ISGC Newsletter
Issue 33 - February 2015

Contents

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

Thomas Battey
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Introduction

This is the thirty-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 posted as a PDF document to the ISGC website on the 1st of even months (or nearest workday) and can either be viewed online or downloaded as an attachment.

All Investigators are invited and encouraged to submit content for the newsletter. Please send content suggestions to Thomas Battey (tbattey@mgh.harvard.edu).

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.

New ISGC Members

The Outreach Committee (Anne-Katrin Giese, John Cole, Laura Heitsch, Jennifer Majersik, Juan Jose Martin, Tatjana Rundek, Daniel Woo) continues to welcome a number of members to the ISGC. If you would like to assist with the Outreach Committee's work, or know someone who would like to join the consortium, please contact Jennifer Majersik(jennifer.majersik@hsc.utah.edu).

Below please find a list of new members to the ISGC in 2015. We encourage you to contact them for collaboration, or simply to welcome them to the group.

Polina Golland, Massachusetts Institute of Technology (USA)
Dharambir Sanghera, University of Oklahoma (USA)

ISGC Project Updates

New Projects:

There are no new project proposals at this time.

Ongoing Projets:

Pharmacogenomics of tPA: Meta-analysis of GWAS and replication analysis

Contact: Israel Fernandez-Cadenas

Date Proposed: September 2014

Aims: To conduct a GWAS to identify genetic variants associated hemorrhagic transformation following treatment of ischemic stroke with tPA.

Status: Identifying and collecting cohort data for meta-analysis.

GISCOME - Genetics of Ischaemic Stroke functional outCOME Study

Contact: Jane Maguire, Arne Lindgren, Christina Jern and Brad Worrall

Date Proposed: February 2013

Aims: (A) To conduct a GWAS to identify genetic variants associated with functional outcome after ischemic stroke;
(B) To replicate the preliminary GWAS results from the discovery cohort.

Status: Preliminary results presented at November 2014 Paris ISGC workshop. Manu script for description of GISCOME in preparation.

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: Replication genotyping of second discovery phase is underway.

ISGC Project Updates

Ongoing Projects (continued):

Looking for genetic risk factors of cervical artery dissections

Contact: Stéphanie Debette and Didier Leys, on behalf of the CADISP group
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: The CADISP manuscript is in the revision process.

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

Contacts: 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: Imaging repository function will be a part of the NINDS-ISGC collaborative U01 grant. Phenotypic and genotypic functionality to be added as a part of a BioInformatics Research Network ARRA grant.

National Institute of Neurological Disorders and Stroke Ischemic Stroke GWAS

Contacts: Steven Kittner
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: Preliminary data presented at November 2014 Paris ISGC workshop. Primary manuscript in preparation.

ISGC Project Updates

Ongoing Projects (continued):

White Matter Hyperintensity GWAS

Contacts: Natalia Rost, Jonathan Rosand

Date Proposed: July 2009

Aims: To discover genetic markers of WMH severity using available genome-wide data and WMH volumes measured on MRI in patients with acute ischemic stroke.

Status: (1) interim GWA summary results to be exchanged between MGH/WTCCC to facilitate future meta-analysis; (2) WMH heritability study completed and pending validation; (3) WMH genetic score previously shown to be associated with incident ischemic stroke risk is pending replication.
A multi-center NIH R01 grant application, The MRI-GENetics Interface Exploration (MRI-GENIE) study has been submitted in June 2013 to further explore the genetic determinants of WMH using ischemic stroke cases (n=3,385) from the NINDS Stroke Genetics Network (SiGN).

MetaStroke: A meta-analysis of genome-wide studies in ischaemic stroke

Contact: Hugh Markus

Date Proposed: December 2009

Aims: Meta-Analysis of genome-wide data in ischemic stroke

Status: Meta-analysis underway.

Genome-wide association study of deep cerebral phenotypes

Contact: Dan Woo

Date Proposed: February 2010

Aims: (1) Specific SNPs/gene regions will be associated with deep cerebral phenotypes (deep/periventricular location of ICH, lacunar stroke or white matter disease) and this association will be independent of traditional risk factors including hypertension. (2) Specific SNPs/gene regions will be associated with deep cerebral phenotypes and will be modified by the presence/duration/severity of hypertension.

