National Human Genome Research Institute

National Institutes of Health

U.S. Department of Health and Human Services

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

National Human Genome Research Institute

National Institutes of Health

U.S. Department of Health and Human Services

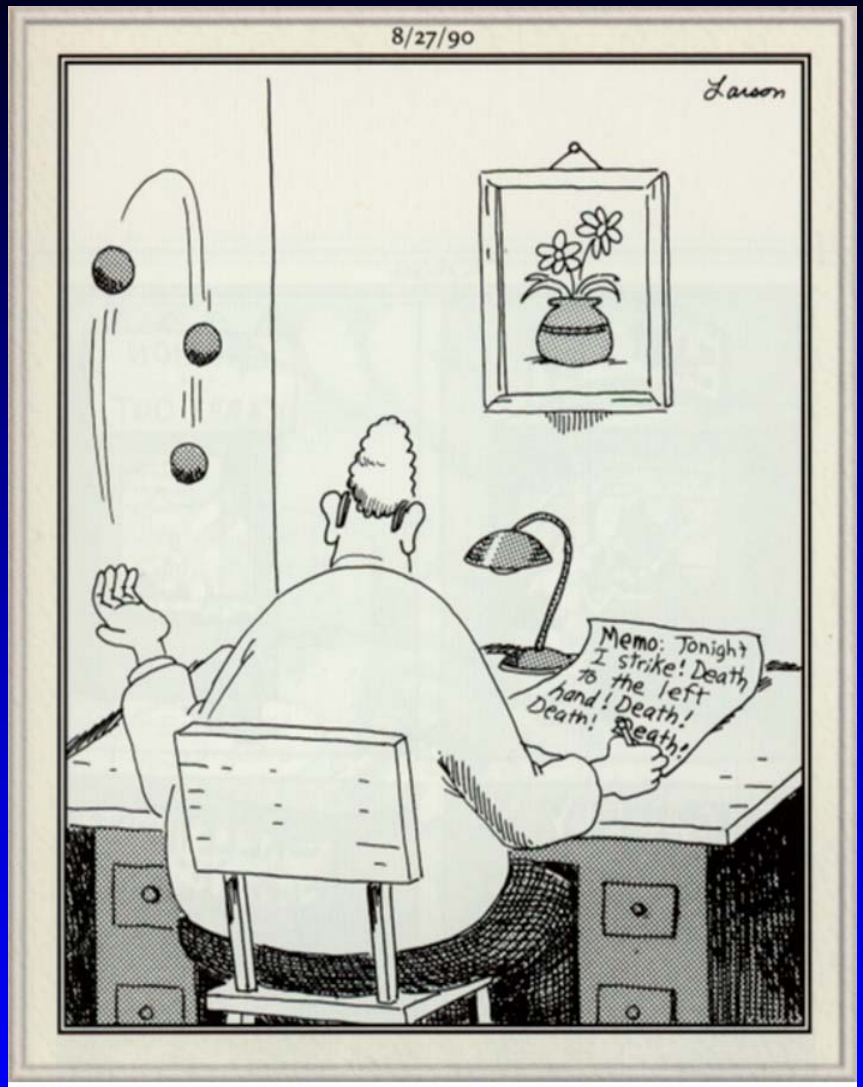
Multi-IC Symposium on Application of Genomic Technologies to Population-Based Studies

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

Goals of Multi-IC Training Symposia

- To identify common, critical issues encountered in applying genomic technologies to population studies
- To develop approaches for prioritizing and conducting population studies using genomic technologies
- To identify new tools needed for conducting genomics-based population studies



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

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

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

STATUS OF RECOMMENDATIONS FROM JUNE 5-6 2006
MULTI-IC SYMPOSIUM ON APPLICATION OF GENOMIC TECHNOLOGIES TO POPULATION-BASED STUDIES
(As of 5/17/07)

