

ICH GWAS Monthly Newsletter

Issue 13 - February 2010

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This is the 13th 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 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

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Recruitment Updates

Sites recruiting prospectively as part of GOCHA

Study site	Period	Warfarin		Total
		Case	Control	
Mass General Hospital	November 2009	3	-	3
	December 2009	1	-	1
	January 2010	2	1	3
University of Michigan	November 2009	-	-	-
	December 2009	-	-	-
	January 2010	-	-	-
University of Virginia	November 2009	-	-	-
	December 2009	1	-	1
	January 2010	-	-	-
Mayo Clinic - Jacksonville	November 2009	-	3	3
	December 2009	-	1	1
	January 2010	-	-	-
University of Florida	November 2009	-	-	-
	December 2009	-	-	-
	January 2010	-	-	-
University of Washington	November 2009	-	-	-
	December 2009	4	-	-
	January 2010	-	-	-
Beth Israel Deaconess Medical Center	November 2009	-	2	2
	December 2009	-	-	-
	January 2010	1	2	3
Totals		12	9	21

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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	Mary	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

Zaitlen N, Paşaniuc B, Gur T, Ziv E, Halperin E.

Leveraging genetic variability across populations for the identification of causal variants.

Am J Hum Genet. 2010;86(1):23-33.

ABSTRACT

Genome-wide association studies have been performed extensively in the last few years, resulting in many new discoveries of genomic regions that are associated with complex traits. It is often the case that a SNP found to be associated with the condition is not the causal SNP, but a proxy to it as a result of linkage disequilibrium. For the identification of the actual causal SNP, fine-mapping follow-up is performed, either with the use of dense genotyping or by sequencing of the region. In either case, if the causal SNP is in high linkage disequilibrium with other SNPs, the fine-mapping procedure will require a very large sample size for the identification of the causal SNP. Here, we show that by leveraging genetic variability across populations, we significantly increase the localization success rate (LSR) for a causal SNP in a follow-up study that involves multiple populations as compared to a study that involves only one population. Thus, the average power for detection of the causal variant will be higher in a joint analysis than that in studies in which only one population is analyzed at a time. On the basis of this observation, we developed a framework to efficiently search for a follow-up study design: our framework searches for the best combination of populations from a pool of available populations to maximize the LSR for detection of a causal variant. This framework and its accompanying software can be used to considerably enhance the power of fine-mapping studies.

Spotlight: Article

Shinawi M, Schaaf CP, Bhatt SS et al.

A small recurrent deletion within 15q13.3 is associated with a range of neurodevelopmental phenotypes

Nat Genet. 2009;41,1269-1271

ABSTRACT

We report a recurrent 680-kb deletion within chromosome 15q13.3 in ten individuals, from four unrelated families, with neurodevelopmental phenotypes including developmental delay, mental retardation and seizures. This deletion likely resulted from nonallelic homologous recombination between low-copy repeats on the normal and inverted region of chromosome 15q13.3. Although this deletion also affects OTUD7A, accumulated data suggest that haploinsufficiency of CHRNA7 is causative for the majority of neurodevelopmental phenotypes in the 15q13.3 microdeletion syndrome.