ISGC ICH Bi-Monthly Newsletter Issue 29 September 2012

Study Updates:

ICH GWAS Investigators Meeting:

To be held during the ISGC Workshop in Krakow, Poland (Date TBA)

Please contact Valerie (vvalant@partners.org) or Sarah (gramansc@UCMAIL.UC.EDU) for additional details

This is the 29th issue of the ISGC ICH bi-monthly newsletter (to be released on the 15th of each month, or nearest workday). This newsletter is a tool for updating all members of the ISGC on aspects of projects relating to Intracerebral Hemorrhage. Both Dr. Jonathan Rosand of Massachusetts General Hospital and Dr. Daniel Woo of The University of Cincinnati oversee this Newsletter. For study specific questions, new topics or feedback, please contact either Valerie Valant or Sarah Gramann who can direct your inquiry toward the investigating researcher.

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Study Updates

ERICH (Ethnic and Racial Variation in Intracerebral Hemorrhage)

Contact Site: University of Cincinnati

Aims: The ERICH study is a multi-center, prospectively recruited case-control study of spontaneous intracerebral hemorrhage. Site selection for enrollment targeted minority populations of African-American and Hispanic populations with a goal of recruiting 1000 cases in each ethnic minority as well as 1000 cases among non-Hispanic Whites. Controls are identified from the same region as the cases through random-digit dialing and all subjects undergo a direct interview and cases undergo an additional chart abstraction, 3, 6 and 12 month follow-up. Centralized neuroimaging review is performed on all cases and every fifth subject has a study-MRI performed.

Status: The ERICH study is up to 1219 cases and 490 controls. The study is overall at 82.5% of target enrollment for their date and improving. We have 1,622 CT scans on cases read (including follow-up scans) as well as 329 MRIs on the cohort of ICH cases.

GERFHS: Genetic and Environmental Risk Factors for Hemorrhagic Stroke

Contact Site: University of Cincinnati

Aims: The GERFHS study is a population-based, prospectively recruited case-control study of spontaneous intracerebral hemorrhage. Demographically mached controls are identified by random digit dialing and a direct interview and chart abstraction is performed on enrolled cases and a chart abstraction on all cases of ICH within the region. Aims: To perform a genome-wide association study of ICH using Affymetrix 6.0 array to identify common variants associated with ICH.

Status: The GERFHS study now has 502 ICH cases enrolled and 420 demographically matched population-based controls enrolled during the current study period. Genotyping is nearly complete on an additional 500 subjects with Affymetrix 6.0 to add to an already genotyped 380 ICH cases and matching controls with buccal swab extraction.

ICH GWAS (Intercerebral Hemorrhage – Genome Wide Association Study)

Contact Site: Massachusetts General Hospital and University of Cincinnati

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: MGH has successfully completed genotyping of 190 Warfarin-cases and 190 Warfarin-controls and are in the process of submitting another 4 plates for GWAS.

ICH Meta-Analysis

Contact Site: Massachusetts General Hospital

Aims: To identify and uncover the common genetic determinants of risk of non-warfarin intracerebral hemorrhage.

Status: No update as of July 2012. *We are planning on including the recently genotyped 190 GOCHA Warfarin-ICH cases and 190 GOCHA Warfarin controls on Illumina OmniExpress into the meta-analysis to better refine our results.*

ExomeChip Genotyping

Contact Site: Massachusetts General Hospital and University of Cincinnati

Aims: To test the rare variant risk hypothesis of ICH in samples which have already completed genotyping through GWAS.

Status: Samples have been plated and are in queue for ExomeChip genotyping at the Broad Institute. Results expected to be received late summer 2012.

Risk Variants for White Matter Hyperintensity (WMH) influence risk of Intracerebral Hemorrhage (ICH)

Contact Site: Massachusetts General Hospital

Aims: 1) To examine whether increasing numbers of common genetic variants associated with hypertension influence the risk of ICH.

Hypothesis: Increasing numbers of CGVs associated with HTN produce additive increases in ICH risk.

2) To examine whether increasing numbers of common genetic variants associated with hypertension influence the radiological features and clinical outcome of ICH.

Hypothesis: Increasing numbers of CGVs associated with HTN produce larger hematomas, as measured upon at admission and at 24 hours, and worsens clinical outcome.

Status: Data analysis completed. Manuscript in preparation.

Effect of blood pressure-related genetic variants on intracerebral hemorrhage volume and outcome

Contact Site: Massachusetts General Hospital

Aims: 1) To evaluate the effect of blood pressure-related risk alleles on the admission volumes of primary intracerebral hemorrhage

2) To evaluate the effect of blood pressure-related risk alleles on the admission volumes of warfarin-related intracerebral hemorrhage

3) To evaluate the effect of blood pressure-related risk alleles on clinical outcome of primary intracerebral hemorrhage

4) To evaluate the effect of blood pressure-related risk alleles on clinical outcome of warfarin-related intracerebral hemorrhage

Status: Analysis completed. Manuscript submitted for publication.

Effect modification by admission blood pressure of the effect of APOE on ICH admission volumes

Contact Site: Massachusetts General Hospital

Aims: 1) To assess differences in effect estimates of APOe on first ICH admission volume across strata of admission blood pressure.

2) To assess differences in effect estimates of APOe on recurrent ICH admission volume across strata of admission blood pressure.

3) To assess differences in effect estimates of APOe on clinical outcome of first and recurrent ICH across strata of admission blood pressure.

Status: Analysis completed. Manuscript in preparation.