Office of Population Genomics: Mission, Goals, Accomplishments

U.S. Department of Health and Human Services
National Institutes of Health
National Human Genome Research Institute

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Senior Advisor to the Director for Population Genomics

December 18, 2007

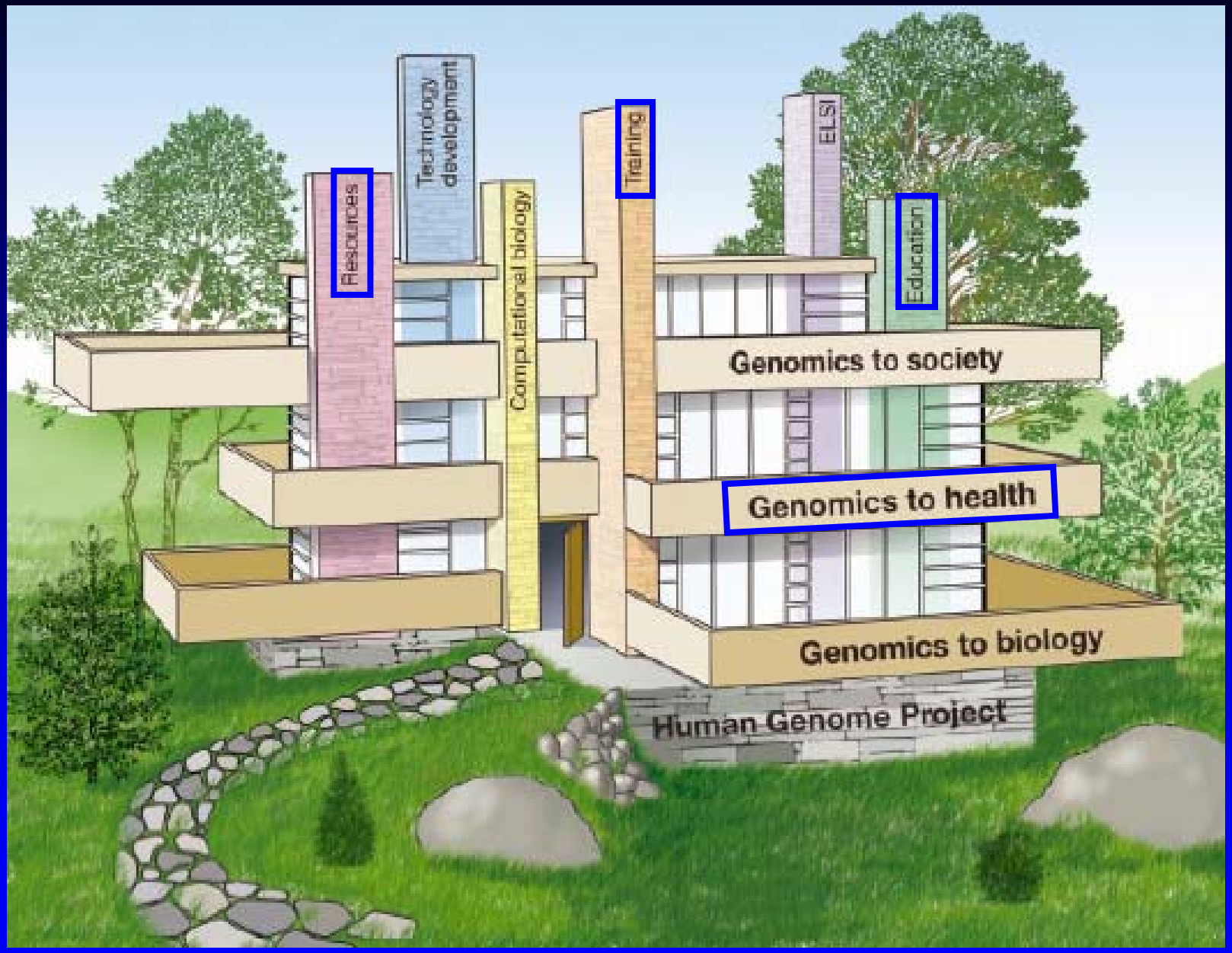
Population Genomics: Mission

NHGRI will facilitate the application of genomic knowledge to health by establishing an Office of Population Genomics, whose mission is to:

Promote multi-disciplinary research in epidemiology and genomics, by applying genomic technologies to existing population and clinical studies, and developing new population resources for investigation of genetic and environmental contributions to complex diseases.

