NEWSLETTER

Marzo 2012

GeneStroke | The Spanish Stroke Genetics Consortium

Estimados compañeros

Os enviamos la tercera Newsletter del consorcio GeneStroke, donde esperamos encontrareis información de vuestro interés, sobre las novedades del consorcio y de la genética en el ictus.

Equipo GeneStroke
www.GeneStroke.com

Contenido:

Artículo de Nature Genetics muy interesante "Genome-wide association study identifies a variant in HDAC9 associated with large vessel ischemic stroke."
¡¡No dejéis de consultarlo!!

El Consorcio pone a vuestra disposición el *Servicio de extracción de DNA* y la participación en la *Colección de muestras Genestroke*.

Más información en www.genestroke.com o contactad con *csoriano@genestroke.com*

Publicaciones con participación de *Genestroke:*

APOE genotype and extent of bleeding and outcome in lobar intracerebral haemorrhage: a genetic association study.
Biffi A, Anderson CD, Jagiella JM, Schmidt H, Kissela B, Hansen BM, Jimenez-Conde J, Pires CR, Ayres AM, Schwab K, Cortellini L, Pera J, Urbanik A, Romero JM, Rost NS, Goldstein JN, Viswanathan A, Pichler A, Enzinger C, Rabionet R, Norrving B, Tirschwell DL, Selim M, Brown DL, Silliman SL, Worrall BB, Meschia JF, Kidwell CS, Broderick JP, Greenberg SM, Roquer J, Lindgren A, Slowik A, Schmidt R, Woo D, Rosand J; on behalf of the International Stroke Genetics Consortium. *Lancet Neurol.* 2011 Aug;10(8):702-709.

Role of the MMP9 gene in hemorrhagic transformations after t-PA treatment in stroke patients.
I. Fernández-Cadenas PhD; A. del Río-Espínola PhD; C. Carrera; S. Domingues-Montanari PhD; M. Mendióroz MD, PhD; P. Delgado MD, PhD; A. Rosell PhD; M. Ribó MD, PhD; D. Giralt; M. Quintana; M. Castellanos MD, PhD; V. Obach MD, PhD; S. Martínez MD, PhD; M.M. Freijo MD, J. Jiménez-Conde MD, PhD; J. Roquer MD, PhD; J. Martí-Fábregas MD, PhD; CA. Molina MD, PhD; J. Álvarez-Sabín MD, PhD; J. Montaner MD, PhD. *Stroke (2012)*

***TTC7B* emerges as a novel risk factor for ischemic stroke through the convergence of several genome-wide approaches.**
Krug, Tiago; Gabriel, João Paulo; Taipa, Ricardo; Fonseca, Maria B.; Domingues-Montanari, Sophie; Fernández Cadenas, Israel; Manso, Helena; Gouveia, Liliana; Sobral, João; Albergaria, Isabel; Gaspar, Gisela; Jiménez-Conde, Jordi; Rabionet, Raquel; Ferro, José; Montaner, Joan; Vicente, Astrid; Silva, Mário Rui; Matos, Ilda; Lopes, Gabriela; Oliveira, Sofia,. *Journal of Cerebral Blood Flow & Metabolism* (2012) (in press)

PROYECTOS GENESTROKE EN ACTIVO

Actualmente tenemos estos proyectos en curso:

¿Quieres realizar un estudio y necesitas colaboraciones? ¡¡¡Envía tu propuesta!!! ¡¡PARTICIPAD!!

Proyecto: **Replicación CONIC**
IP: Sophie Domingues-Montanari (Hospital Vall d'Hebron)
Estado: Se han genotipado y esta en fase de análisis.

Proyecto: **RICAD**
IP: Gavin Lucas (grupo de Investigación Cerebrovascular del Hospital del Mar)
Estado: Se han genotipado y esta en fase de análisis.

Proyecto: **GWALA!!** (Bases genéticas de la leucoaraiosis. Estudio de Genome Wide Association en población española.).
IP: Jordi Jiménez Conde (Hospital del Mar).
Estado: Pendiente de comenzar la genotipación de las muestras.

Proyecto: **GWAs GenotPA**
IP: Israel Cadenas (Hospital Vall d'Hebron)
Estado: En la fase inicial, este año se espera tener los resultados del GWAs.

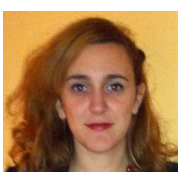
Proyecto: **GODS project** (Genetic contribution to functional Outcome and Disability after Stroke)
IP: Jordi Jiménez Conde (Hospital del Mar).
Estado: Concedido el proyecto presentado a *La Marató de TV3*.