Status: List of interested studies compiled and in the process of developing a data transfer agreement. In addition, we are awaiting the completion of the Wellcome Trust effort as it would constitute a major contribution of small vessel ischemic strokes.

ISGC Project Updates

Ongoing Projects (continued):

Genetics of cerebral venous thrombosis (CVT)

Contact: Pankaj Sharma
Date Proposed: May 2010
Aims: To recruit DNA from CVT patients in order to undertake a GWAS.
Status: Awaiting receipt of Wellcome Trust control data for final analysis.

Replication of associations detected in a the Meta-stroke meta-analysis of genome-wide studies in ischaemic stroke

Contact: Hugh Markus
Date Proposed: September 2010
Aims: Replication of findings from the initial MetaStroke collaboration in novel cohorts of Caucasian and other ethnic groups.
Status: Analysis in progress

Consortium of Minority Population genomewide-Association Studies of Stroke (COMPASS)

Contact: Brad Worrall
Date Proposed: December 2010
Aims: Meta-analysis of cohorts and case-control studies with GWAS data for individuals of African descent and other minority groups.
Status: No update at this time.

ISGC Project Updates

Ongoing Projects (continued):

Replication of Ischemic Stroke Genes Discovered from Exome Sequencing

Contact: Steve Rich

Date Proposed: March 2011

Aims: Replication of genes discovered in NHLBI Exome Sequencing Project in ischemic stroke cases with small or large vessel strokes.

Status: The examination of rare variants in ischemic stroke in collaboration with the NHLBI Exome Sequencing Project (ESP) has made significant progress. The ESP Executive Committee has approved the use of 3,000 case samples and 3,000 control samples to be genotyped with the ExomeChip, a custom 300,000 SNP array (as designed by Illumina) with rare variants residing in exomes and additional content. These samples will be split with WHI and the ISGC, and restricted to those samples with existing GWAS data (for imputation), deep phenotyping (for use with other targeted traits), and both cases and controls from the same sites, with IRB approval for extensive sharing of information and deposition of data into dbGaP. The two studies that had samples meeting these criteria and immediately available for shipment to the University of Washington (the ESP genotyping site for ischemic stroke) were GEOS and ISGS. These samples are being sent for evaluation with anticipated completion of genotyping in Q1 2012.

Genetic studies of recurrent stroke

Contact: Brad Worrall, Michele Sale, Keith Keene

Date Proposed: February 2011

Aims: Meta-analysis and replication of GWAS in recurrent ischemic stroke.

Status: No update at this time.

Next Generation Sequencing in Lacunar Stroke and Small Vessel Disease

Contact: Anna Bersano

Date Proposed: April 2011

Aims: Perform Next-Generation Sequencing on subjects with lacunar stroke and small vessel disease. Novel mutations will be replicated via direct genotyping in an additional 1000 cases and 1000 controls .

Status: No update at this time.

ISGC Project Updates

Ongoing Projects (continued):

GWA meta-analysis of carotid plaque and intima-media thickness (IMT)

Contact: Pankaj Sharma
Date Proposed: June 2011
Aims: Meta-analysis of existing GWA data in those subjects who have had carotid imaging in order to use carotid disease as a surrogate for vascular disease.
Status: Analysis is underway.

Genome-wide Heritability of Ischemic Stroke in Caucasians.

Contact: Braxton Mitchell
Date Proposed: August 2011
Aims: Examine the heritability of ischemic stroke using genome wide SNPs for early vs. late onset IS and determining stroke subtype
Status: No update at this time.

GWAS of Stroke/TIA in Patients with Atrial Fibrillation

Contact: Mina Chung, Sudha Seshadri
Date Proposed: October 2011
Aims: Perform a GWAS meta-analysis of stroke/TIA within AF cases
Status: No update at this time.