Population-Based Research Methods

- Findings can be generalized to broad population, not just to those coming to clinical care
- Phenotypes (diseases, traits, risk factors) and environmental exposures defined in valid, reproducible, and transportable manner
- Generally need to be large to reduce sampling variation and spurious findings, allow meaningful subgroup analyses representative of diversity of US population



Collins et al, *Nature* 2003; 422:835-47.

Genomics to Health: Grand Challenges

- II-1: Develop strategies for identifying the genetic contributions to disease and drug response
- II-2: Develop strategies for identifying gene variants that contribute to good health and resistance to disease
- II-3: Develop genome-based approaches to prediction of disease susceptibility and drug response, early detection of illness, and molecular taxonomy of disease states
- II-5: Investigate how genetic risk information is conveyed in clinical settings, how that information influences health strategies and behaviours, and how these affect health outcomes and costs.

Initial Goals of Population Genomics at NHGRI: October 2005 - present

- Establish *research resources* to identify genes related to complex diseases and their environmental modifiers.
- Improve *analysis strategies* for relating genotypic to phenotypic data.
- Build successful *NIH-wide collaborations* in population-based genomic research.
- Develop *novel* population research approaches.
- Support *cross-disciplinary training* for geneticists, epidemiologists, clinical researchers, and clinicians.

Goal #1: Collect and make widely available standardized genetic, environmental, and phenotypic data on meticulously characterized individuals with appropriate consent.

- GAIN (six complex diseases)
- GEI GWA component, “GENEVA” (S Chanock, L Cardon, J Murray, D Schwartz)
- Genome-Wide Studies in Biorepositories with Electronic Medical Records, “eMERGE” (R Chisholm, C Chute, B Koenig)
- Public Consultation to Inform the Design of Large-Scale Studies, RFA HG-06-008
- High-Priority Phenotype and Exposure Measures for GWA Studies, “PhenX”

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GWA Data Generation

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GWA Infrastructure

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GWA Data and Infrastructure

Goal #2: Improve analysis strategies for relating genotypic to phenotypic data, evaluating modifiers of those relationships, and assessing the impact of diverse ancestral origins.

- Methods development for GWA, RFA-HL-05-011 (ENDGAME project)
- Methods development for G x E interactions: GEI RFA-HL-07-010
- Methodologic efforts in course of other GWA studies
- Standardized database structures for genotypes and phenotypes (dbGaP)
- Analytic capacity of OPG staff