Proyecto: **METICUS** (Patrón de METilación como marcador de inestabilidad de placa carotídea en pacientes con ICtUS isquémico)
IP: Israel Cadenas (Hospital Vall d'Hebron)
Estado: Pendiente financiación. Se ha solicitado a la *Fundación Ramón Areces* (XVI Concurso Nacional para la Adjudicación de Ayudas a la Investigación en Ciencias de la Vida y de la Materia).

Proyecto: **GLAM-Stroke** (GLobAl Methylation of ischemic stroke)
IP: Carolina Soriano (Hopital del Mar)
Estado: : En la fase inicial de análisis.

Para solicitar más información sobre los proyectos, contactar con:

Carolina Soriano
(csoriano@genestroke.com)



Sophie Domingues
(sdomingues@genestroke.com)

NOVEDADES SOBRE GENÉTICA y EPIGENÉTICA EN EL ICTUS:

Genome-wide association study identifies a variant in HDAC9 associated with large vessel ischemic stroke. The International Stroke **Genetics** Consortium (ISGC); the **Wellcome Trust** Case Control Consortium 2 (WTCCC2), Bellenguez C, Bevan S, Gschwendtner A, Spencer CC, Burgess AI, Pirinen M, Jackson CA, Traylor M, Strange A, Su Z, Band G, Syme PD, Malik R, Pera J, Norrving B, Lemmens R, Freeman C, Schanz R, James T, Poole D, Murphy L, Segal H, Cortellini L, Cheng YC, Woo D, Nalls MA, Müller-Myhsok B, Meisinger C, Seedorf U, Ross-Adams H, Boonen S, Wloch-Kopec D, Valant V, Slark J, Furie K, Delavaran H, Langford C, Deloukas P, Edkins S, Hunt S, Gray E, Dronov S, Peltonen L, Gretarsdottir S, Thorleifsson G, Thorsteinsdottir U, Stefansson K, Boncoraglio GB, Parati EA, Attia J, Holliday E, Levi C, Franzosi MG, Goel A, Helgadottir A, Blackwell JM, Bramon E, Brown MA, Casas JP, Corvin A, Duncanson A, Jankowski J, Mathew CG, Palmer CN, Plomin R, Rautanen A, Sawcer SJ, Trembath RC, Viswanathan AC, Wood NW, Worrall BB, Kittner SJ, Mitchell BD, Kissela B, Meschia JF, Thijs V, Lindgren A, Macleod MJ, Slowik A, Walters M, Rosand J, Sharma P, Farrall M, Sudlow CL, Rothwell PM, Dichgans M, Donnelly P, Markus HS. **Nat Genet**. 2012 Feb 5;44(3):328-333. doi: 10.1038/ng.1081.

Abstract

Genetic factors have been implicated in stroke risk, but few replicated associations have been reported. We conducted a genome-wide association study (GWAS) for ischemic stroke and its subtypes in 3,548 affected individuals and 5,972 controls, all of European ancestry. Replication of potential signals was performed in 5,859 affected individuals and 6,281 controls. We replicated previous associations for cardioembolic stroke near *PITX2* and *ZFHX3* and for large vessel stroke at a 9p21 locus. We identified a new association for large vessel stroke within *HDAC9* (encoding histone deacetylase 9) on chromosome 7p21.1 (including further replication in an additional 735 affected individuals and 28,583 controls) (rs11984041; combined $P = 1.87 \times 10^{-11}$; odds ratio (OR) = 1.42, 95% confidence interval (CI) = 1.28–1.57). All four loci exhibited evidence for heterogeneity of effect across the stroke subtypes, with some and possibly all affecting risk for only one subtype. This suggests distinct genetic architectures for different stroke subtypes.

Epigenome-wide association studies for common human diseases.
Rakyan VK, Down TA, Balding DJ, Beck S. **Nat Rev Genet.** 2011 Jul 12;12(8):529-41. doi: 10.1038/nrg3000. Review

Abstract

Despite the success of genome-wide association studies (GWASs) in identifying loci associated with common diseases, a substantial proportion of the causality remains unexplained. Recent advances in genomic technologies have placed us in a position to initiate large-scale studies of human disease-associated epigenetic variation, specifically variation in DNA methylation. Such epigenome-wide association studies (EWASs) present novel opportunities but also create new challenges that are not encountered in GWASs. We discuss EWAS design, cohort and sample selections, statistical significance and power, confounding factors and follow-up studies. We also discuss how integration of EWASs with GWASs can help to dissect complex GWAS haplotypes for functional analysis.

Are Myocardial Infarction-Associated Single-Nucleotide Polymorphisms Associated With Ischemic Stroke?