Genome Wide Association Study of Plasma Fibrinogen

Contact: Christopher O'Donnell
Date Proposed: November 2011
Aims: To conduct a meta-analysis of GWA studies on plasma levels of fibrinogen with the goal of identifying novel loci that underlie variation in plasma fibrinogen concentration.
Status: No update at this time.

Pharmacogenomics GWAS of tPA-induced Haemorrhagic Transformation

Contact: Christopher Levi and Jane Maguire
Date Proposed: November 2011
Aims: To identify SNPs associated with haemorrhagic transformation of acute ischemic stroke after intravenous tPA therapy using a pharmacogenomic-focused GWAS.
Status: Although unfunded, we are currently recruiting from two Australian sites, and collaborating with ISGC groups for future pooling of further samples.

ISGC Project Updates

Ongoing Projects (continued):

Genome-wide association study of incident stroke-wave 2

Contact: Stéphanie Debette, Will Longstreth, and Sudha Seshadri on behalf of the CHARGE Consortium

Date Proposed: June 2012

Aims: Our aim is to perform a second wave Incident Stroke GWAS meta-analysis within the CHARGE consortium, including a larger number of cohorts, using 1000G imputation, and including extension to other ethnic groups if large enough samples can be collected.

Status: Meta-analysis for GWAS of all stroke, ischemic stroke, cardioembolic ischemic stroke, non-cardioembolic ischemic stroke was presented at the Lund meeting. 14 prospective longitudinal cohort studies included in analysis, 15th cohort will be added shortly for discovery phase. Replication will be sought immediately after.

GRECAS Project: Genotyping Risk and Efficacy of Clopidogrel or Aspirin following Stroke

Contact: Israel Fernandez-Cadenas and Joan Montaner

Date Proposed: September 2012

Aims: Replication Study. This is a pharmacogenomic study, the main objective is: to find genetic risk factors associated with Aspirin or Clopidogrel clinical resistance, considering clinical resistance as new vascular recurrences during a follow up of one year.

Status: The first plates with the samples for the replication stage have been sent to the genotyping center.

ISGC Project Updates

Ongoing Projects (continued):

Genetics on post stroke functional outcome: Candidate gene study of post stroke functional outcome including replication

Contact: Arne Lindgren, Christina Jern, Brad Worrall and Jane Maguire,

Date Proposed: February 2013

Aims: (A) To conduct a candidate gene replication study of 3 SNPs associated with post stroke functional outcome; 1 SNP in the GPIIIa gene known for its prothrombotic function and 2 SNPs in the COX-2 gene known for its function in the inflammatory pathway; (B) To conduct a candidate gene replication study of 2 SNPs associated with post stroke functional outcome in a gene known to have a protective effect against oxidative stress; (C) To examine if a candidate gene in the SDF-1/CXCR4/7 pathway is related to post stroke functional outcome; (D) We will also consider examining whether the ApoE epsilon 4 polymorphism is related to poor outcome in a large group of ischemic stroke patients.

Status: In Progress

A Joint meta-analysis of gene x aspirin interactions in ischemic stroke to identify variants related to aspirin resistance

Contact: Christopher John Oldmeadow and John Attia

Date Proposed: February 2013

Aims: Discovery study to confirm loci involved in gene x aspirin interaction in stroke patients . We performed a genome-wide gene x environment-interaction study on a predominantly elderly European cohort of stroke cases with self-reported medication history and found evidence of a locus on chromosome 7p32 (3 SNPs). We propose to meta-analyse this region (consisting of 4 SNPs) using summary statistics from participating groups using the Joint Meta Analysis (JMA) method (described in Manning et al, Genetic Epidemiology 2011).

Status: Seeking ISGC Collaborators

ISGC Project Updates

Completed 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: Manuscript published.

*Bellenguez C, Bevan S, Gschwendtnew A, et al., on behalf of the International Stroke Genetics Consortium (ISGC) & the Wellcome Trust Case Control Consortium 2 (WTCCC2). Genome-wide association study identifies a variant in HDAC9 associated with large vessel ischemic stroke. *Nature Genetics*. 2012;44(3):328-333.

