ICH GWAS Monthly Newsletter
Issue 15 - May 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
8:30-10:00 am

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This is the 15th 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

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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	**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

Tobacco and Genetics Consortium

Genome-wide meta-analyses identify multiple loci associated with smoking behavior

Nat Genet. 2010;42(5):441-7.

ABSTRACT

Consistent but indirect evidence has implicated genetic factors in smoking behavior. We report meta-analyses of several smoking phenotypes within cohorts of the Tobacco and Genetics Consortium (n = 74,053). We also partnered with the European Network of Genetic and Genomic Epidemiology (ENGAGE) and Oxford-GlaxoSmithKline (Ox-GSK) consortia to follow up the 15 most significant regions (n > 140,000). We identified three loci associated with number of cigarettes smoked per day. The strongest association was a synonymous 15q25 SNP in the nicotinic receptor gene CHRNA3 (rs1051730[A], beta = 1.03, standard error (s.e.) = 0.053, P = 2.8 x 10(-73)). Two 10q25 SNPs (rs1329650[G], beta = 0.367, s.e. = 0.059, P = 5.7 x 10(-10); and rs1028936[A], beta = 0.446, s.e. = 0.074, P = 1.3 x 10(-9)) and one 9q13 SNP in EGLN2 (rs3733829[G], beta = 0.333, s.e. = 0.058, P = 1.0 x 10(-8)) also exceeded genome-wide significance for cigarettes per day. For smoking initiation, eight SNPs exceeded genome-wide significance, with the strongest association at a nonsynonymous SNP in BDNF on chromosome 11 (rs6265[C], odds ratio (OR) = 1.06, 95% confidence interval (CI) 1.04-1.08, P = 1.8 x 10(-8)). One SNP located near DBH on chromosome 9 (rs3025343[G], OR = 1.12, 95% CI 1.08-1.18, P = 3.6 x 10(-8)) was significantly associated with smoking cessation.

Spotlight: Article

Sanna S, Pitzalis M, Zoledziewska M et al.

Variants within the immunoregulatory CBLB gene are associated with multiple sclerosis

Nat Genet. 2010 May 9

ABSTRACT

A genome-wide association scan of approximately 6.6 million genotyped or imputed variants in 882 Sardinian individuals with multiple sclerosis (cases) and 872 controls suggested association of CBLB gene variants with disease, which was confirmed in 1,775 cases and 2,005 controls (rs9657904, overall P = 1.60 x 10(-10), OR = 1.40). CBLB encodes a negative regulator of adaptive immune responses, and mice lacking the ortholog are prone to experimental autoimmune encephalomyelitis, the animal model of multiple sclerosis.