC bioinformatics* 2007;8:436.

4.4 NHANES III Collaborative Genomics Project

U.S. Genome Variation Estimates

In 2008, OPHG reported study results on allele frequency and genotype prevalence estimates of selected candidate gene variants for U.S. population. This study was conducted in collaboration with researchers from across CDC and the National Cancer Institute. The study measured and evaluated 90 variants in 50 candidate genes from DNA collected from 7,159 participants aged 12 years or older in the Third National Health and Nutrition Examination Survey (NHANES III). These variants and genes were selected based on their potential significance to public health. The estimates were calculated by age, sex, and race/ethnicity among non-Hispanic whites, non-Hispanic blacks, and Mexican-Americans. These estimates are the start of a comprehensive databank of human genetic variation in the United States that will serve as an important reference for future investigations into the role genes play in disease. Some possible future investigations using these estimates might explore how genes affect population-level risk for disease and how genetic variants might contribute to health disparities. These estimates are also available online at www.cdc.gov/genomics/population/genvar.htm.

Chang M, Lindegren ML, Butler MA, Chanock SJ, Dowling NF, Gallagher M, et al. [Prevalence in the United States of Selected Candidate Gene Variants: Third National Health and Nutrition Examination Survey \(NHANES III\), 1991-1994](#). *American Journal of Epidemiology* 2009 Jan 1;169(1):54-66. Epub 2008 Oct 20.

Beyond Gene Discovery (BGD) Workshop

On March 3, 2008, OPHG hosted the first Beyond Gene Discovery workshop entitled *Developing the Genome Profile of the U.S. Population and Assessing the Role of Genetic Variation in Health and Disease* to discuss data access issues of the NHANES III DNA bank for public health research purposes and to develop an analytical plan for how these data may be used. The purpose of the workshop was to launch a far-reaching initiative to assess the genome profile of the U.S. population using nationally representative samples and to provide access to research datasets for investigators interested in genotype-phenotype analyses. The workshop convened CDC programs, federal partners, academia, and the private sector to review the Beyond Gene Discovery (BGD) plans, discuss analytic issues and develop solutions regarding models for accessing research datasets that maintain human subjects protections. A major outcome of the workshop was the agreement for the National Center for Health Statistics (NCHS) at CDC to establish and fund the first Remote Data Center in Atlanta, Georgia.

NHANES Publications in FY2008

In addition to the major achievement of the [*Prevalence in the United States of Selected Candidate Gene Variants: Third National Health and Nutrition Examination Survey \(NHANES III\), 1991-1994*](#) paper, the following paper based on the NHANES III data was published:

Yang QH, Botto LD, Gallagher M, Friedman JM, Sanders CL, Koontz D, et al. Prevalence and effects of gene-gene and gene-nutrient interactions on serum folate and serum total homocysteine concentrations in the United States: findings from the third National Health and Nutrition Examination Survey DNA Bank. *Am J Clin Nutr.* 2008 Jul;88(1):232-46.

4.5 Seed Funding for Public Health Genomics Research

In 2008, OPHG awarded seed funding for five new CDC projects to integrate genomics into existing public health research and programs. Priority was given to those projects with potential to demonstrate health impact within a two-year period. Descriptions of these projects can be found at: <http://www.cdc.gov/genomics/activities/fund2008.htm>.

4.6 Other OPHG Achievements

10th Anniversary Meeting of Public Health Genomics at CDC

In January 2008, OPHG hosted a meeting to highlight progress and achievements in genomics and to discuss future directions. Richard Campanelli of the U.S. Department of Health and Human Services, Julie Gerberding, MD, MPH, director of CDC, and other CDC directors gave welcoming remarks. National and international public health and genomics experts presented on emerging topics, including genome-wide association, human genome epidemiology, family history, genetic testing, and genomics translation research. A scientific poster session showcased a broad scope of more than 70 genomics projects currently being done or recently completed by CDC programs and partners, and other organizations. About 170 scientists and professionals from across CDC and partners from other federal agencies, state health departments, academic and research institutions, and nonprofit organizations attended the event.

OPHG achievements during the last 10 years are described in the following publications:

- 10 Years of Public Health Genomics at CDC 1997-2007 (www.cdc.gov/genomics/activities/file/print/2007-12_10yr_web.pdf)
- Khoury MJ, Bowen S, Bradley LA, Coates R, Dowling NF, Gwinn M, et al. A Decade of Public Health Genomics in the United States: Centers for Disease Control and Prevention 1997-2007. *Public Health Genomics.* 2008 Sep 3. [Epub ahead of print]

National Surveys of Direct-To-Consumer Nutrigenomic Tests

In 2008, OPHG utilized two national surveys (HealthStyles and DocStyles) to assess awareness and use of direct-to-consumer personal genome scans among U.S. consumers as well as knowledge of and experiences with these scans among U.S. physicians. OPHG also assessed knowledge of and exposure to EGAPP recommendations among U.S. physicians. Preliminary analyses of these data indicate

that one in five consumers surveyed were aware of these personal genome scans, but very few had actually used them. OPHG also worked with three state health departments to assess U.S. consumer awareness and use of these scans using the 2009 Behavioral Risk Factor Surveillance System.

5.0 OPHG-Funded State Achievements in FY2008

5.1 Michigan Department of Community Health (MDCH)

Public Health Issue

State health departments have the legal mandate for newborn screening, which involves the collection of blood samples from all babies born in the state and testing these samples for a variety of rare disorders. Each state maintains policies for protecting and storing the residual blood samples.

Over 160 biomarkers and compounds have been measured in residual blood samples, such as genetic material (DNA), proteins (the gene products), infectious agents (e.g., viruses), and harmful metals (e.g., lead). These samples provide an important resource that can be used in epidemiology studies, for example, to measure the frequency of genetic variations in a population or to understand how genes interact with environmental exposures.