	Near-Term Administrative Action Items:	**Leadership**	**Status**
1.	Key elements of consent for genome-wide association studies (GWAS) should be collected, updated frequently, and made available to ICs and possibly to the outside community. A repository of model consent forms could be developed.	Symposium Panel 3, in collaboration with Nabel GWAS Data Sharing Committee	Sample consents from current NIDDK, NIGMS, NIMH, and NINDS repositories, and draft consent elements for NHGRI Medical Sequencing program, have been made available for review at http://www.genome.gov/Pages/Extranets/PopulationGenomicsTraining/consent.cfm
2.	Examples or collections of successful consortium agreements and genotyping quality control standards would be helpful.	Nabel Committee, with NIH/OD	Sample data use and consortium agreements and policies from current NCI, NHLBI, NIDDK, NIGMS, and NIMH programs have been made available for review at http://www.genome.gov/Pages/Extranets/PopulationGenomicsTraining/agreements.cfm

Status of Key Recommendations from 2006 Multi-IC Symposium

Near-Term Administrative Action Items	Progress
Post key elements of consent	Done
Post successful consortium agreements	Done
Develop common data elements for GWA studies	NCBI; RFA HG-07-006
Standards for quality of genotyping and sequencing data	
Sequencing to follow-up GWA signals	Done
Standards for defining validity and replication of GWA findings	Done

Status of Additional Recommendations

- 3 of 4 “Intermediate-Priority Goals” in progress or completed, fourth is:

  Assess benefits and risks of electronically tracking research use of GWA data; consider asking that GWA study name be used in abstracts of publications.
- 18 of 36 “Other Recommendations” in progress or completed

Some 6/6/06 Recommendations to be Revisited?

24. Encourage addition of ancillary phenotypic and exposure measures to existing studies.

25. Provide incentives for analysis of datasets in large population studies, and collaborating with population study investigators.

35. “Federate” very large capacity, infrequently used data outside of central databases.

37. Need “cosmopolitan” GWA panel that will work in numerous or all populations.

Some 6/6/06 Recommendations to be Revisited?

38. Cost-effective technologies needed for characterizing 10-10,000 SNPs.

39. Develop better methods for scoring structural variation.

41. Need effective methods for targeted resequencing or 100kb-1Mb regions.

46. Need better methods for optimizing efficient use of limited DNA.

Some 6/6/06 Recommendations to be Revisited?

38. Cost-effective technologies needed for characterizing 10-10,000 SNPs.

39. Develop better methods for scoring structural variation.

41. Need effective methods for targeted resequencing or 100kb-1Mb regions.

46. Need better methods for optimizing efficient use of limited DNA.

Genome-wide association study of prostate cancer identifies a second risk locus at 8q24

Meredith Yeager[1,2], Nick Orr[3], Richard B Hayes[2], Kevin B Jacobs[4], Peter Kraft[5], Sholom Wacholder[2], Mark J Minichiello[6], Paul Fearnhead[7], Kai Yu[2], Nilanjan Chatterjee[2], Zhaoming Wang[1,2], Robert Welch[1,2],

Multiple regions within 8q24 independently affect risk for prostate cancer

Christopher A Haiman[1], Nick Patterson[2], Matthew L Freedman[2,3], Simon R Myers[2], Malcolm C Pike[1], Alicja Waliszewska[2,4,5], Julie Neubauer[2,4], Arti Tandon[2,4], Christine Schirmer[2,4], Gavin J McDonald[2,4],

Genome-wide association study identifies a second prostate cancer susceptibility variant at 8q24

Julius Gudmundsson[1,17], Patrick Sulem[1,17], Andrei Manolescu[1,17], Laufey T Amundadottir[1,17], Daniel Gudbjartsson[1], Agnar Helgason[1], Thorunn Rafnar[1], Jon T Bergthorsson[1], Bjarni A Agnarsson[2],

nature genetics

May 2007, Volume 39 No 5 pp 569-688

Genomics of common diseases

Sciencexpress Report

A Genome-Wide Association Study of Type 2 Diabetes in Finns Detects Multiple Susceptibility Variants

Laura J. Scott,[1] Karen L. Mohlke,[2] Lori L. Bonnycastle,[3] Cristen J. Willer,[1] Yun Li,[1] William L. Duren,[1] Michael R. Erdos,[3] Heather M. Stringham,[1] Peter S. Chines,[3] Anne U. Jackson,[1] Ludmila Prokunina-