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: Manuscript in press at G3: Genes, Genomes, Genetics

*Cheng Y-C, O'Connell JR, Cole, JW, Stine OC, Dueker N, McArdle PF, Sparks MJ, Shen J, Laurie CC, Nelson S, Doheny KF, Ling H, Pugh EW, Bott TG, Brown Jr. RD, Meschia JF, Nalls M, Rich SS, Worrall B, Andreson CD, Biffi A, Cortellini L, Furie KL, Rost NS, Rosand J, Manolio TA, Kittner SJ, Mitchell BD. Genome-wide association analysis of ischemic stroke in young adults. *G3: Genes, Genomes, Genetics*. 2011 Nov 1; 1(6):505-514.

ISGC Project Updates

Completed Projects (continued):

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 published.

*Arsava EM, Ballabio E, Benner T et. al.; on behalf of the International Stroke Genetics Consortium. The Causative Classification of Stroke system: An international reliability and optimization study. *Neurology*. 2010 Oct 5;75(14):1277-1284.

Replication of Chr. 9q21region 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: The project has been stalled due to a lack of sample collection.

Australian GWAs in ischaemic stroke

Contact: Christopher Levi, John Attia, Jane Maguire and Liz Holliday

Date Proposed: May 2008

Aims: To identify snps associated with acute ischaemic stroke

Status: We demonstrated that the most common mechanistic form of ischaemic stroke, large artery atherosclerosis (LAA) is influenced by a genetic component. We identified a new LAA susceptibility locus on chromosome 6p21.1. We then replicated this susceptibility locus in 1,715 LAA cases and 52,695 population controls from 10 independent population cohorts. We are currently participating in discovery and replication cohorts with various ISGC members. Manuscript published.

Holliday EG, Maguire JM, Evans TJ, et al, on behalf of the International Stroke Genetics Consortium. Common variants at 6p21.1 are associated with large artery atherosclerotic stroke. *Nat Genet.* 2012;44(10):1147-51.

ISGC Project Updates

Completed Projects (continued):

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 published.

*Lemmens R, Buysschaert I, Geelen V, et.al. International Stroke Genetics Consortium. The Association of the 4q25 Susceptibility Variant for Atrial Fibrillation With Stroke Is Limited to Stroke of Cardioembolic Etiology. *Stroke*. 2010;41(9):1850-7.

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 published.

*International Stroke Genetics Consortium; Wellcome Trust Case-Control Consortium 2. Failure to validate association between 12p13 variants and ischemic stroke. *New England Journal of Medicine*. 2010;362(16):1547-1550.

ISGC Project Updates

Completed 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: Manuscript published.

*Olsson S, Melander O, Jood K, Smith JG, Lövkvist H, Sjögren M, Engström G, Norrving B, Lindgren A, Jern C, the International Stroke Genetics Consortium (ISGC). A genetic variant on chromosome 12p13 does not show association to ischemic stroke in three Swedish case-control studies. *Stroke.* 2010; 42(1):214-6.

Genes and Response to Aspirin in Secondary Stroke Prevention, GRASSP

Contact: Agnieszka Slowik, Joanna Pera

Date Proposed: June 2010

Aims: To establish genetic markers of aspirin efficiency, aspirin resistance, aspirin intolerance, and increased risk aspirin-related adverse effects in ischemic stroke patients with different stroke etiologies. To develop clinically useful and cost-effective test(s) allowing predict responses to aspirin treatment, and to avoid/ reduce adverse effects .

Status: Grant submitted, project not funded at this time.

ISGC Project Updates

Completed Projects (continued):

Association of myocardial infarction-associated SNPs with ischemic stroke: a meta-analysis of European Caucasian populations

Contact: Braxton Mitchell, Yu-Ching Cheng

Date Proposed: July 2010

Aims: The goal of this project is to extend previous work (e.g., the ISGC analysis of the chr 9 SNP on stroke) to determine if: (1) other MI-associated SNPs are associated with ischemic stroke; and (2) if associations of these additional SNPs are dependent on stroke subtype and/or age of stroke onset.

Status: Manuscript published.