Program Example

Since 1965, blood samples have been collected from almost every newborn in Michigan as part of their newborn screening program. Currently, the Michigan state public health laboratory screens newborns for 49 rare disorders; in addition, hospitals screen all newborns for hearing loss. In the early 1980s, the lab began to store all residual newborn screening samples for 21½ years based on a ruling by the state Attorney General's office. Based on a 1999 recommendation by the Governor's Commission on Genetic Privacy and Progress, the state legislature amended the public health code in 2000 to allow use of the blood specimens for medical research during the retention period as long as the research is conducted in a manner that preserves confidentiality and human subject protections. In early 2009, lab policy was revised to store all samples indefinitely unless parents (or legal guardians) request that their baby's sample: 1) be destroyed after screening is completed, or 2) not be used for any research. There are currently over three million samples in storage.

The genomics program in the Michigan Department of Community Health, in collaboration with many partners and stakeholders, is developing a biobank of residual blood samples for use in public health and medical research. Key partners include the major state research universities and the Van Andel Institute. The University of Michigan (UM) Center for Public Health and Community Genomics (CPHCG) and Michigan State University (MSU) Center for Ethics and Humanities in the Life Sciences have provided important support and consultation in developing and implementing a plan for community engagement to inform the public and assess support for a population-based biorepository. During 2008, approaches to community assessment and engagement included a series of four questions on the Behavioral Risk Factor Survey about public support for different types of research using dried blood spots; a deliberative jury process

with in-depth examination of relevant issues; a full-day discussion session with MSU students; development of a FAQ booklet and PowerPoint presentation for use in informational sessions; a series of 10 focus groups reaching various vulnerable populations and different geographic areas of the state; as well as several presentations to a variety of professional groups. An informational webpage with online survey was prepared and will be available in the Spring of 2009 for all Michigan citizens over age 18 to share their opinions on the biobank.

The genomics program also worked closely with the state laboratory director, Wayne State University, and a steering committee on development of a business plan that outlines a mission and vision, timeline, possible governance structure, steps toward implementation and funding needs related to establishing a biobank. Program staff members were also involved in working with the department's institutional review board (IRB) to identify needed policies for ensuring human subjects protection; to begin designing a process for parental consent for storage of future specimens; and to develop methods for incorporating public input in the identification of research priorities through establishment of a Community Values Advisory Board.

Implications and Impact

Since Michigan first began newborn screening for Phenylketonuria (PKU), more than five million infants have been screened, and over 4,150 babies have been identified with disorders for which there are effective treatments. The state newborn screening program has saved lives and improved the quality of life for Michigan's children and their families. With rapid scientific advances in technology, it is now possible to use residual samples for additional public health purposes. The creation of a permanent biobank of residual blood samples is an important first step in establishing public health infrastructure to support new research and public health practices that will contribute to improving future health outcomes for Michigan residents.

5.2 Utah Department of Health Chronic Disease Genomics Program

Public Health Issue

In Utah, Hispanic/Latino students make up nearly 50% of all students in some school districts. Requests from teachers for educational materials in Spanish have increased. Also, wide achievement gaps in science, based on mandatory statewide tests, also demonstrate a need for culturally-appropriate health and genetics education materials.

Program Example

Starting in 2005, the Utah Department of Health collaborated with the University of Utah Genetic Science Learning Center, high school teachers, and Hispanic/Latino community members in Salt Lake City to adapt existing 5th and 10th grade classroom curricula to be culturally and linguistically appropriate for Hispanic/Latino students. Program staff developed these curricula based on recommendations from a Hispanic/Latino Community Advisory Committee.

The 5th grade curriculum, *Introduction to Heredity*, consists of five classroom activities, three take-home family activities, and a teacher guide. The 10th grade curriculum, *Using*

Family History to Improve Your Health, consists of four classroom activities, a promotional video, two take-home activities, and accompanying teacher materials.

Implications and Impact

The 5th and 10th grade curriculum meet national and state-level Health Education and Biology Standards and are available free of charge in English and Spanish (<http://learn.genetics.utah.edu>). Classroom testing of these curriculum were favorable.

In 2007, the 5th grade curriculum was classroom tested with six 5th grade teachers and 159 students (54.2% Hispanic/Latino, 20.5% White, 14.5% Asian/Pacific Islander, 4.2% African American, 3.7% American Indian/Alaska Native, 3.2% Other). The materials received high ratings for their cultural appropriateness, student engagement, and achieving the intended learning objectives. The take-home activities were effective in engaging parents in their child's education.

In 2008, the 10th grade curriculum was tested with six high school health education teachers and approximately 499 students (49.5% Hispanic). Teachers reported that the videos and take-home guide were culturally appropriate and conveyed the importance of family health history, and the classroom activities were engaging.

6.0 Future Directions

In 2009, OPHG will continue to strengthen its genomics translation initiative by establishing a network of government agencies, academic and research institutions, healthcare plans, consumer advocacy groups, biotechnology industries, and other organizations around common goals for using genomics in preventing disease, improving treatments, and reducing health disparities. OPHG is also more effectively using public-private partnerships in evaluating genetic tests. Additionally, OPHG will support more extensive genotyping, which will expand the human genetic variation data bank and make these data more accessible to the scientific research community.

7.0 Publication List

This section provides a list of all scientific articles by OPHG staff published in peer-reviewed journals in FY2008.

1. Berry RJ, Carter HK, and Yang QH. Cognitive impairment in older Americans in the age of folic acid fortification. *Am J Clin Nutr.* 2007;86: 265-267.
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