Sciencexpress Report

Genome-Wide Association Analysis Identifies Loci for Type 2 Diabetes and Triglyceride Levels

Sciencexpress Report

Replication of Genome-Wide Association Signals in U.K. Samples Reveals Risk Loci for Type 2 Diabetes

Eleftheria Zeggini,[1,2*] Michael N. Weedon,[3,4*] Cecilia M. Lindgren,[1,2*] Timothy M. Frayling,[3,4*] Katherine S. Elliott,[2] Hana Lango,[3,4] Nicholas J. Timpson,[2,5] John R. B. Perry,[3,4] Nigel W. Rayner,[1,2] Rachel M. Freathy,[3,4] Jeffrey C. Barrett,[2] Beverley Shields,[4] Andrew P. Morris,[2] Sian Ellard,[4,6] Christopher J. Groves,[1] Lorna W. Harries,[4] Jonathan L. Marchini,[7] Katharine R. Owen,[1] Beatrice Knight,[4]

A genome-wide association study identifies novel risk loci for type 2 diabetes

Robert Sladek[1,2,4], Ghislain Rocheleau[1]*, Johan Rung[4]*, Christian Dina[5]*, Lishuang Shen[1], David Serre[1], Philippe Boutin[5], Daniel Vincent[4], Alexandre Belisle[4], Samy Hadjadj[6], Beverley Balkau[7], Barbara Heude[7], Guillaume Charpentier[8], Thomas J. Hudson[4,9], Alexandre Montpetit[4], Alexey V. Pshezhetsky[10], Marc Prentki[10,11], Barry I. Posner[2,12], David J. Balding[13], David Meyre[5], Constantin Polychronakos[1,3] & Philippe Froguel[5,14]

Sciencexpress Report

A Common Variant in the *FTO* Gene Is Associated with Body Mass Index and Predisposes to Childhood and Adult Obesity

Timothy M. Frayling,[1,2*] Nicholas J. Timpson,[3,4*] Michael N. Weedon,[1,2*] Eleftheria Zeggini,[3,5*] Rachel M. Freathy,[1,2] Cecilia M. Lindgren,[3,5] John R. B. Perry,[1,2] Katherine S. Elliott,[3] Hana Lango,[1,2] Nigel W. Rayner,[3,5] Beverley Shields,[2] Lorna W. Harries,[2] Jeffrey C. Barrett,[3] Sian Ellard,[2,6] Christopher J. Groves,[5] Bridget Knight,[2] Ann-Marie Patch,[2,6] Andrew R. Ness,[7] Shah Ebrahim,[8] Debbie A. Lawlor,[9] Susan M. Ring,[9] Yoav Ben-Shlomo,[9] Marjo-Riitta Jarvelin,[10,11] Ulla Sovio,[10,11] Amanda J. Bennett,[5] David Melzer,[1,12] Luigi Ferrucci,[13] Ruth J. F. Loos,[14] Inês Barroso,[15] Nicholas J. Wareham,[14] Fredrik Karpe,[5] Katharine R. Owen,[5] Lon R. Cardon,[3] Mark Walker,[16] Graham A. Hitman,[17] Colin N. A. Palmer,[18] Alex S. F. Doney,[19] Andrew D. Morris,[19] George Davey-Smith,[4] The Wellcome Trust Case Control Consortium,[20] Andrew T. Hattersley,[1,2†‡] Mark I. McCarthy[3,5†]

12 April 2007

Sciencexpress Report

A Common Allele on Chromosome 9 Associated with Coronary Heart Disease

Ruth McPherson,[1]*† Alexander Pertsemlidis,[2]* Nihan Kavaslar,[1] Alexandre Stewart,[1] Robert Roberts,[1] David R. Cox,[3] David A. Hinds,[3] Len A. Pennacchio,[4] Anne Tybjaerg-Hansen,[5] Aaron R. Folsom,[6] Eric Boerwinkle,[7] Helen H. Hobbs,[2,9] Jonathan C. Cohen[2,8]†