Cheng YC, Anderson CD, Bione S, et al, on behalf of the International Stroke Genetics Consortium. Are myocardial infarction—-associated single-nucleotide polymorphisms associated with ischemic stroke? *Stroke*. 2012;43(4):980-986.

International Stroke Genetics Consortium Project Protocols and Standards

Contact: Jennifer Majersik and Jane Maguire

Date Proposed: January 2013

Aims: The goal of this paper is to describe clinical and research criteria agreed upon by the ISGC to standardize data collection of stroke cases & controls across continents. Criteria will include definitions and requirements for harmonization of phenotypes, neuroimaging, genotyping definitions and requirements, and ethics. (There will be a separate paper by Thomas Battey and others on how to biobank.) It is anticipated that in addition to providing ISGC members with agreed clinical and research parameters, this paper will aid and encourage investigators in underrepresented countries & continents to contribute their cohorts to stroke genetic research.

Status: Manuscript published.

Majersik J.J., Cole J.W., Golledge J., Rost N.S., Chan Y.Y., Gurol M.E., Lindgren A.G., Woo D., Fernandez-Cadenas I., Chen D.T., Thijs V., Worrall B.B., Kamal A., Bentley P., Wardlaw J.M., Ruigrok Y.M., Battey T.W.K., Schmidt R., Montaner J., Giese A., Roquer J., Jimenez-Conde J., Lee C., Ay H., Martin J.J., Rosand J. and Maguire J., on behalf of the International Stroke Genetics Consortium. Recommendations from the International Stroke Genetics Consortium, Part 1: Standardized phenotypic data collection. *Stroke*. 2015;46(1):279-84.

ISGC Project Updates

Completed Projects (continued):

The ISGC: Establishment of a biorepository for stroke genetic research

Contact: Thomas Battey and Jonathan Rosand

Date Proposed: February 2013

Aims: To describe how one academic health center and an international consortium of researchers collaborated to organize and implement a stroke genetic research bio-repository. This paper will not only provide details on how to set-up a research biorespository, but will also help under-represented countries & continents to contribute their cohorts to stroke genetic research. (There will be a separate paper by Jenny Majersik and Jane Maguire on ISGC phenotyping protocols and standards).

Status: Manuscript published.

Battey T.W.K., Valant V., Baedorf Kassis S., Kourkoulis C., Lee C., Anderson C.D., Falcone G.J., Jimenez-Conde J., Fernandez-Cadenas I., Pare G., Rundek T., James M.L., Lemmens R., Lee T.H., Tatlisumak T., Kittner S.J., Lindgren A., Mateen F.J., Berkowitz A.L., Holliday E.G., Majersik J., Maguire J., Sudlow C. and Rosand J., on behalf of the International Stroke Genetics Consortium. Rec ommendations from the International Stroke Genetics Consortium, Part 2: Bio logical sample collection and storage. *Stroke.* 2015;46(1):285-90.

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

METASTROKE
Contact: Martin Dichgans

ISGC Grants Awarded

- Wellcome Trust Genome-Wide Association Study for Ischemic Stroke (WTCCC2)
- Australian Stroke Genetics Collaborative Group
- The Baltimore-Washington Young Stroke Study (GEI)
- Gene Discovery for Warfarin-Related Intracerebral Hemorrhage (ICH GWAS)
- Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH)
- NINDS-Stroke Genetics Network (SiGN) Study

ISGC Publications (2009-2011)

2009:

Gschwendtner A, Bevan S, Cole JW, et. al.; on behalf of the International Stroke Genetics Consortium. Sequence variants on chromosome 9p21.3 confer risk for atherosclerotic stroke. *Ann Neurol.* 2009;65(5):531-9.

2010:

International Stroke Genetics Consortium; Wellcome Trust Case-Control Consortium 2. Failure to validate association between 12p13 variants and ischemic stroke. *N Engl J Med.* 2010;362 (16):1547-50.

Lemmens R, Buysschaert I, Geelen V, et. al.; on behalf of the International Stroke Genetics Consortium. The association of the 4q25 susceptibility variant for atrial fibrillation with stroke is limited to stroke of cardioembolic etiology. *Stroke.* 2010;41(9):1850-7.

