



ISGC NEWSLETTER

ISSUE 4- FEBRUARY 2010

Contents

Introduction	2
Founding Principles	2
ISGC Project List	
Ongoing Projects	3
Other ISGC Projects	6
ISGC Website Update	7
6th International Workshop in Cincinnati	8
7th International Workshop in Edinburgh	9
8th International Workshop in Miami	10

If you'd like to suggest a topic or article for a future newsletter, or if you'd like to give general feedback, please contact:

Lynelle Cortellini
(lcortellini@partners.org).

Introduction

This is the third issue of the bi-monthly newsletter for the International Stroke Genetics Consortium. The ISGC newsletter will serve to keep investigators updated on ongoing projects, new project proposals, meetings, and publications.

The newsletter will be sent to participants on the 1st of even months (or nearest workday) as an email attachment.

All Investigators are invited and encouraged to submit content for the newsletter. Please send content suggestions to Lynelle Cortellini (lcortellini@partners.org).

ISGC Founding Principles

Cerebrovascular disease is a complex disorder influenced by variation in many genetic and non-genetic exposures, each of which contributes only a small influence to disease risk. Therefore large (larger than any single center can assemble on its own) well-characterized samples will be necessary to discover these exposures.

Principles of Collaboration:

- 1) The ISGC is open to all who can contribute
- 2) All contributions will be fairly recognized in publications
- 3) We work together in a spirit of cooperation and open communication in order to promote the best science in the present and the best science in the future.

ISGC Project Updates

Ongoing Projects:

Wellcome Trust Case Control Consortium Ischemic Stroke GWAS

Contact: Hugh Markus

Date Proposed: July 2007

Aims: Determine whether there are genetic determinants of ischemic stroke that can be identified using GWAS and whether these determinants predispose individuals to specific subtypes of stroke.

Status: Genotyping of Phase I completed, replication in European cohort to begin in late Spring on Illumina ImmunoChip. Meta-analysis with other interested ISGC collaborators with GWAS data on ischemic stroke samples and with deCode to begin in late Spring.

NIH-funded ICH GWAS

Contact: Jonathan Rosand

Date Proposed: January 2008

Aims: This multi-center genome-wide association study (GWAS) is designed to identify genetic determinants of:

- 1) Risk of intracerebral hemorrhage (ICH) using a case-control design
- 2) Clinical course of ICH using a cohort design of individuals who have suffered an ICH.

Status: Genotyping in progress, meta-analysis with U Cincinnati group in progress.

A genome-wide association study of early onset ischemic stroke

Contact: Braxton Mitchell, Steven Kittner

Date Proposed: January 2008

Aims: To carry out a GWAS of early onset stroke

- 1) Conduct a staged GWAS in the U of Maryland sample
- 2) Replicate associations detected in Aim 1 in an independent set of young-onset stroke cases controls from collaborators in the ISGC.
- 3) Determine if SNPs robustly associated with early onset stroke in both the Maryland and IGSC cohorts are also associated with older onset stroke.

Status: Further developments include: 1. GWAS analysis underway: 1M SNPs genotyped on Illumina Omni Quad platform through the NHGRI-sponsored GENEA Consortium. Collaboration established with two additional early onset stroke cohorts for a combined meta-analysis: (a) 1,500 cases from Pakistan (Dr. Danish Saleheen); and (b) 1,000 cases from Germany (Dr. Arndt Rolf).

2. Genotyping completed for 50K Illumina CVD chip for analysis of common and rare SNPs in CVD candidate genes proceeding.

ISGC Projects

Ongoing Projects (continued):

Replication of Chr. 9q21 region in stroke cases and matched controls in Chinese population

Contacts: Xingyu Wang, Lisheng Liu

Date Proposed: March 2008

Aims: To replicate the findings of the Chromosome 9p21 projects of the ISGC within a Chinese cohort.

Status: Manuscript being drafted, to be presented in Cincinnati

International Validation of a Computerized Algorithm for Etiologic Classification of Ischemic Stroke: The Causative Classification of Stroke System (CCS)

Contact: Hakan Ay, Jonathan Rosand

Date Proposed: March 2008

Aims: This is an ISGC-wide study to validate a computerized system for etiologic classification of ischemic stroke.

Status: Manuscript submitted

Relationship of genetic markers for common risk factors for stroke with ischemic cerebrovascular disease

Contact: Vincent Thijs

Date Proposed: June 2008

Aims: Determine whether SNPs associated with well known risk factors for ischemic stroke like diabetes, elevated LDL, myocardial infarction and atrial fibrillation are associated with ischemic cerebrovascular disease using a case control design.

Status: Manuscript being drafted

Looking for genetic risk factors of cervical artery dissections

Contact: Stéphanie Debette on behalf of Didier Leys

Date Proposed: February 2009

Aims: A replication study to test whether the polymorphisms associated with CAD in the GWAS within the CADISP-consortium are also associated with CAD in other independent populations, in order to exclude spurious associations.

Status: Genotyping in final phase, results expected soon. The replication study is in the final phase of recruitment

ISGC Projects

Ongoing Projects (continued):

The International Stroke Genetics Consortium Informatics Platform: A tool for Efficient Collaboration and Rapid Discovery

Contacts: Lynelle Cortellini, Steve Bevan, Jonathan Rosand

Date Proposed: February 2009

Aims: 1) Compile a publically-available web-based catalog of all clinical characteristics, radiographic studies, genetic data and available biological samples collected for subjects with ischemic stroke and controls.
2) Enrich characterization of stroke patients by classifying all subjects according to the biologically-based Causative Classification of Stroke System and creating a central repository of de-identified neuroimaging data on patients with stroke.

Status: Ethics Committee submission in progress.

