ICH GWAS Monthly Newsletter
Issue 14 - April 2010

In this issue:


ICH GWAS
Investigators Meeting

To be held just prior to the start of the ISGC 7th International Workshop Edinburgh, Scotland:


Thursday, June 17th, 2010
Time TBD

ICH GWAS Monthly Newsletter Issue 14 - April 2010

This is the 14th issue of the monthly newsletter for the ICH GWAS Study Group. This newsletter is meant to be a tool to keep investigators participating in the ICH GWAS updated on all aspects of this project, including phenotyping, genotyping, data analysis and logistics.

The newsletter will be sent out to participants on the 15th of each month (or nearest workday) as an email attachment from the Program Manager at the Coordinating Center.

If you want to add topics to the next newsletter, or you'd like to give general feedback to the Newsletter Design Team please contact:
Lynelle Cortellini
(lcortellini@partners.org).

Currently Active ICH GWAS Sub-projects

This section of the ICH GWAS Newsletter lists all sub-projects proposed by Investigators. Contact information for each specific subproject is listed. All Investigators who have contributed samples are invited to submit proposals. Once submitted, proposals are circulated to all investigators for comment and approval. The ICH GWAS Sub-project proposal form can be obtained from the ICH GWAS section of the ISGC website or by contacting the Coordinating Center (see contact info for this topic).

Currently active Sub-Projects

ApoE Candidate Gene Study in ICH

Aims: Investigate the role of ApoE in ICH using a large-scale candidate-gene approach.

Current Status:

Meta-analysis completed. Manuscript drafted and circulated to participating Investigators for review and approval.

Requirements for Participation:

N/A: Data gathering complete

Contact: Alessandro Biffi, MD
Massachusetts General Hospital
abiffi@partners.org

Consent Status in the determination of the phenotype spectrum in hemorrhagic stroke genetic research

Aims: Investigate the impact of consent status (self-consent, enrollment by proxy authorization, or waiver of consent because subject died prior to inclusion) in the ICH phenotypic spectrum in GOCHA / ICH GWAS

Current Status:

Currently available data was obtained from approximately 550 individuals (169 self-consented, 142 enrolled post mortem, and 239 enrolled via surrogate) from 7 sites. Analysis will be focused on preliminary comparisons among the 3 groups in relation to demographics (sex, race, age), risk factors, warfarin status, INR, and hemorrhage characteristics. This was presented as a poster at the International Stroke Conference in San Antonio in February.

Requirements for Participation:

As previously discussed, one group not currently represented in the data consists of patients who are eligible but who decline to participate in genetic studies. We anticipate being able to generate basic demographics on "refusers" from the MGH and UVA sites. If other individual sites have reasonably complete data on individuals who refused participation they are welcome to submit them for analysis.

Contact: Bradford B. Worrall, MD, MSc
University of Virginia Health System
bbw9r@virginia.edu

For further info on this topic please contact:
Lynelle Cortellini, M.Sc.
lcortellini@partners.org

Recruitment Updates

Sites recruiting prospectively as part of GOCHA

Study site	Period	Warfarin		Total
		Case	Control	
Mass General Hospital	January 2010	2	1	**3**
	February 2010	-	1	**1**
	March 2010	1	-	**1**
University of Michigan	January 2010	-	-	**-**
	February 2010	-	-	**-**
	March 2010	-	-	**-**
University of Virginia	January 2010	-	-	**-**
	February 2010	1	-	**1**
	March 2010	-	-	**-**
Mayo Clinic - Jacksonville	January 2010	-	-	**-**
	February 2010	-	1	**1**
	March 2010	-	-	**-**
University of Florida	January 2010	-	-	**-**
	February 2010	-	-	**-**
	March 2010	-	-	**-**
University of Washington	January 2010	-	-	**-**
	February 2010	1	-	**1**
	March 2010	1	-	**1**
Beth Israel Deaconess Medical Center	January 2010	1	2	**3**
	February 2010	-	-	**-**
	March 2010	-	1	**1**
Totals		**7**	**6**	**13**

Sites recruiting prospectively as part of ICH GWAS

Principal Investigator		Institution	Country of Origin	Status
Last Name	First Name			
Majersik	Jennifer	University of Utah	US	Joining
Thijs	Vincent	University Hospital Leuven	Belgium	Joining
Slowik	Agnieszka	Jagiellonian University, Krakow	Poland	Joined
Schmidt	Reinhold	Medical University Graz	Austria	Joined
Dichgans	Martin	Ludwig Maximilians University, Munich	Germany	Joined

