



ISGC NEWSLETTER

ISSUE 1- AUGUST 2009

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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 first issue of the bi-monthly newsletter for the International Stroke Genetics Consortium, initiated at the suggestion of members at last month's workshop in Munich. 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 Projects

Completed Projects:

Chromosome 9p21

Contact: Martin Dichgans

Date Proposed: October 2007

Aims: To determine whether the chromosome 9p21 locus is significantly associated with risk of ischemic stroke, independent of the reported association of with coronary artery disease and myocardial infarction.

Status: Publication accepted- Gschwendtner et.al. *Annals of Neurology*, May 2009.

Genome Wide Association Study of Ischemic Stroke

Contacts: Agnieszka Slowik, Daniel Woo

Date Proposed: January 2008

Aims: Grant application to the Polish Government: Our two institutes propose to submit a request to the Polish government for funding of a genome-wide association study for acute ischemic stroke using our existing cases and controls.

Status: Grant not funded

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

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

ISGC Projects

Ongoing Projects (continued):

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: Genotyping in progress

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

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 near completion

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

ISGC Projects

Ongoing Projects (continued):

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 ongoing

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: Grant under review

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: Jonathan Rosand, James Meschia

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 completed

ISGC Projects

New Projects:

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

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– this new proposal is available on the ISGC website

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

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

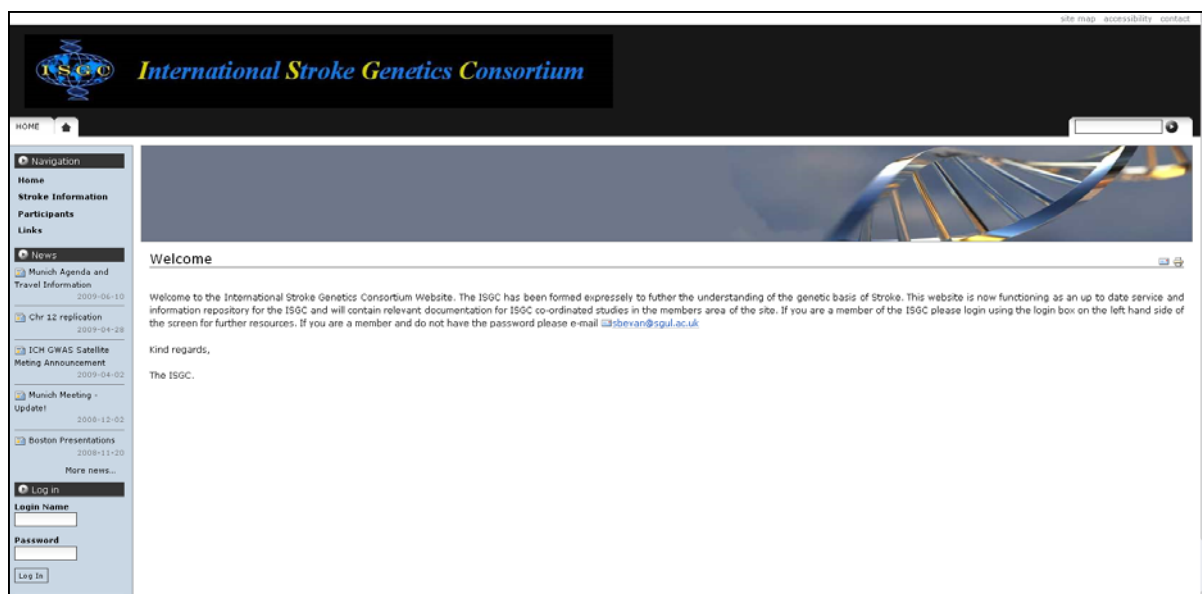
Contact: Jonathan Rosand

Website Update

Thanks to everyone who presented at the 6th International Workshop in Munich. We would like to post as many of the presentations as possible on the website in the Members Only section. Members are encouraged to share part or all of their presentations.

We are in the process of implementing some of the suggestions we received at the ISGC workshop, including more information and pictures of the Consortium and improved stroke genetics content on the public site. If you have additional web-site 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: Munich, Germany



Thank you to everyone who attended the 6th International Workshop in Munich, Germany. This was our largest meeting yet, with attendance reaching more than 70 investigators.

We hope you enjoy some of the images from the meeting and the Bavarian Alps trip below. Additional pictures will be available on the ISGC website.



7th International Workshop: Cincinnati OH, USA

The 7th International Workshop of the ISGC is scheduled for January 7-8, 2010 in Cincinnati OH, USA. Inaugurating a new tradition in which co-chairs from different continents will preside, the Cincinnati workshop will be organized by Daniel Woo and Stéphanie Debette. Please contact Dan (woodl@ucmail.uc.edu) or Stéphanie (sdebette@bu.edu) with any meeting specific questions.