National Institute of Neurological Disorders and Stroke Ischemic Stroke GWAS

Contacts: Steven Kittner, James Meschia

Date Proposed: March 2009

Aims: Funding of an ischemic stroke genetics consortium in order to perform a genome wide association study in ischemic stroke patients and matched controls.

Status: Grant under review

Chromosome 12 and risk of ischemic stroke: A replication study

Contacts: James Meschia, Andrew Singleton, Jonathan Rosand

Date Proposed: April 2009

Aims: Replication effort through the ISGC of the CHARGE discovery of two SNPs on chromosome 12 that were over-represented among cases with ischemic stroke, compared to controls.

Status: Manuscript In Press with NEJM

White Matter Hyperintensity GWAS

Contacts: Natalia Rost, Jonathan Rosand

Date Proposed: July 2009

Aims: Perform a meta-analysis of the white matter hyperintensity volumes in patients with acute ischemic stroke and available GWAS data in order to achieve the necessary power to discover genetic associations between WMH volume and risk of stroke.

Status: Genotyping in progress, new sites joining

ISGC Projects

Ongoing Projects (continued):

Are established candidate gene polymorphisms for blood pressure, coronary heart disease, atrial fibrillation, lipid metabolism and hemostatic and inflammatory pathways also related to ischemic stroke risk in populations from the Southwest of Sweden?

Contacts: Arne Lindgren, Christina Jern, Olle Melander

Date Proposed: July 2009

Aims: To examine if SNPs related to phenotypes are related to ischemic stroke risk in a homogenous population sample from the Southwest of Sweden.

Status: Recently completed genotyping of 3600 patients and 2500 controls regarding 66 candidate SNP's from the above areas of interest.

Other Projects Involving ISGC Members

Genetic and Environmental Risk Factors for Hemorrhagic Stroke

Contact: Daniel Woo

Australian Stroke Genetics Collaborative Group

Contact: Chris Levi, John Attia

NHLBI Initiative on White Matter Disease

Contact: Paul Nyquist

INTERSTROKE

Contact: Guillaume Pare

Mitochondrial Genetics and Risk of Stroke

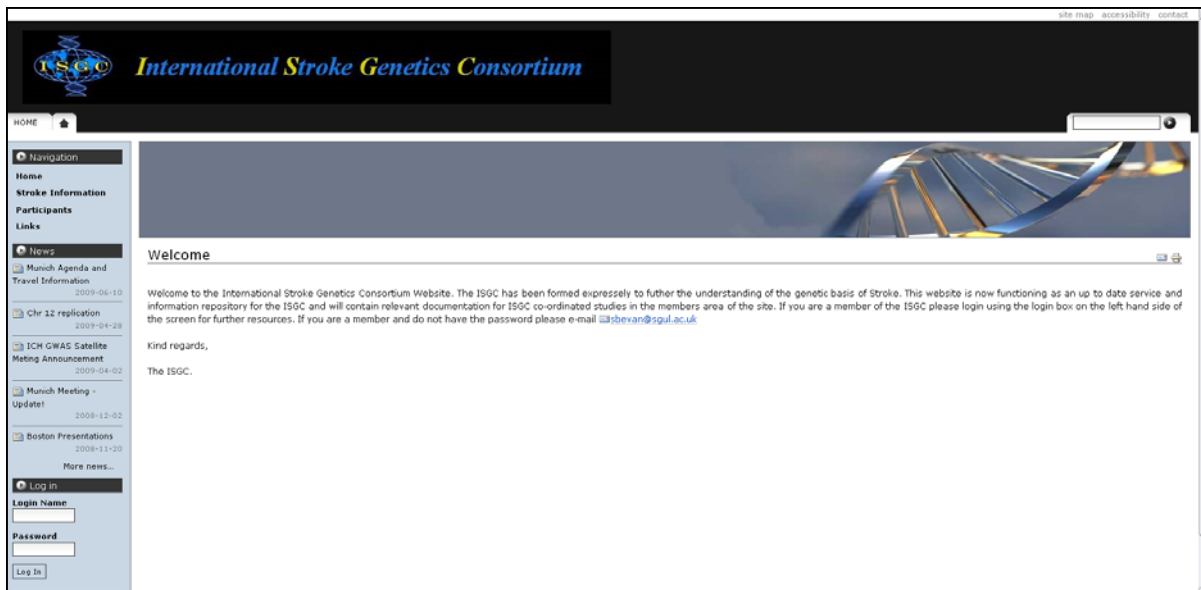
Contact: Jonathan Rosand

Website Update

Thanks to everyone who submitted a short bio and picture for the website! All bios received have been posted. If you would still like to submit a bio and picture, you can email them to either Lynelle or Steve.

If you have additional website content or layout suggestions, please email Lynelle Cortellini (lcortellini@partners.org) or Steve Bevan (sbevan@sgul.ac.uk) with your ideas.

Thank you!



6th International Workshop: Cincinnati OH, USA



Thank you to everyone who attended the 6th International Workshop in Cincinnati OH, USA. In spite of winter travel hazards, we had a great turnout. Thank you again to Dan Woo and Stephanie DeBette for organizing and hosting this meeting

We hope you enjoy some of the images from the meeting.



7th International Workshop: Edinburgh, Scotland

Our next ISGC European Workshop will take place on June 17 and 18, 2010. This meeting will be hosted by Cathie Sudlow (cathie.sudlow@ed.ac.uk) and Brad Worrall (bbw9r@virginia.edu). Additional details will be sent out as they are received.



8th International Workshop: Miami FL, USA

As was announced last month, the next US ISGC workshop will take place in Miami, Florida, USA. The meeting will take place in January, 2011- specific dates will be announced shortly.