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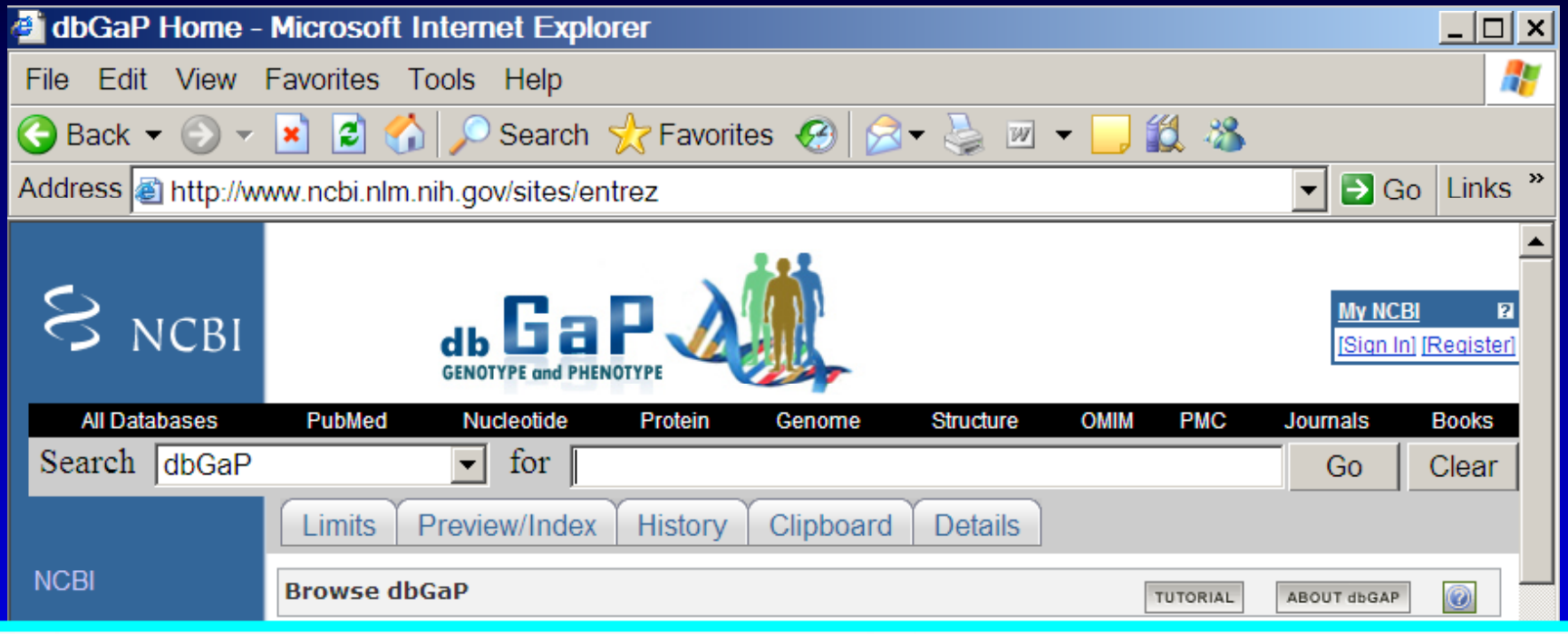
dbGaP Entry Page (through PubMed)



Collaborative Association Study of Psoriasis	August 13, 2008	35	3	2875	Case-control
Framingham SHARe	October 19, 2008	13183	132	17354	Community-based, longitudinal, family-based cohort

Needs for Analytic Capabilities within OPG

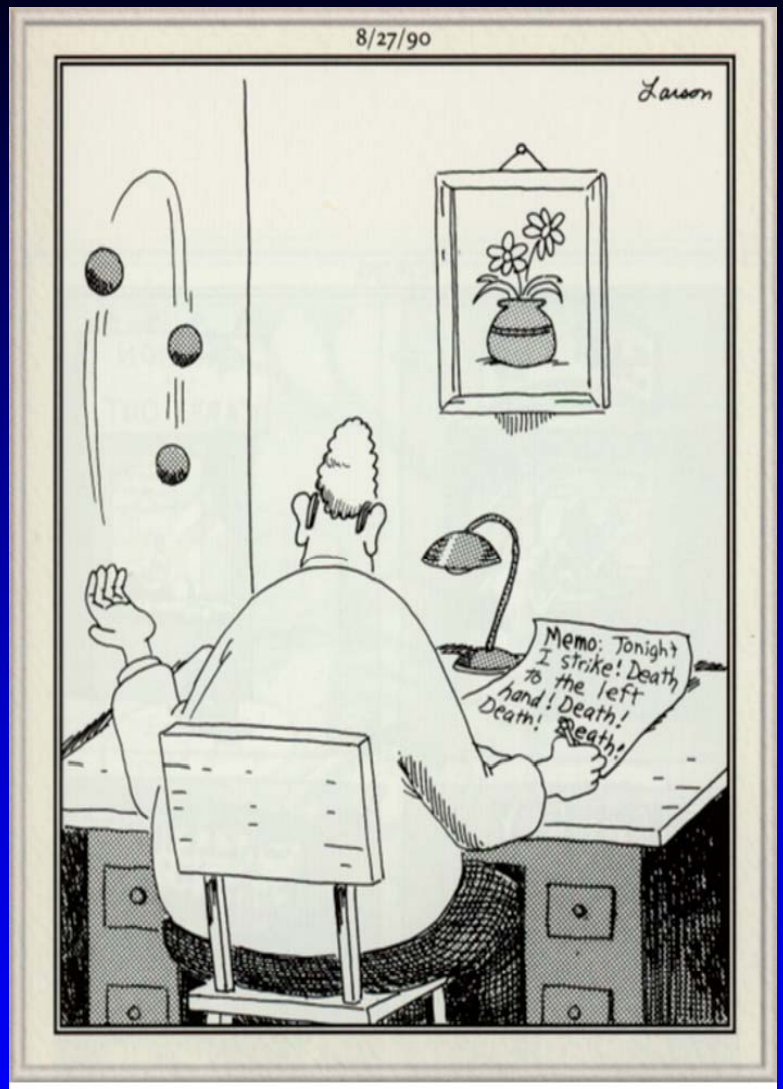
- Programmatic Priorities
  - Planning: identify conditions of high public health priority
  - Design: estimate sample size and power
  - Sampling: project US census estimates
  - Pooling and integration: assess comparability of phenotype measures, population samples
  - Quality control: genotyping QC, reproduce NCBI association analyses