Arsava EM, Ballabio E, Benner T, et. al.; on behalf of the International Stroke Genetics Consortium. The Causative Classification of Stroke system: An international reliability and optimization study. *Neurology.* 2010;75(14):1277-1284.

Biffi A, Sonni A, Anderson CD, et al.; on behalf of the International Stroke Genetics Consortium. Variants at APOE Influence Risk of Deep and Lobar Intracerebral Hemorrhage. *Ann Neurol.* 2010;68(6):934-43.

2011:

Anderson CD, Biffi A, Rahman R, et. al, on behalf of the International Stroke Genetics Consortium. Common mitochondrial sequence variants in ischemic stroke. *Ann Neurol.* 2011; 69(3):471-80.

Olsson S, Melander O, Jood K, Smith JG, Lövkvist H, Sjögren M, Engström G, Norrving B, Lindgren A, Jern C, the International Stroke Genetics Consortium (ISGC). A genetic variant on chromosome 12p13 does not show association to ischemic stroke in three Swedish case-control studies. *Stroke.* 2011;42(1):214-6.

Biffi A, Anderson CD, Jagiella JM, et.al., on behalf of the International Stroke Genetics Consortium. APOE genotype and extent of bleeding and outcome in lobar intracerebral haemorrhage: a genetic association study. *Lancet Neurology.* 2011;10(8):702-709.

ISGC Publications (2012-2013)

2012:

International Stroke Genetics Consortium (ISGC); Wellcome Trust Case Control Consortium 2 (WTCCC2), Bellenguez C, et al. Genome-wide association study identifies a variant in HDAC9 associated with large vessel ischemic stroke. *Nature Genetics.* 2012;44(3):328-333.

Cheng YC, Anderson CD, Bione S, et al, on behalf of the International Stroke Genetics Consortium. Are myocardial infarction—-associated single-nucleotide polymorphisms associated with ischemic stroke? *Stroke.* 2012;43(4):980-986.

Falcone GJ, Biffi A, Devan WJ, et al, on behalf of the International Stroke Genetics Consortium. Burden of Risk Alleles for Hypertension Increases Risk of Intracerebral Hemorrhage. *Stroke.* 2012;43(11):2877-2883.

Holliday EG, Maguire JM, Evans TJ, et al, on behalf of the International Stroke Genetics Consortium. Common variants at 6p21.1 are associated with large artery atherosclerotic stroke. *Nat Genet.* 2012;44(10):1147-51.

Traylor M, Farrall M, Holliday EG, et al, on behalf of the International Stroke Genetics Consortium. Genetic risk factors for ischaemic stroke and its subtypes (the METASTROKE Collaboration): a meta-analysis of genome-wide association studies. *Lancet Neurol.* 2012;11 (11):951-962.

2013:

Williams FM, Carter AM, Hysi PG, et al, on behalf of the International Stroke Genetics Consortium. Ischemic stroke is associated with the ABO locus: The EuroCLOT study. *Ann Neurol.* 2013;73(1):16-31.

Anderson CD, Biffi A, Nalls MA, et al, on behalf of the International Stroke Genetics Consortium. Common variants within oxidative phosphorylation genes influence risk of ischemic stroke and intracerebral hemorrhage. *Stroke.* 2013;44(3):612-9.

Falcone GJ, Biffi A, Devan WJ, et al, on behalf on the GOCHA investigators. Burden of Blood Pressure-Related Alleles is Associated with Larger Hematoma Volume and Worse Outcome in Intracerebral Hemorrhage. *Stroke.* 2013;44(2):321-6.

Devan WJ, Falcone GJ, Anderson CD, et al. on behalf of the International Stroke Genetics Consortium. Heritability Estimates Identify a Substantial Genetic Contribution to Risk and Outcome of Intracerebral Hemorrhage. *Stroke.* 2013;44(6):1578-83.

