NEWSLETTER

Junio 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

GCGGCGCGGAGGCTGGCCCGGGACGCGCCCGGAGCCCAGGGAAGGAGGGAGGAGGGGAGGGTCGCGG
CCGGCCGCCATGGGGCCGGGGGCCCGTGGCCGCCGCCGCCGCCGTCGCCCGATGTCGCCGCCACCGC
CACCGCCACCCGTGCGGGCGCTGCCCCTGCTGCTGCTGCTAGCGGGGCCGGGGGCTGCAGGTGAGGG
GCCGGGACCTGGCGGATGGGACGAGGGCGGCAGA**TITULARES**GGGGGAGTGCAAGAACCCCCAAG
GCCGGGGCTGGCGGGGGTTCATGGGAGGCAGGAACCAGGGTCGGGGAAGGGGCGCAGGAGCCCGGCT

Contenido:

OFERTA ANTICRISIS

EXTRACCIÓN DNA GRATIS

Para más información contacta con nosotros

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:*

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)

A Predictive Clinical-Genetic Model of t-PA Response in Acute Ischemic Stroke.
A. del Río-Espínola,* PhD,[1] I. Fernández-Cadenas,* PhD,[1] D. Giralt, BSc,[1] A. Quiroga,[2] M. Gutiérrez-Agulló, MSc,[3] M. Quintana, BSc,[4] P. Fernández-Álvarez, MSc,[2] S. Domingues-Montanari, PhD,[1] M. Mendióroz, MD, PhD,[1] P. Delgado, MD, PhD,[1] N. Turck, PhD,[5] A. Ruíz, PhD,[6] M. Ribó, MD, PhD,[4] M. Castellanos, MD, PhD,[7] V. Obach, MD, PhD,[8] S. Martínez, MD, PhD,[9] M.M. Freijo, MD,[10] J. Jiménez-Conde, MD, PhD,[11] E. Cuadrado-Godia, MD,[11] J. Roquer, MD, PhD,[11] P. Chacón, PhD,[3] J. Martí-Fábregas, MD, PhD,[9] J.C. Sánchez, PhD,[5] GRECOS investigators,[12] and J. Montaner,* MD PhD. Annals of Neurology 2012 (in press).

PROYECTOS GENESTROKE EN ACTIVO

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

Actualmente tenemos estos proyectos en curso:

Proyecto: **Replicación CONIC**
IP: Sophie Domingues-Montanari (Hospital Vall d'Hebron)
Estado: Terminado.
Resultado: Los SNPs no se han replicado.

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: Genotipándose.

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

Para solicitar más información sobre los proyectos, contactar con:

Carolina Soriano
(csoriano@genestroke.com)

NOVEDADES SOBRE GENÉTICA y EPIGENÉTICA EN EL ICTUS:

TTC7B emerges as a novel risk factor for ischemic stroke through the convergence of several genome-wide approaches.

Krug T, Gabriel JP, Taipa R, Fonseca BV, Domingues-Montanari S, Fernandez-Cadenas I, Manso H, Gouveia LO, Sobral J, Albergaria I, Gaspar G, Jiménez-Conde J, Rabionet R, Ferro JM, Montaner J, Vicente AM, Silva MR, Matos I, Lopes G, Oliveira SA. **J Cereb Blood Flow Metab.** 2012 Jun;32(6):1061-72.

Abstract

We hereby propose a novel approach to the identification of ischemic stroke (IS) susceptibility genes that involves converging data from several unbiased genetic and genomic tools. We tested the association between IS and genes differentially expressed between cases and controls, then determined which data mapped to previously reported linkage peaks and were nominally associated with stroke in published genome-wide association studies. We first performed gene expression profiling in peripheral blood mononuclear cells of 20 IS cases and 20 controls. Sixteen differentially expressed genes mapped to reported whole-genome linkage peaks, including the TTC7B gene, which has been associated with major cardiovascular disease. At the TTC7B locus, 46 tagging polymorphisms were tested for association in 565 Portuguese IS cases and 520 controls. Markers nominally associated in at least one test and defining associated haplotypes were then examined in 570 IS Spanish cases and 390 controls. Several polymorphisms and haplotypes in the intron 5-intron 6 region of TTC7B were also associated with IS risk in the Spanish and combined data sets. Multiple independent lines of evidence therefore support the role of TTC7B in stroke susceptibility, but further work is warranted to identify the exact risk variant and its pathogenic potential.

Rare variants in ischemic stroke: an exome pilot study.

