International Stroke Genetics Consortium

4th International Workshop: November 6 and 7, 2008, Boston, MA USA

Meeting Minutes

I. Welcome/Introductions/Goals for Meeting (Jonathan Rosand)

- History of ISGC
  - Workshops held thus far
- Funded Projects
- Principles
  - Anyone with the resources and/or expertise to contribute is invited to join

II. ISGC Project Presentations

A. Sequence Variants on Chromosome 9p21 Confer Risk of Atherosclerotic Stroke (J. Rosand for Martin Dichgans)

B. Wellcome Trust Case Control Consortium Ischemic stroke GWAS (Hugh Markus)

- GWAS of IS in European and US cohort
- Three stage design
  - 1: Initial GWAS in European cohort
  - 2: Replication in European cohort
  - 3: Replication in US cohort

C. Preparing for Anticipated NINDS GWAS Initiative (Steven Kittner, James Meschia, Stephen Rich)

- April 2008, NINDS held an advisory meeting that examined the following:
  - Role of NINDS repository
  - Ability of sites to conform to data sharing policies
  - Minimum required phenotypic information
- Proposed Specific Aims:
  - 1: Obtain phenotypic information and DNA from 7100 cases and 7100 controls from the ISGC sites in North America (ISGC-NA)
  - 2: Perform imputation and meta-analyses within the ISGC-NA
  - 3: Perform in silico meta-analysis with the WTCCC
  - 4: Replicate findings in other cohorts e.g. CHARGE

D. Project Proposal Mechanism

- The ISGC project proposal form is available online: all investigators interested in leading a collaborative project should complete this form and send to info@strokegenetics.org. Once it is received, the proposal will be circulated to the group
  - At present, all project proposals are circulated, however, in the future, screening may become necessary

III. Introduction to Broad Institute (Stacey Gabriel: Broad Institute)

- History of the Broad Institute
- Overview of the Genetic Analysis Platform (GAP) and structure
- Effect of the Hap Map project at the Broad Institute
- Broad Institute is a NCRR National Genotyping Center of the NIH
- Protection of data within the Broad and the GAP database
- Overview of CARe portal

IV. ISGC Informatics Platform (Michael Dinsmore, Lynelle Cortellini, J. Rosand)

- Demonstration of the ISGC Informatics Platform
- In progress:

- Study proposal and application mechanism
- Proposed date use approval procedure

- Investigators still have complete control over their own data and approvals for use
- A project proposal regarding the Informatics Platform will be circulated to the group in the next month or so

V. Related Studies

A. Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium Ischemic Stroke GWAS (Monique Breteler)

- Results from IS GWAS

B. GWAS of Blood Pressure (Christopher Newton-Cheh: Broad Institute/Massachusetts General Hospital)

C. GWAS of Blood Lipids and MI (Sekar Kathiresan: Broad Institute/Massachusetts General Hospital)

VI. Discussion: How to make Consortia Work for Your Career and Your Trainees' Careers

VII. Special presentation (James Gusella)

- "Mendelian diseases as complex phenotypes"
- Evolving techniques from linkage studies, to candidate gene studies, to GWAS

VIII. Brief review of projects involving ISGC members (Part 1)

A. Causative Classification of Stroke (CCS) study (Hakan Ay)

- Paper in progress

B. Genes and Environment Interactions Study (GEI) (Braxton Mitchell)

- GWAS of ischemic stroke interactions with smoking

C. WMH GWAS (Natalia Rost)

- GWAS of white matter disease in ischemic stroke population

D. Intracerebral Hemorrhage (ICH) GWAS (J. Rosand)

- Funding for a multicenter ICH GWAS from the National Institute of Neurological Disorders and Stroke (NINDS) at MGH
- All sites with ICH samples and matched controls are encouraged to participate

E. Cincinnati ICH GWAS (Daniel Woo)

- Genetic and Environmental Risk Factors for Hemorrhagic Stroke (GERFHS)
  - Population-based study of individuals in the Cincinnati area
  - Blood and buccal swab samples available: 99.4% genetic concordance between the two types of samples from the same individual
  - 1:2 case:control ratio
- REasons for Geographic and Racial Differences in Stroke (REGARDS)
  - 50% white, 50% black; 50% from Stroke Belt, 50% outside Stroke Belt; 50% male, 50% female
  - ~30,000 subjects

F. Australian GWAS (Christopher Levi)

- Australian Stroke Genetics Collaborative Group
  - Funding to do GWAS through Fall 2009
  - Multi-site enrollment: Newcastle, Perth, Gosford, Adelaide
  - Single-phase: 1500 cases, 1500 controls
  - Genotyping on Illumina 610 platform

G. Looking ahead: Standardizing prospective data collection for all centers (Arne Lindgren & S. Kittner)

- Future enrollment suggestions
  - Minimum set of defined variables that are defined by the ISGC in addition to local definitions
    - Would include: stroke classification, risk factors, etc.
- Sample Handling recommendations
- Discussion regarding whether to publish methods in literature