Needs for Analytic Capabilities within OPG

- Scientific Priorities
  - Efficiency: QT analysis studying extremes vs entire distribution
  - Cost: gains in coverage and power with increased marker density
  - Diversity: what AIMs add to self-identified race/ethnicity as measures of risk
  - Generalizability: biases involved in traditional vs universal control groups
  - Recruitment and retention: need for scientific outlet and career development

Goal #3: Build successful collaborations in population-based genetic research across multiple conditions with other NIH Institutes and Centers, other agencies, and the private sector.

- Multi-IC symposia on population resources and genomic technologies
- GAIN and GEI collaborations NIH-wide
- Harmonization of data sharing policies NIH-wide
- Population genomics opportunities with other ICs



Innocent and carefree, Stuart's left hand didn't know what the right was doing.

Larson, G. *The Complete Far Side*. 2003.

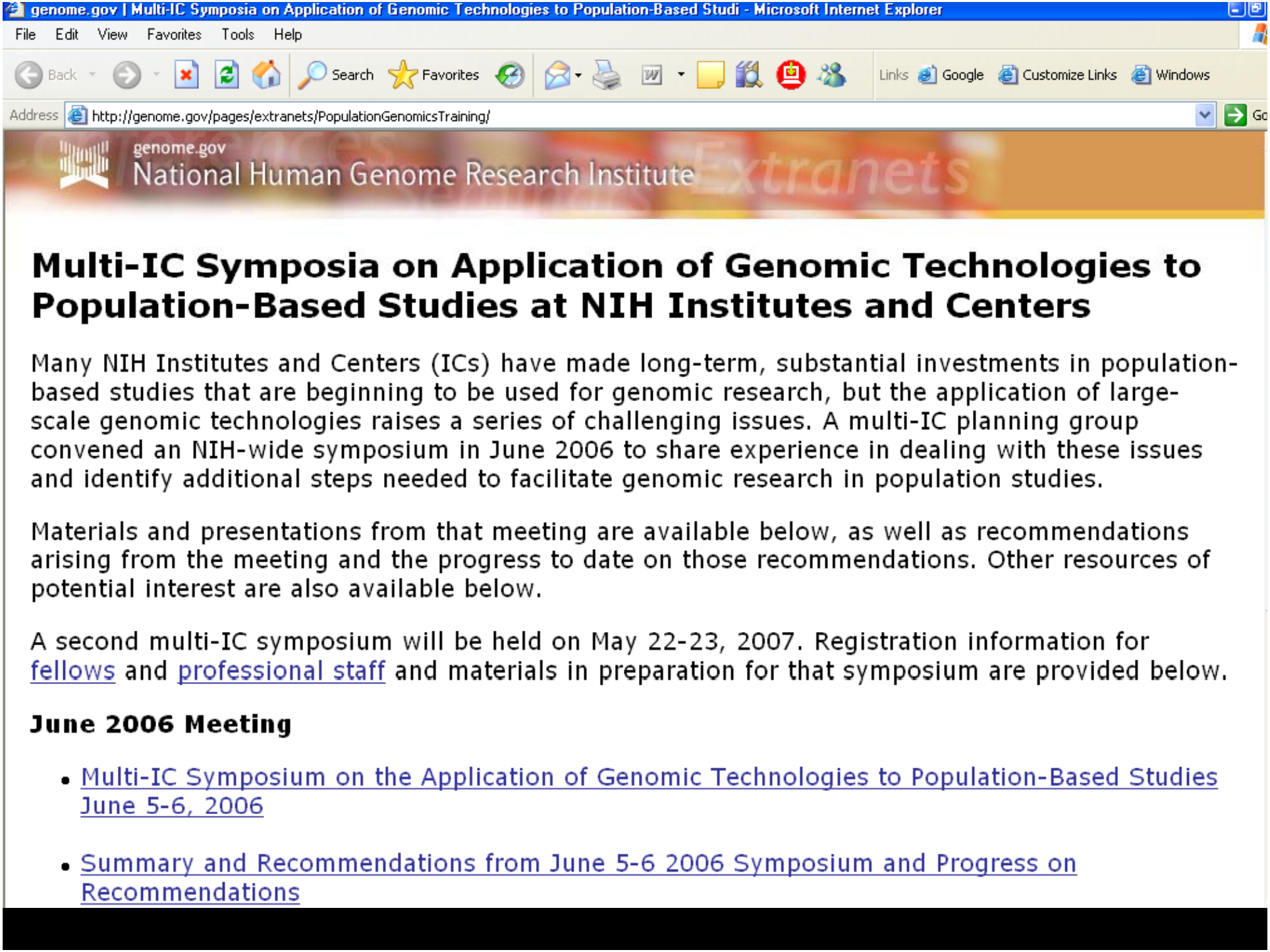
Multi-IC Symposium on Application of Genomic Technologies to Population-Based Studies