Cole JW, Stine OC, Liu X, Pratap A, Cheng Y, Tallon LJ, Sadzewicz LK, Dueker N, Wozniak MA, Stern BJ, Meschia JF, Mitchell BD, Kittner SJ, O'Connell JR. **PLoS One.** 2012;7(4)

Abstract

The genetic architecture of ischemic stroke is complex and is likely to include rare or low frequency variants with high penetrance and large effect sizes. Such variants are likely to provide important insights into disease pathogenesis compared to common variants with small effect sizes. Because a significant portion of human functional variation may derive from the protein-coding portion of genes we undertook a pilot study to identify variation across the human exome (i.e., the coding exons across the entire human genome) in 10 ischemic stroke cases. Our efforts focused on evaluating the feasibility and identifying the difficulties in this type of research as it applies to ischemic stroke. The cases included 8 African-Americans and 2 Caucasians selected on the basis of similar stroke subtypes and by implementing a case selection algorithm that emphasized the genetic contribution of stroke risk. Following construction of paired-end sequencing libraries, all predicted human exons in each sample were captured and sequenced. Sequencing generated an average of 25.5 million read pairs (75 bp×2) and 3.8 Gbp per sample. After passing quality filters, screening the exomes against dbSNP demonstrated an average of 2839 novel SNPs among African-Americans and 1105 among Caucasians. In an aggregate analysis, 48 genes were identified to have at least one rare variant across all stroke cases. One gene, CSN3, identified by screening our prior GWAS results in conjunction with our exome results, was found to contain an interesting coding polymorphism as well as containing excess rare variation as compared with the other genes evaluated. In conclusion, while rare coding variants may predispose to the risk of ischemic stroke, this fact has yet to be definitively proven. Our study demonstrates the complexities of such research and highlights that while exome data can be obtained, the optimal analytical methods have yet to be determined.

Genome-wide association analysis identifies susceptibility loci for migraine without aura.

Freilinger T, Anttila V, de Vries B, Malik R, Kallela M, Terwindt GM, Pozo-Rosich P, Winsvold B, Nyholt DR, van Oosterhout WP, Artto V, Todt U, Hämäläinen E, Fernández-Morales J, Louter MA, Kaunisto MA, Schoenen J, Raitakari O, Lehtimäki T, Vila-Pueyo M, Göbel H, Wichmann E, Sintas C, Uitterlinden AG, Hofman A, Rivadeneira F, Heinze A, Tronvik E, van Duijn CM, Kaprio J, Cormand B, Wessman M, Frants RR, Meitinger T, Müller-Myhsok B, Zwart JA, Färkkilä M, Macaya A, Ferrari MD, Kubisch C, Palotie A, Dichgans M, van den Maagdenberg AM; **International Headache Genetics Consortium**.
Nat Genet. 2012 doi: 10.1038/ng.2307

Abstract

Migraine without aura is the most common form of migraine, characterized by recurrent disabling headache and associated autonomic symptoms. To identify common genetic variants associated with this migraine type, we analyzed genome-wide association data of 2,326 clinic-based German and Dutch individuals with migraine without aura and 4,580 population-matched controls. We selected SNPs from 12 loci with 2 or more SNPs associated with P values of <1 × 10(-5) for replication testing in 2,508 individuals with migraine without aura and 2,652 controls. SNPs at two of these loci showed convincing replication: at 1q22 (in MEF2D; replication P = 4.9 × 10(-4); combined P = 7.06 × 10(-11)) and at 3p24 (near TGFBR2; replication P = 1.0 × 10(-4); combined P = 1.17 × 10(-9)). In addition, SNPs at the PHACTR1 and ASTN2 loci showed suggestive evidence of replication (P = 0.01; combined P = 3.20 × 10(-8) and P = 0.02; combined P = 3.86 × 10(-8), respectively). We also replicated associations at two previously reported migraine loci in or near TRPM8 and LRP1. This study identifies the first susceptibility loci for migraine without aura, thereby expanding our knowledge of this debilitating neurological disorder.

Distinct DNA methylomes of newborns and centenarians.