[1]Division of Cardiology, University of Ottawa Heart Institute, Ottawa K1Y4W7, Canada. [2]Donald W. Reynolds Cardiovascular Clinical Research Center and the Eugene McDermott Center for Human Growth and Development, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA. [3]Perlegen Sciences, Mountain View, CA 94043; USA. [4]Genomics Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA & U.S. Department of Energy Joint Genome Institute, Walnut Creek, CA 94598, USA. [5]Department of Clinical Biochemistry, Rigshospitalet, Copenhagen University Hospital, Copenhagen DK-2100, Denmark. [6]Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN 55454, USA. [7]Human Genetics Center and Institute for Molecular Medicine, University of Texas Health

Sciencexpress Report

A Common Variant on Chromosome 9p21 Affects the Risk of Myocardial Infarction

Anna Helgadottir,[1]* Gudmar Thorleifsson,[1]* Andrei Manolescu,[1]* Solveig Gretarsdottir,[1] Thorarinn Blondal,[1] Aslaug Jonasdottir,[1] Adalbjorg Jonasdottir,[1] Asgeir Sigurdsson,[1] Adam Baker,[1] Arnar Palsson,[1] Gisli Masson,[1] Daniel Gudbjartsson,[1] Kristinn P. Magnusson,[1] Karl Andersen,[2] Allan I. Levey,[3] Valgerdur M. Backman,[1] Sigurborg Matthiasdottir,[1] Thorbjorg Jonsdottir,[1] Stefan Palsson,[1] Helga Einarsdottir,[1] Steinunn Gunnarsdottir,[1] Arnaldur Gylfason,[1] Viola Vaccarino,[3] W. Craig Hooper,[3] Muredach P. Reilly,[4] Christopher B. Granger,[5] Harland Austin,[3] Daniel J Rader,[4] Svati H. Shah,[5] Arshed A. Quyyumi,[3] Jeffrey R. Gulcher,[1] Gudmundur Thorgeirsson,[3] Unnur Thorsteinsdottir,[1] Augustine Kong,[1]† Kari Stefansson[1]†

Objectives

- Share initial NIH-wide experience with GWA studies, including scientific and programmatic problems encountered and solutions employed
- Facilitate collaborations for replication and follow-up studies (sequencing, expression, genome-wide methylation, function, etc)
- Examine different models for data analysis and follow up of GWA findings, and approaches for maximizing use of GWA data

Institutes and Centers Heavily Involved in GWA Studies

- National Cancer Institute
- National Heart, Lung, and Blood Institute
- National Human Genome Research
- National Institute of Mental
- National Institute of
- National Libra
- Nationa
- Nati
- Natio
- Natio
- National Institute on Alcohol Abuse and Alcoholism
- National Institute of Diabetes and Digestive and Kidney Diseases
- National Institute of Drug Abuse

Totally My Bad!

Institutes and Centers Heavily Involved in GWA Studies

- National Cancer Institute
- National Heart, Lung, and Blood Institute
- National Human Genome Research Institute
- National Institute of Mental Health
- National Institute of Neurological Disorders and Stroke
- National Library of Medicine
- National Center for Research Resources
- National Center for Advancing Translational Sciences
- National Institute on Aging
- National Institute on Alcohol Abuse and Alcoholism
- National Institute of Diabetes and Digestive and Kidney Diseases
- National Institute of Drug Abuse

Totally My Bad!