James Battey, NIDCD
Stephen Chanock, NCI
Katrina Gwinn-Hardy, NINDS
Teri Manolio, NHGRI
Rebekah Rasooly, NIDDK
Winifred Rossi, NIA
Gerald Sharp, NIAID

June 5-6, 2006

Objectives of Symposium

- To identify common, critical issues encountered in applying genomic technologies to population studies and creative approaches to solving them
- To develop approaches for prioritizing and conducting population studies using genomic technologies
- To identify new tools for genomics, phenotyping, and database standardization required for GWA and sequence-based studies.


genome.gov | Multi-IC Symposia on Application of Genomic Technologies to Population-Based Studi - Microsoft Internet Explorer
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Address http://genome.gov/pages/extranets/PopulationGenomicsTraining/
genome.gov
National Human Genome Research Institute
Extranets
Multi-IC Symposia on Application of Genomic Technologies to Population-Based Studies at NIH Institutes and Centers
Many NIH Institutes and Centers (ICs) have made long-term, substantial investments in population-based studies that are beginning to be used for genomic research, but the application of large-scale genomic technologies raises a series of challenging issues. A multi-IC planning group convened an NIH-wide symposium in June 2006 to share experience in dealing with these issues and identify additional steps needed to facilitate genomic research in population studies.
Materials and presentations from that meeting are available below, as well as recommendations arising from the meeting and the progress to date on those recommendations. Other resources of potential interest are also available below.
A second multi-IC symposium will be held on May 22-23, 2007. Registration information for fellows and professional staff and materials in preparation for that symposium are provided below.
June 2006 Meeting
Multi-IC Symposium on the Application of Genomic Technologies to Population-Based Studies June 5-6, 2006
Summary and Recommendations from June 5-6 2006 Symposium and Progress on Recommendations

Second Multi-IC Symposium on Application of Genomic Technologies to Population Studies: Facilitating Collaboration in GWA Studies

Stephen Chanock, NCI
Katrina Gwinn, NINDS
Thomas Lehner, NIMH
Teri Manolio, NHGRI
Christopher O'Donnell, NHLBI
Jim Ostell, NLM

May 22-23, 2007

Third Multi-IC Symposium on Population Genomics: Lessons Learned from GWA Studies