Cheng YC, Anderson CD, Bione S, Keene K, Maguire JM, Nalls M, Rasheed A, Zeginigg M, Attia J, Baker R, Barlera S, Biffi A, Bookman E, Brott TG, Brown RD Jr, Chen F, Chen WM, Ciusani E, Cole JW, Cortellini L, Danesh J, Doheny K, Ferrucci L, Franzosi MG, Frossard P, Furie KL, Golledge J, Hankey GJ, Hernandez D, Holliday EG, Hsu FC, Jannes J, Kamal A, Khan MS, Kittner SJ, Koblar SA, Lewis M, Lincz L, Lisa A, Matarin M, Moscato P, Mychaleckyj JC, Parati EA, Parolo S, Pugh E, Rost NS, Schallert M, Schmidt H, Scott RJ, Sturm JW, Yadav S, Zaidi M; GARNET Collaborative Research Group; GENEVA Consortium, Boncoraglio GB, Levi CR, Meschia JF, Rosand J, Sale M, Saleheen D, Schmidt R, Sharma P, Worrall B, Mitchell BD; on behalf of the *International Stroke Genetics Consortium*. **Stroke**. 2012 Feb 23. [Epub ahead of print]

Abstract

BACKGROUND AND PURPOSE: Ischemic stroke (IS) shares many common risk factors with coronary artery disease (CAD). We hypothesized that genetic variants associated with myocardial infarction (MI) or CAD may be similarly involved in the etiology of IS. To test this hypothesis, we evaluated whether single-nucleotide polymorphisms (SNPs) at 11 different loci recently associated with MI or CAD through genome-wide association studies were associated with IS.

METHODS: Meta-analyses of the associations between the 11 MI-associated SNPs and IS were performed using 6865 cases and 11 395 control subjects recruited from 9 studies. SNPs were either genotyped directly or imputed; in a few cases a surrogate SNP in high linkage disequilibrium was chosen. Logistic regression was performed within each study to obtain study-specific βs and standard errors. Meta-analysis was conducted using an inverse variance weighted approach assuming a random effect model.

RESULTS: Despite having power to detect odds ratio of 1.09-1.14 for overall IS and 1.20-1.32 for major stroke subtypes, none of the SNPs were significantly associated with overall IS and/or stroke subtypes after adjusting for multiple comparisons.

CONCLUSIONS: Our results suggest that the major common loci associated with MI risk do not have effects of similar magnitude on overall IS but do not preclude moderate associations restricted to specific IS subtypes. Disparate mechanisms may be critical in the development of acute ischemic coronary and cerebrovascular events.

DNA methylation patterns associate with genetic and gene expression variation in HapMap cell lines.

Bell JT, Pai AA, Pickrell JK, Gaffney DJ, Pique-Regi R, Degner JF, Gilad Y, Pritchard JK.
Genome Biol. 2011;12(1):R10. Epub 2011 Jan 20. Erratum in: Genome Biol. 2011;12(6):405.

Abstract

BACKGROUND: DNA methylation is an essential epigenetic mechanism involved in gene regulation and disease, but little is known about the mechanisms underlying inter-individual variation in methylation profiles. Here we measured methylation levels at 22,290 CpG dinucleotides in lymphoblastoid cell lines from 77 HapMap Yoruba individuals, for which genome-wide gene expression and genotype data were also available.

RESULTS: Association analyses of methylation levels with more than three million common single nucleotide polymorphisms (SNPs) identified 180 CpG-sites in 173 genes that were associated with nearby SNPs (putatively in cis, usually within 5 kb) at a false discovery rate of 10%. The most intriguing trans signal was obtained for SNP rs10876043 in the disco-interacting protein 2 homolog B gene (DIP2B, previously postulated to play a role in DNA methylation), that had a genome-wide significant association with the first principal component of patterns of methylation; however, we found only modest signal of trans-acting associations overall. As expected, we found significant negative correlations between promoter methylation and gene expression levels measured by RNA-sequencing across genes. Finally, there was a significant overlap of SNPs that were associated with both methylation and gene expression levels.

CONCLUSIONS: Our results demonstrate a strong genetic component to inter-individual variation in DNA methylation profiles. Furthermore, there was an enrichment of SNPs that affect both methylation and gene expression, providing evidence for shared mechanisms in a fraction of genes.

¿BUSCAS FINANCIACIÓN?

Actualmente...

Instituto Carlos III -Convocatorias y ayudas Acción Estratégica de Salud

FIS, PFIS, Sara Borell, Miguel Servet, CIBERS, RETICS

Puedes consultar las bases de la convocatoria en el BOE:

http://www.boe.es/boe/dias/2012/03/02/pdfs/BOE-A-2012-3035.pdf

INTERNATIONAL STROKE CONFERENCE 2012
SESSIONS: FEBRUARY 1-3
EXHIBITS: FEBRUARY 1-2

Advances in Stroke Genetics: The American Stroke Association

Presentaciones recomendadas

***Necesario disponer de cuenta de "Sessions on Demand" o abrirse una nueva para acceder al contenido)**

Gene Expression for the Diagnosis of Stroke and TIA.
Glen Jickling, MD, FRCPC, Sacramento, CA.

