ICH GWAS Monthly Newsletter
Issue 11 - November 2009

In this issue:


Please mark your calendars
with the date
for the next

ICH GWAS Conference Call:


Tuesday, November 17th 2009
10 - 11 AM, Eastern USA time

This is the eleventh 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:

Genotyping has been completed on approximately 500 ICH cases and healthy controls.
Interim data analysis completed.
Further genotyping performed in the next month.
Additional data from several ICH GWAS Investigators ready for meta-analysis.

Requirements for Participation:

In silico ApoE genotype data (raw genotyped data preferred).
Required phenotype data points are identical to the ICH GWAS minimal and additional requirements.

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.

Requirements for Participation:

As discussed at the ICH GWAS Investigator Meeting in Munich, 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		Non Warfarin		Total
		Case	Control	Case	Control	
Mass General Hospital	August 2009	-	1	7	-	**8**
	September 2009	4	-	11	-	**15**
	October 2009	3	-	8	-	**11**
University of Michigan	August 2009	-	-	-	-	**-**
	September 2009	-	-	-	-	**-**
	October 2009	-	-	-	-	**-**
University of Virginia	August 2009	-	-	1	-	**1**
	September 2009	-	-	1	3	**4**
	October 2009	-	-	1	-	**1**
Mayo Clinic - Jacksonville	August 2009	-	1	2	1	**4**
	September 2009	-	-	-	2	**2**
	October 2009	-	2	1	1	**4**
University of Florida	August 2009	1	1	-	-	**2**
	September 2009	-	1	-	-	**1**
	October 2009	-	-	-	-	**-**
University of Washington	August 2009	2	-	-	-	**2**
	September 2009	-	-	-	-	**-**
	October 2009	1	-	-	-	**1**
Beth Israel Deaconess Medical Center	August 2009	-	-	-	-	**-**
	September 2009	-	-	-	-	**-**
	October 2009	-	1	-	-	**1**
Totals		**11**	**7**	**32**	**7**	**57**

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	
Lindgren	Arne	University Hospital, Lund	Sweden	153	167	**Yes**
Macleod	Marie	University of Aberdeen	GB	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	GB	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

Soranzo N., Spector TD., Mangino M., et al.

A genome-wide meta-analysis identifies 22 loci associated with eight hematological parameters in the HaemGen consortium

Nat Genet. 2009 Nov;41(11):1182-90.

ABSTRACT

The number and volume of cells in the blood affect a wide range of disorders including cancer and cardiovascular, metabolic, infectious and immune conditions. We consider here the genetic variation in eight clinically relevant hematological parameters, including hemoglobin levels, red and white blood cell counts and platelet counts and volume. We describe common variants within 22 genetic loci reproducibly associated with these hematological parameters in 13,943 samples from six European population-based studies, including 6 associated with red blood cell parameters, 15 associated with platelet parameters and 1 associated with total white blood cell count. We further identified a long-range haplotype at 12q24 associated with coronary artery disease and myocardial infarction in 9,479 cases and 10,527 controls. We show that this haplotype demonstrates extensive disease pleiotropy, as it contains known risk loci for type 1 diabetes, hypertension and celiac disease and has been spread by a selective sweep specific to European and geographically nearby populations.

Spotlight: Article

Ganesh SK., Zakai AN., van Rooij FJA., et al.

Multiple loci influence erythrocyte phenotypes in the CHARGE Consortium

Nat Genet. 2009 Oct;41(11):1191-98.

ABSTRACT

Measurements of erythrocytes within the blood are important clinical traits and can indicate various hematological disorders. We report here genome-wide association studies (GWAS) for six erythrocyte traits, including hemoglobin concentration (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and red blood cell count (RBC). We performed an initial GWAS in cohorts of the CHARGE Consortium totaling 24,167 individuals of European ancestry and replication in additional independent cohorts of the HaemGen Consortium totaling 9,456 individuals. We identified 23 loci significantly associated with these traits in a meta-analysis of the discovery and replication cohorts (combined P values ranging from 5 x 10(-8) to 7 x 10(-86)). Our findings include loci previously associated with these traits (HBS1L-MYB, HFE, TMPRSS6, TFR2, SPTA1) as well as new associations (EPO, TFRC, SH2B3 and 15 other loci). This study has identified new determinants of erythrocyte traits, offering insight into common variants underlying variation in erythrocyte measures.