ISGC Publications (2013-2014)

2013 (Cont.):

Adib-Samii P, Rost N, Traylor M, et al. on behalf of the International Stroke Genetics Consortium. 17q25 Locus is associated with white matter hyperintensity volume in ischemic stroke, but not with lacunar stroke status. *Stroke.* 2013;44(6):1609-1615.

Yadav S, Cotlarciuc I, Munroe PB, et al. on behalf of the International Stroke Genetics Consortium. Genome-wide analysis of blood pressure variability and ischemic stroke. *Stroke.* 2013;44(10):2703-2709.

Biffi A, Anderson, CD, Falcone GJ, et al. on behalf of the International Stroke Genetics Consortium. Novel insights into the genetics of intracerebral hemorrhage. *Stroke.* 2013;44(6 Suppl 1):S137.

2014:

Dichgans M, Malik R, König IR, et al. on behalf of the METASTROKE Consortium; the CARDIoGRAM consortium; the C4D consortium; the International Stroke Genetics Consortium. Shared Genetic Susceptibility to Ischemic Stroke and Coronary Artery Disease: A Genome-Wide Analysis of Common Variants. *Stroke.* 2014;45(1)24-36.

Radmanesh F, Devan WJ, Anderson CD, Rosand J, Falcone GJ; Alzheimer's Disease Neuroimaging Initiative (ADNI). Accuracy of imputation to infer unobserved APOE epsilon alleles in genome-wide genotyping data. *Eur J Hum Genet.* 2014;22(10):1239-42.

Woo D, Falcone GJ, Devan WJ, et al., on behalf of the International Stroke Genetics Consortium. Meta-Analysis of Genome-Wide Association Studies Identifies 1q22 as a Susceptibility Locus for Intracerebral Hemorrhage. *Am J Hum Genet.* 2014;94(4):511-21.

Falcone GJ, Malik R, Dichgans M, Rosand J. Current concepts and clinical applications of stroke genetics. *Lancet Neurol.* 2014;13(4): 405-418.

Cotlarciuc I, Malik R, Holliday EG, et al., on behalf of METASTROKE and the International Stroke Genetics Consortium. Effect of genetic variants associated with plasma homocysteine levels on stroke risk. *Stroke.* 2014;45(7):1920-4.

Falcone GJ, Radmanesh F, Brouwers HB, et al., on behalf of the International Stroke Genetics Consortium. APOE ε variants increase risk of warfarin-related intracerebral hemorrhage. *Neurology.* 2014;83(13):1139-46.

ISGC Publications (2014-Present)

2014 (cont.):

Traylor M, Makela KM, Kilarski LL, et al., on behalf of METASTROKE, the International Stroke Genetics Consortium, and the Wellcome Trust Case Control Consortium 2. a novel MMP-12 locus is associated with large artery atherosclerotic stroke using a genome-wide age -at-onset informed approach. *PLoS Genet.* 2014;10(7):e1004469.

Kilarski LL, Achteberg S, Devan WJ, et al., on behalf of the GARNET Collaborative Research Group, Wellcome Trust Case Control Consortium 2, Australian Stroke Genetic Collaborative, the METASTROKE Consortium, and the International Stroke Genetics Consortium. Meta-analysis in more than 17,900 cases of ischemic stroke reveals a novel association at 12q24.12. *Neurology*. 2014;83(8):678-85.