Sites recruiting retrospectively as part of ICH GWAS

Principal Investigator		Institution	Country of Origin	Number of Cases	Number of Controls	Samples received by Genotyping Center
Last Name	First Name					
Dichgans	Martin	Munich	Germany	50	50	**Yes**
Lindgren	Arne	University Hospital, Lund	Sweden	153	167	**Yes**
Macleod	Mary	University of Aberdeen	UK	40	40	
Markus	Hugh	St. George's, University of London	UK	200	200	
Melander	Olle	Malmo University Hospital	Sweden	100	300	
Montaner	Joan	Vall d'Hebron Hospital	Spain	169	176	**Yes**
Rothwell	Peter	Oxford	UK	40	40	
Roquer	Jaume	Hospital del Mar	Spain	200	200	**Yes**
Schmidt	Reinhold	Medical University Graz	Austria	42	400	**Yes**
Slowik	Agnieszka	Jagiellonian University	Poland	224	420	**Yes**
Sudlow	Cathie	Western General, Edinburgh	UK	40	40	

Data presented in the table above are estimates of the number of samples each participating center has pledged to provide for the ICH GWAS. Actual numbers of samples analyzed will vary depending on DNA and phenotype quality.

For further info on this topic please contact:

Alessandro Biffi, M.D.

abiffi@partners.org

Spotlight: Article

Ritchie MD, Denny JC, Crawford DC et al.

Robust Replication of Genotype-Phenotype Associations across Multiple Diseases in an Electronic Medical Record

Am J Hum Genet. 2010;April 1

ABSTRACT

Large-scale DNA databanks linked to electronic medical record (EMR) systems have been proposed as an approach for rapidly generating large, diverse cohorts for discovery and replication of genotype-phenotype associations. However, the extent to which such resources are capable of delivering on this promise is unknown. We studied whether an EMR-linked DNA biorepository can be used to detect known genotype-phenotype associations for five diseases. Twenty-one SNPs previously implicated as common variants predisposing to atrial fibrillation, Crohn's disease, multiple sclerosis, rheumatoid arthritis, or type 2 diabetes were successfully genotyped in 9483 samples accrued over 4 mo into BioVU, the Vanderbilt University Medical Center DNA biobank. Previously reported odds ratios (ORPR) ranged from 1.14 to 2.36. For each phenotype, natural language processing techniques and billing-code queries were used to identify cases (n = 70–698) and controls (n = 808–3818) from deidentified health records. Each of the 21 tests of association yielded point estimates in the expected direction. Previous genotype-phenotype associations were replicated ($p < 0.05$) in 8/14 cases when the ORPR was > 1.25, and in 0/7 with lower ORPR. Statistically significant associations were detected in all analyses that were adequately powered. In each of the five diseases studied, at least one previously reported association was replicated. These data demonstrate that phenotypes representing clinical diagnoses can be extracted from EMR systems, and they support the use of DNA resources coupled to EMR systems as tools for rapid generation of large data sets required for replication of associations found in research cohorts and for discovery in genome science.

Spotlight: Article

Yasuno K, Bilguvar K, Bijilenga P. et al.

Genome-wide association study of intracranial aneurysm identifies three new risk loci

Nature Genetics (2010); April 4

ABSTRACT

Saccular intracranial aneurysms are balloon-like dilations of the intracranial arterial wall; their hemorrhage commonly results in severe neurologic impairment and death. We report a second genome-wide association study with discovery and replication cohorts from Europe and Japan comprising 5,891 cases and 14,181 controls with ~832,000 genotyped and imputed SNPs across discovery cohorts. We identified three new loci showing strong evidence for association with intracranial aneurysms in the combined dataset, including intervals near RBBP8 on 18q11.2 (odds ratio (OR) = 1.22, P = 1.1 × 10−12), STARD13-KL on 13q13.1 (OR = 1.20, P = 2.5 × 10−9) and a gene-rich region on 10q24.32 (OR = 1.29, P = 1.2 × 10−9). We also confirmed prior associations near SOX17 (8q11.23–q12.1; OR = 1.28, P = 1.3 × 10−12) and CDKN2A-CDKN2B (9p21.3; OR = 1.31, P = 1.5 × 10−22). It is noteworthy that several putative risk genes play a role in cell-cycle progression, potentially affecting the proliferation and senescence of progenitor-cell populations that are responsible for vascular formation and repair.