To Be Determined…

Spring, 2008

Participation in IC Advisory Meetings and Symposia

- NIAMS (4/06): Scientific Retreat, Advisory Council
- NIAID (5/06): MACS/WHIS Investigators
- NIDA (6/06): Genetics Consortium
- NIGMS (7/06): Roadmap Biomedical Computing Centers
- NHLBI (9/06): Ancillary Pharmacogenetics Investigators
- NCI (10/06): Cancer Cohort Consortium
- NEI (10/06): Vision Research Investigators
- NCI (11/06): Board of Scientific Advisors
- CC (11/06): Functional Genomics of Injury and Illness
- CDC (1/07): Influenza Public Health Genomics

Participation in IC Advisory Meetings and Symposia

- NIMH (2/07): Future Directions in Genetic Epidemiology
- NEI (2/07): AREDS2 Genetics Advisory Meeting
- ORD (2/07): Genetics of Rare Diseases
- CDC/NCI (2/07): Public Health Genomics
- NCCAM (2/07): Population Study Designs
- VA Genomics (3/07): GWA Data Sharing
- ODS (5/07): Genetics of Complex Traits
- NIDDK (5/07): Diabetic Nephropathy
- FDA (5/07): QC Consortium, GWA Studies
- NIAID (6/07): Clinical Research Network, GWA and HIV

Participation in IC Advisory Meetings and Symposia

- FDA (7/07): QC Consortium, Data Sharing
- NIA (8/07): GWA and Alzheimer Disease
- NHGRI Short Course (8/07): Population Genomics
- Physician Assistants (9/07): GWA Studies
- NLM (9/07): Board of Regents, GWA Data Policies
- NCI (11/07): Cancer Cohorts Consortium
- NIA (12/07): Longevity Consortium and GWA
- IOM (12/07): Effectiveness Research and GWA
- CDC (12/07): GWA and Predictive Health
- CDC (1/07): Integrating GWA into Knowledge Base

Criteria for Supporting New Research Opportunities in Population Genomics

- Meets scientific goals of population genomics program
- Meets scientific goals of NHGRI as a whole (technology; genomic scale; clinical care)
- Catalyzes or facilitates genomic research (paradigm-setting; unsupportable by 1-2 ICs)
- Meets key policy or administrative goals (minority health/disparities; cost-effective)

Goal #4: Develop novel population research approaches that are optimally designed to capture information on genetic and environmental risk factors and their interactions.

- Clinical trials of pharmacogenomic-directed treatment: warfarin dosing
- Pharmacogenomic-directed drug selection: abacavir hypersensitivity
- Genes predicting good health and disease resistance
- Molecular classification of disease
- Dynamic nature of genome in longitudinal studies, including epigenetic changes