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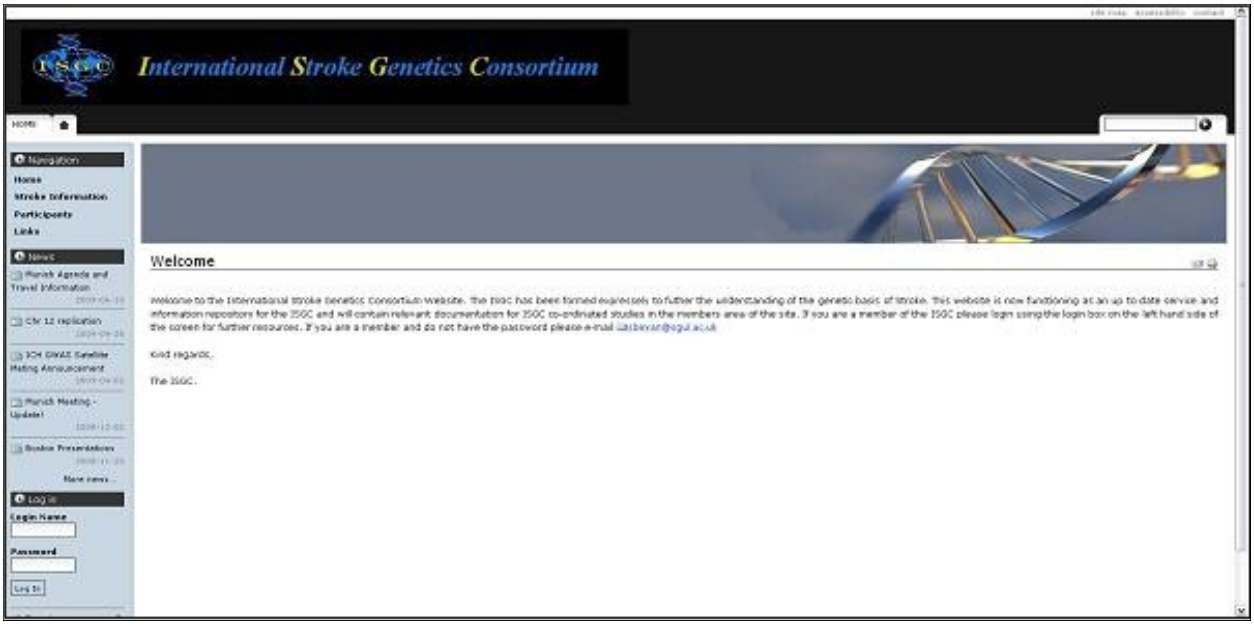
Website Update

The ISGC website can be found at www.strokegenetics.org. Please consider submitting a short bio and a picture for the website! If you are interested, please email them to Steve.

If you have additional website content or layout suggestions, please email Steve Bevan (snb31@medschl.cam.ac.uk) with your ideas.

Thank you!



Upcoming Conference Deadlines

2015

American Academy of Neurology

Abstract Deadline: Passed
Meeting Date: April 18-25, 2015
Meeting Location: Washington, DC (USA)

European Stroke Conference

Abstract Deadline: Passed
Meeting Date: May 12-15, 2015
Meeting Location: Vienna, Austria

International Stroke Genetics Consortium Meeting

Abstract Deadline: April 30, 2015
Meeting Date: June 4-5, 2015
Meeting Location: Hamilton, ON (Canada)

American Neurological Association

Abstract Deadline: March 31, 2015
Meeting Date: September 27-29, 2015
Meeting Location: Chicago, IL (USA)

American Society of Human Genetics

Abstract Deadline: June 11, 2015
Meeting Date: October 6-10, 2015
Meeting Location: Baltimore, MD (USA)

2016

International Stroke Conference

Abstract Submission: Opens May 20, 2015
Meeting Date: February 17-19, 2016
Meeting Location: Los Angeles, CA (USA)

17th International Workshop: Hamilton, Ontario

The 17th International Workshop of the ISGC will be held June 4-5 2015 in Hamilton, Ontario and will be hosted by Guillaume Pare (pareg@mcmaster.ca).

Please stay tuned for a conference program, website, and information on travel and lodging arrangements. Registration is available at the following link: https://conferencereg.mcmaster.ca/go/conferences/ISGC%E2%80%902015.

Note: Talks by meeting presenters who have shared their slides are available for viewing after each workshop on the ISGC website (www.strokegenetics.org).

18th International Workshop: Barcelona, Spain

The 18th International Workshop of the ISGC will be held on October 22-23, 2015 in Paris, France by Israel Fernandez-Cadenas and Jordi Jimenez-Conde.

Please stay tuned for a conference program, website, and information on travel and lodging arrangements as they become available this summer.

Note: Talks by meeting presenters who have shared their slides are available for viewing after each workshop on the ISGC website (www.strokegenetics.org).