Heyn H, Li N, Ferreira HJ, Moran S, Pisano DG, Gomez A, Diez J, Sanchez-Mut JV, Setien F, Carmona FJ, Puca AA, Sayols S, Pujana MA, Serra-Musach J, Iglesias-Platas I, Formiga F, Fernandez AF, Fraga MF, Heath SC, Valencia A, Gut IG, Wang J, Esteller M. **Proc Natl Acad Sci U S A.** 2012

Abstract

Human aging cannot be fully understood in terms of the constrained genetic **setting. Epigenetic drift is an alternative means of explaining age-associated alterations. To address this issue, we performed whole-genome bisulfite sequencing (WGBS) of newborn and centenarian genomes. The centenarian DNA had a lower DNA methylation content and a reduced correlation in the methylation status of neighboring cytosine-phosphate-guanine (CpGs) throughout the genome in comparison with the more homogeneously methylated newborn DNA. The more hypomethylated CpGs observed in the centenarian DNA compared with the neonate covered all genomic compartments, such as promoters, exonic, intronic, and intergenic regions. For regulatory regions, the most hypomethylated sequences in the centenarian DNA were present mainly at CpG-poor promoters and in tissue-specific genes, whereas a greater level of DNA methylation was observed in CpG island promoters. We extended the study to a larger cohort of newborn and nonagenarian samples using a 450,000 CpG-site DNA methylation microarray that reinforced the observation of more hypomethylated DNA sequences in the advanced age group. WGBS and 450,000 analyses of middle-age individuals demonstrated DNA methylomes in the crossroad between the newborn and the nonagenarian/centenarian groups. Our study constitutes a unique DNA methylation analysis of the extreme points of human life at a single-nucleotide resolution level.**

XXI European Stroke Conference

Contribuciones de los miembros del consorcio:

Comunicación Oral. GRECOS project: the use of genetic markers in the prediction of vascular recurrence after a first ischemic stroke.

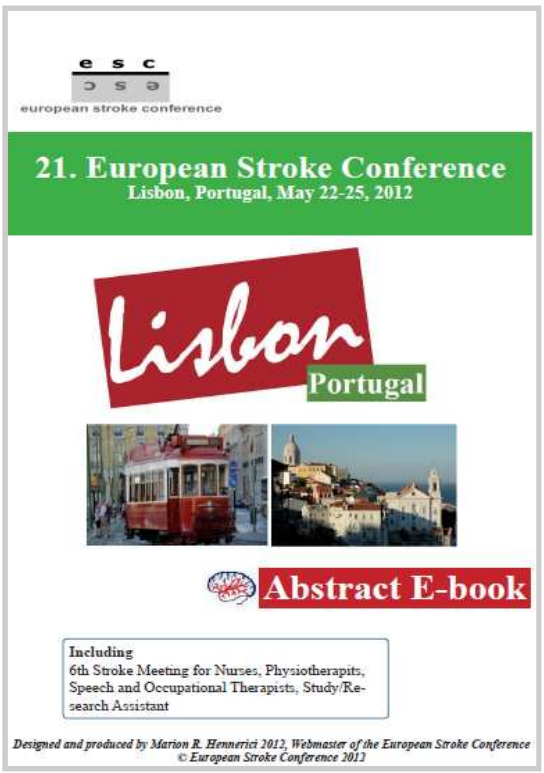
I Fernandez-Cadenas, M. Mendioroz, E. Palomeras, A. Aboix, M. Ribo, D. Canovas, J. Krupinski, J. Arenillas, N. Perez de la Ossa, J. Martí-Fàbregas, J. Roquer10, J. Masjuan, J. Serena, F. Purroy, J. Montaner. GRECOS study Group

E-Póster (best posters). Contribution of Genetic Variants Associated with Blood Pressure in Risk of Stroke Depending on Stroke Subtype. The Spanish Genetic Stroke Consortium (Genestroke).

J. Jimenez-Conde, G. Lucas, C. Soriano, E. Giralt-Steinhauer, A. Rodriguez-Campello, A. Ois, E. Cuadrado-Godia, I. Fernandez-Cadenas, S. Domingues, J. Krupinski, V. Obach, S. Martinez, E. Goyenechea, J. Roquer, J.A. Iniesta.

Póster. Epigenetics of ischemic stroke subtypes.

C. Soriano, J. Jiménez-Conde, E. Giralt-Steinhauer, A. Ois, A. Rodríguez-Campello, E. Cuadrado-Godia, J. Roquer.



Aquí podéis encontrar todas las comunicaciones presentadas en el congreso.

Próximo año…

LONDRES

CONGRESOS Y REUNIONES DE INTERÉS 2012-2013

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

16th 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)

22nd European stroke conference, May 28-31, 2013. London (UK)

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Sugerencias…
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Estamos en la web!
www.GeneStroke.com

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