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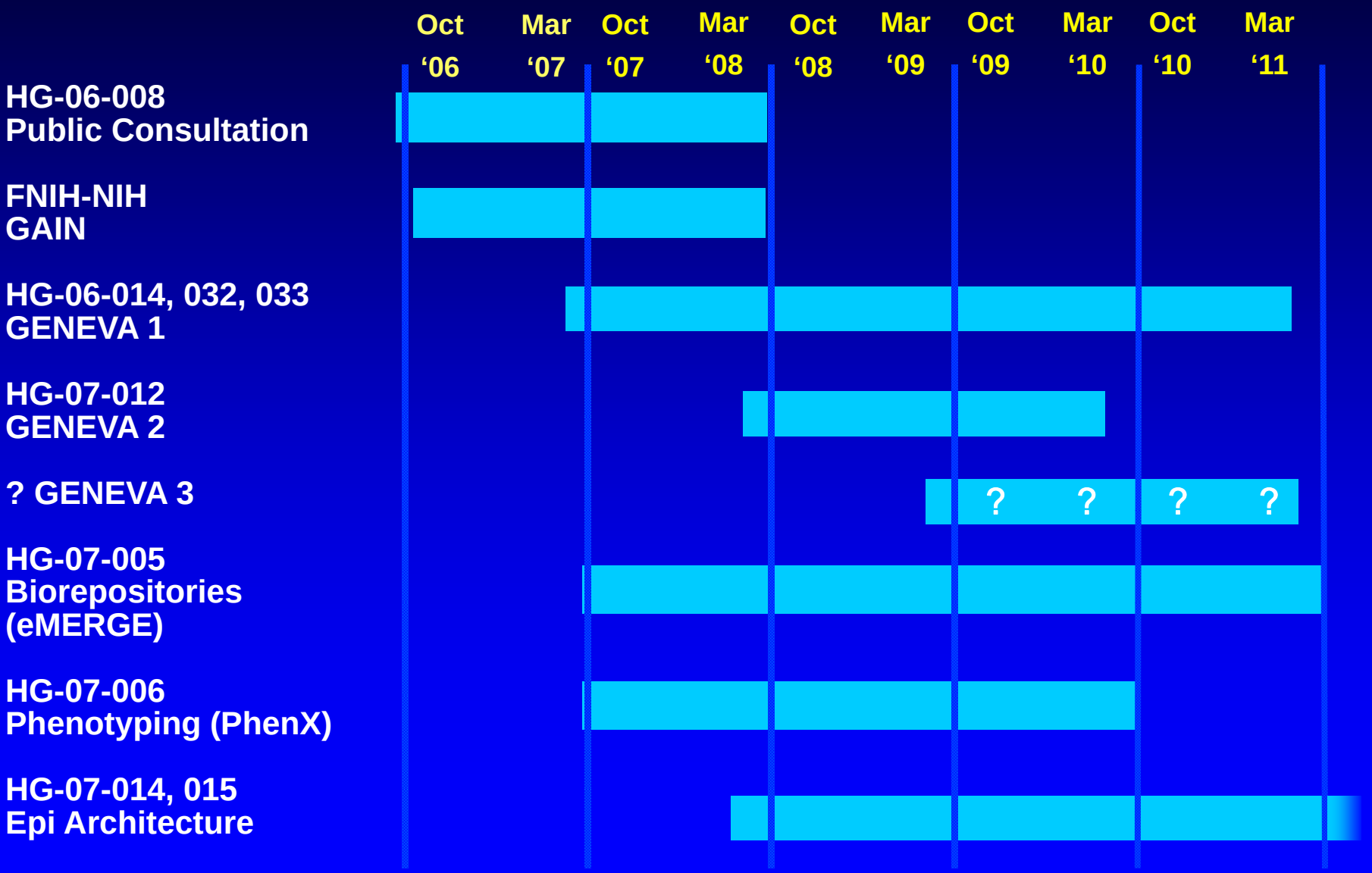
Goal #5: Support training of geneticists in epidemiologic research methods, of epidemiologists in genomic methods, and of clinical researchers and clinicians in applying genomic technologies to promote health and reduce disease.

- Course development for AAFP hemochromatosis component, 2006
- Multi-IC symposia training components, 2006-2008
- GEI-SER symposium, “GWA Studies for the Rest of Us,” June 2007
- ASHG seminar on bias, “Designing Geneticists,” October 2007
- Sabbatical opportunities (course development, critical assessment of methods and bias in GWA studies)

OPG Studies Timeline



Genome-Wide Studies to Health

	GAIN	GEI	Biorepositories	Consultation	Phenotyping	Epi Arch

Genome-Wide Studies to Health

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Discovery GWA	++	++	+			

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Replication		+			+	

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Discovery GWA	++	++	+			
Replication		+			+	
Disseminate Individual Data	++	++	+			

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Discovery GWA	++	++	+			
Replication		+			+	
Disseminate Individual Data	++	++	+			
Address Consent, Commun Concerns		+	++	++		

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Discovery GWA	++	++	+			
Replication		+			+	
Disseminate Individual Data	++	++	+			
Address Consent, Commun Concerns		+	++	++		
Improve Phenotypic Characterization			++		++	
Harmonize Data Across Studies		+	+		++	+

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Discovery GWA	++	++	+			
Replication		+			+	
Disseminate Individual Data	++	++	+			
Address Consent, Commun Concerns		+	++	++		
Improve Phenotypic Characterization			++		++	
Harmonize Data Across Studies		+	+		++	+
Analyze Associations	+	++	+			++
Assess Health Impact			+			++

Mia Diggs, Program Assistant
Emily Harris, Epidemiologist
Lucia Hindorff, Epidemiologist
Heather Junkins, Program Analyst
Lisa McNeil, Program Analyst
Erin Ramos, Epidemiologist
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