IX. ISGC Project Management Discussion (science, collaboration, timelines, future sample collection, phenotyping etc.)

- Proposed Projects:
  - ISGC Symposium at ASHG meeting, fall 2009, Hawaii USA (Worrall)
  - Standardization of prospective data (Lindgren/Kittner)
  - ISC satellite meeting in San Diego (Worrall)
  - CCS follow-up: assessment of performance in cases from sites other than Massachusetts General Hospital, especially non-US sites (Sudlow)
    - May be added as part of the ISGC-NA data harmonization effort

X. Special topics

A. Novel Strategies to Analyze Existing Datasets (Paul deBakker)

B. Copy Number Variation (Amanda Elliot)

C. Risk Assessment of Cerebrovascular Events (RACE) Study and the Pakistan Risk Of Myocardial Infarction Study (PROMIS) (Danish Salaheen)

- Pakistani cohort

D. Taiwan stroke study (Ida Chen)

- 4300 stroke patients per year in 4 Taiwanese hospitals, with potential of adding 2 more hospitals with 2600 stroke patients per year
- Examine different rates of cardiovascular disease and ischemic heart disease in East vs. West populations

E. Cervical Artery Dissections and Ischemic Stroke Patients (CADISP) (Stéphanie Debette)

- Cervical artery dissection in young European adults
- GWAS to begin in 1/2009

X. ISGC Website (L. Cortellini)

- Website address: www.strokegenetics.org
- Members only section
  - Log in on home page
  - Username and password: ISGCparticipant
    - Please do not change the username or password!
  - We hope to have individual passwords for each investigator in the near future
- Areas in Members Only section for each project
  - Each project has own password protection
- All ISGC forms, meeting minutes, etc. to be posted here
- Any questions, please email info@strokegenetics.org

XI. Concluding discussion, planning the 5th international workshop in Europe

- Munich was chosen as the location for the 5th International Workshop

- Dates will be June 25-27, 2009

XII. Action Items

1. Project proposals to be circulated: please email Project Proposal forms to info@strokegenetics.org for circulation to the group
2. If investigators are interested in working to address phenotypic consistency across sites, please contact Brad Worrall or James Meschia. Brad and James are collecting a random sample of 20 case review forms from each site to review for TOAST accuracy.

International Stroke Genetics Consortium

4th International Workshop: November 6 and 7, 2008, Boston, MA USA

Attendee List

Beth Israel Deaconess Medical Center, Boston MA, USA	Magdy Selim
Boston University School of Medicine, Boston MA, USA	Philip Wolf, Sudah Seshadri, Stephanie Debette, Aleksandra Pikula
Cardiovascular and Stroke Genetics Working Group at Emory University, Atlanta GA, USA	Salina Waddy
Cedars Sinai Medical Center, Los Angeles CA, USA	Ida Chen
Celera, Alameda CA, USA	May Luke
Chang Gung Memorial Hospital, Kaohsiung County, Taiwan	Ku-Chou Chang
Erasmus University, Rotterdam, Netherlands	Monique Breteler
Framingham Heart Study, Framingham MA, USA	Christopher O'Donnell
Hammersmith Hospitals & Imperial College London, UK	Pankaj Sharma
Jagiellonian University, Krakow, Poland	Agnieszka Slowik
John Hunter Hosp, University of Newcastle, New Lambdon NSW, Australia	Christopher Levi
Linkou Medical Center, Taoyuan, Taiwan	Tsong-Hai Lee
Lund University, Malmö University Hosp, Malmö, Sweden	Olle Melander, Philippe Burri
Lund University, University Hosp, Lund, Sweden	Arne Lindgren
Massachusetts General Hospital, Deane Institute, Broad Institute, Boston MA, USA	Jonathan Rosand, Natalia Rost, Hakan Ay, Lynelle Cortellini, Alessandro Biffi, Jordi Jimenez-Conde, A. Gregory Sorensen, Steven Greenberg
Milan University, Milan Italy	Anna Bersano
Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria	Akintomi Olugbodi
Sahlgrenska University Hospital, Goteborg, Sweden	Christina Jern, Katarina Jood
St. George's University, London, United Kingdom	Steve Bevan, Hugh Markus
University Hospitals Leuven, Belgium	Vincent Thijs
University of Cambridge, Cambridge, UK	Danish Saleheen
University of Cincinnati, Cincinnati OH, USA	Daniel Woo
University of Edinburgh; Western General Hospital, Edinburgh, Scotland	Cathie Sudlow
University of Maryland School of Medicine, Baltimore MD, USA	Steven Kittner, Braxton Mitchell, Patrick McArdle, Mark Dobbins, Mary Sparks
University of Texas Heath Sciences Center, Houston TX, USA	Myriam Fornage
University of Utah, Salt Lake City UT, USA	Jennifer Majersik
University of Virginia, Charlottesville VA, USA	Stephen Rich, Michele Sale, Bradford Worrall
University of Washington, Seattle WA, USA	Will Longstreth
Vall d'Hebron Hospital, Barcelona, Spain	Israel Fernandez-Cadenas