Topics to be Addressed Today

- Replication Studies - Stephen
  (false positives, criteria, collaboration)
- Follow-Up Studies - Thomas
  (fine-mapping, sequencing, new technologies)
- Cross-Study Analysis - Chris
  (consortia, combining platforms, multiple traits, common controls)
- Data Sharing - Jim
  (databases, receiving data, quality control)
- Consent/Approvals - Kat
  (data sharing, layered or older consents)

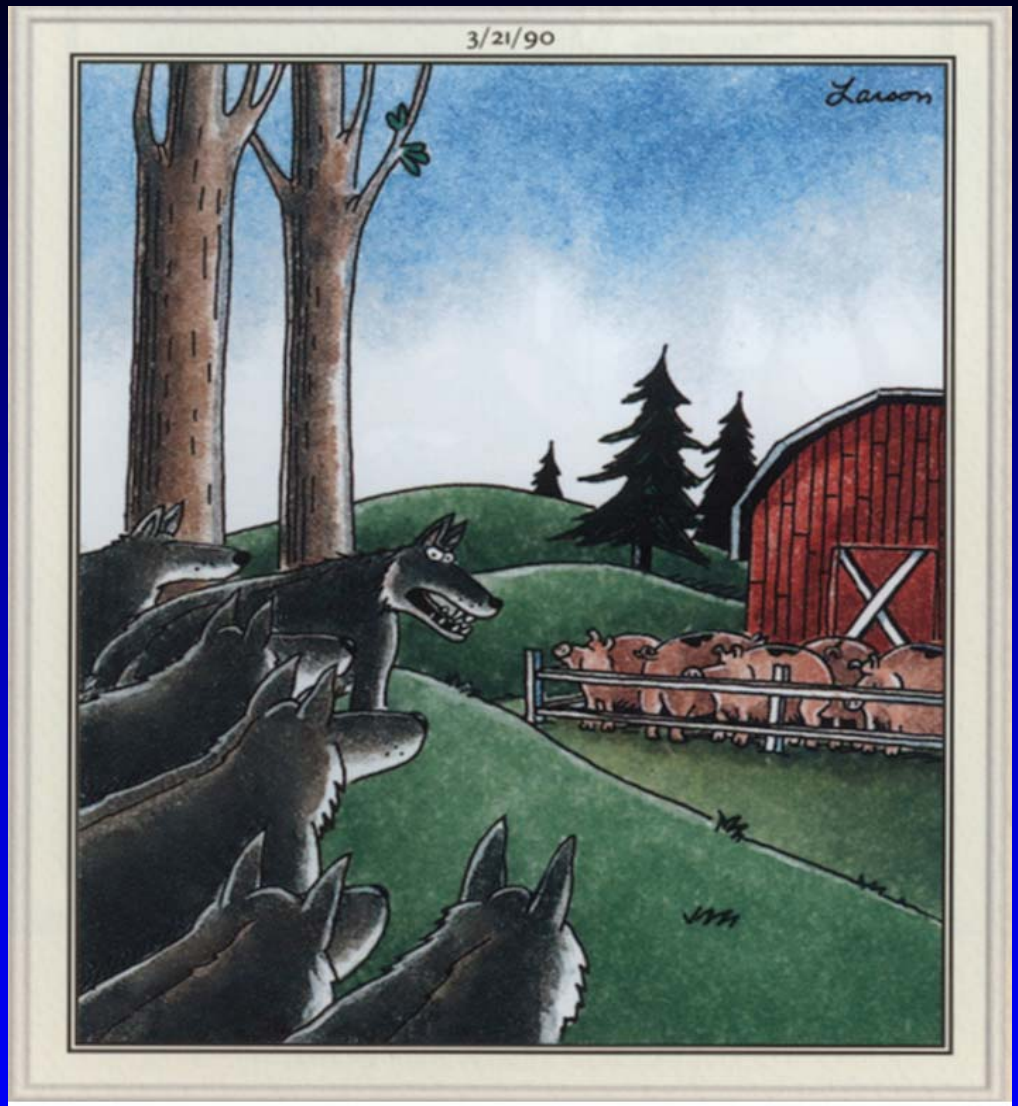
Things We'd Like to Do in the Next 9 Hours

- Stimulate active discussion and interchange on GWA studies among ICs (or even within ICs…)
- Identify obstacles to be overcome and tools needed to facilitate these studies
- Come away with at least three new inter-IC (or intra-IC?) collaborations in GWA studies

Things We WON'T Do in the Next 9 Hours

- Decide or even discuss policies related to GWA studies

- Prescribe or proscribe any GWA practices for any IC



I say we do it ... and trichinosis be damned!"

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