Genetics of Cerebral Artery Dissection.
Stephanie Debette, MD, PhD, Boston, MA.

Genetics of Atrial Fibrillation. Patrick T Ellinor, MD, PhD, Boston, MA.

Unlocking the Genetics of Vascular Cognitive Impairment.
Sudha Seshadri, MBBS, MD, Boston, MA

Cognitive Function, APOE and Small Vessel Stroke in African Americans.
Cheryl Bushnell, MD, MHSc, FAHA, Winston Salem, NC.

CONGRESOS Y REUNIONES DE INTERÉS 2012-2013

International Stroke Genetics Conference. April 12-13, 2012. Newcastle, Australia.

21rt European stroke conference, May 22-25, 2012. Lisbon, Portugal.

22nd Meeting of European Neurological Society. June 9-12, 2012. Prague, Czech Republic.

The European Human Genetics Conference 2012 in conjunction with the European Meeting on Psychosocial Aspects of Genetics 2012, June 23-26, 2012. Nuremberg, Germany.

6th EFNS Congress, September 08- 11, 2012. Stockholm, Sweden.

3rd Canadian Stroke Congress, September 29-October 2nd, 2012. Calgary, Alberta.

8th World Stroke Congress, October 10-13, 2012. Brasilia, Brazil.

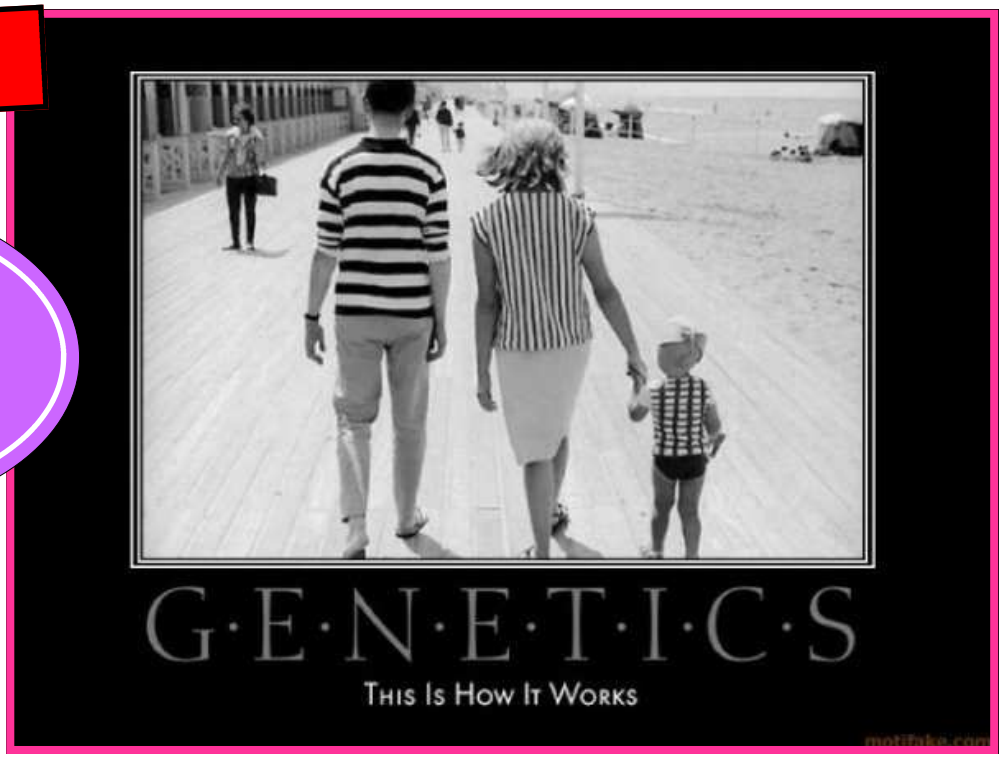
Society for Neuroscience (SFN) Annual Meeting: Neuroscience 2012, October 13-17, 2012. New Orleans, USA.

American Society of Human Genetics (ASHG) 62nd Annual Meeting, November 6-10, 2012. San Francisco, USA.

SEN 2012 - LXIV Reunión Anual de la Sociedad Española de Neurología, 20 al 24 de Noviembre de 2012. Barcelona.

International Stroke Conference, Febrary 6-8, 2013. Honolulu, Hawaii (USA)

GE, GE, GE…



Sugerencias…
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www.GeneStroke.com

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