ICH GWAS Monthly Newsletter Issue 12 - December 2009

In this issue:


Please remember: our ICH GWAS Investigator's Meeting will be held in conjunction with the ISGC meeting on January 7th in Cincinnati OH, USA. Additional meeting details, including the agenda, will be sent out shortly.


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		Total
		Case	Control	
Mass General Hospital	September 2009	4	-	**4**
	October 2009	3	-	**3**
	November 2009	3	-	**3**
University of Michigan	September 2009	-	-	**-**
	October 2009	-	-	**-**
	November 2009	-	-	**-**
University of Virginia	September 2009	-	-	**-**
	October 2009	-	-	**-**
	November 2009	-	-	**-**
Mayo Clinic - Jacksonville	September 2009	-	-	**-**
	October 2009	-	2	**2**
	November 2009	-	3	**3**
University of Florida	September 2009	-	1	**1**
	October 2009	-	-	**-**
	November 2009	-	-	**-**
University of Washington	September 2009	-	-	**-**
	October 2009	1	-	**1**
	November 2009	-	-	**-**
Beth Israel Deaconess Medical Center	September 2009	-	-	**-**
	October 2009	-	1	**1**
	November 2009	-	2	**2**
Totals		**11**	**9**	**20**

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

Selvaraju Veeriah, Barry S Taylor, Shasha Meng et al.

Somatic mutations of the Parkinson's disease–associated gene PARK2 in glioblastoma and other human malignancies

Nat Genet. 2009 Nov 29. Epub ahead of print

ABSTRACT

Mutation of the gene PARK2, which encodes an E3 ubiquitin ligase, is the most common cause of early-onset Parkinson's disease1, 2, 3. In a search for multisite tumor suppressors, we identified PARK2 as a frequently targeted gene on chromosome 6q25.2–q27 in cancer. Here we describe inactivating somatic mutations and frequent intragenic deletions of PARK2 in human malignancies. The PARK2 mutations in cancer occur in the same domains, and sometimes at the same residues, as the germline mutations causing familial Parkinson's disease. Cancer-specific mutations abrogate the growth-suppressive effects of the PARK2 protein. PARK2 mutations in cancer decrease PARK2's E3 ligase activity, compromising its ability to ubiquitinate cyclin E and resulting in mitotic instability. These data strongly point to PARK2 as a tumor suppressor on 6q25.2–q27. Thus, PARK2, a gene that causes neuronal dysfunction when mutated in the germline, may instead contribute to oncogenesis when altered in non-neuronal somatic cells.

Spotlight: Article

Chris Wallace, Deborah J Smyth, Meeta Maisuria-Armer et al.

The imprinted DLK1-MEG3 gene region on chromosome 14q32.2 alters susceptibility to type 1 diabetes

Nat Genet. Dec 6. Epub ahead of print

ABSTRACT

Genome-wide association (GWA) studies to map common disease susceptibility loci have been hugely successful, with over 300 reproducibly associated loci reported to date1. However, these studies have not yet provided convincing evidence for any susceptibility locus subject to parent-of-origin effects. Using imputation to extend existing GWA datasets2, 3, 4, we have obtained robust evidence at rs941576 for paternally inherited risk of type 1 diabetes (T1D; ratio of allelic effects for paternal versus maternal transmissions = 0.75; 95% confidence interval (CI) = 0.71–0.79). This marker is in the imprinted region of chromosome 14q32.2, which contains the functional candidate gene DLK1. Our meta-analysis also provided support at genome-wide significance for a T1D locus at chromosome 19p13.2. The highest association was at marker rs2304256 (odds ratio (OR) = 0.86; 95%CI = 0.82–0.90) in the TYK2 gene, which has previously been associated with systemic lupus erythematosus5 and multiple sclerosis6.