NEWSLETTER

GeneStroke | The Spanish Stroke Genetics Consortium

Estimados compañeros

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

Equipo GeneStroke
www.GeneStroke.com

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TITULARES

PRÓXIMAMENTE en Barcelona:

I CURSO DE FORMACIÓN Y ACTUALIZACIÓN EN GENÉTICA DE LAS ENFERMEDADES COMPLEJAS

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GeneStroke

18th Workshop of the International Stroke Genetics Consortium

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Últimas publicaciones con participación de *GeneStroke:*

New **An Inflammatory Polymorphisms Risk Scoring System for the Differentiation of Ischemic Stroke Subtypes.**

Muiño E, Krupinski J, Carrera C, Gallego-Fabrega C, Montaner J, Fernández-Cadenas I. **Mediators Inflamm**. 2015.

Common variation in COL4A1/COL 4A2 is associated with sporadic cerebral small vessel disease.

K Rannikmäe, …, J **Jimenez-Conde**, **J Montaner**, …, Jonathan Rosand, Cathie LM Sudlow on behalf of the Metastroke Consortium, the CHARGE WMH Group, the ISGC ICH GWAS Study Collaboration, the WMH in ischemic stroke GWAS Study Collaboration and the International Stroke Genetics Consortium. **Neurology. 2015 Mar 3.**

Agreement between TOAST and CCS ischemic stroke classification: The NINDS SiGN Study.

McArdle PF, …, **Jiménez-Conde J**, **Roquer J**, …, Worrall BB, On behalf of the NINDS SiGN Study. **Neurology. 2014 Oct 28.**

Pathogenic Ischemic Stroke Phenotypes in the NINDS-Stroke Genetics Network. Ay H, **Giralt E,** Grewal RP, Gwinn K, Jern C, **Jiménez-Conde J**, …, Worrall BB, Meschia JF. **Stroke. 2014 Dec.**

Recommendations from the International Stroke Genetics Consortium, Part 2: Biological Sample Collection and Storage.

Thomas Battey, …, **Jordi Jiménez-Conde, Israel Fernandez-Cadenas**, Guillaume Paré, Cathie Sudlow and Jonathan Rosand on behalf of the International Stroke Genetics Consortium. **Stroke. 2015 Jan.**

PROYECTOS GENESTROKE EN ACTIVO

Actualmente tenemos estos proyectos en curso:

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

Proyecto: **GWALA!! (Bases genéticas de la leucoaraiosis. Estudio de Genome Wide Association en población española)**
IP: Jordi Jiménez Conde (Hospital del Mar)
Estado: En fase de publicación

Proyecto: **GWAs GenotPA (Estudio de Genome-Wide Association en pacientes tratados con tPA)**
IP: Israel Fernández Cadenas (Vall d'Hebron Institut de Recerca i Mútua de Terrassa)
Estado: En fase de replicación

Proyecto: **GODS project (Genetic contribution to functional Outcome and Disability after Stroke)**
Coord y IP grupo: Jordi Jiménez Conde (Hospital del Mar); *IP grupo*: Israel Fernández Cadenas (Vall d'Hebron); *IP grupo*: Xavier Estivill (Centro de Regulación Genómica); *IP grupo*: Jerzy Krupinski (Mútua Terrassa); *IP grupo*: Cristòfol Vives (Hospital Son Espases)
Estado: En fase de análisis

Proyecto: **Cardioembolic Exome (Secuenciación de exoma completo de pacientes con ictus cardioembólicos)**
IP: Israel Fernández Cadenas (Vall d'Hebron Institut de Recerca i Mútua de Terrassa)
Estado: En fase de publicación

Proyecto: **GRECAS Project (Genotyping Risk and Efficacy of Clopidogrel or Aspirin following Stroke)**
IP: Israel Fernández Cadenas (Vall d'Hebron Institut de Recerca i Mútua de Terrassa)
Estado: En fase de análisis

Proyecto: **EWAS-Stroke (Estudio de Epigenome-Wide Association en los subtipos etiológicos de ictus isquémico)**
IP: Carolina Soriano (Hospital del Mar)
Estado: En fase de publicación

Proyecto: **ChiCHOS (Case/Control study to analyse tHe genetic risk factOrs of ischemic Stroke)**
IP: Israel Fernández Cadenas (Vall d'Hebron Institut de Recerca i Mútua de Terrassa)
Estado: En fase de análisis

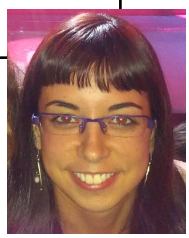
Proyecto: **Pharmastroke (Epigenética en pacientes tratados con antiagregantes)**
IP: Israel Fernández Cadenas (Vall d'Hebron Institut de Recerca i Mútua de Terrassa)
Estado: En fase de publicación

Proyecto: **MENEAS (MEthylation of DNA depending on Nutrition and Exercise habits. Developing a marker of "biological Age" and risk of Stroke)**
IP: Jordi Jiménez Conde (Hospital del Mar)
Estado: En fase de análisis

Proyecto: **EWAL (Estudio de Epigenome Wide Association en Leucoaraiosis. Contribución de la epigenética en el envejecimiento cerebral.** International Stroke Genetics Consortium (ISGC))
IP: Jordi Jiménez Conde (Hospital del Mar)
Estado: Financiado. Pendiente iniciar

Proyecto: **GENERACIÓN (Estudio GENÉtico de mutaciones RAras en el ictus isquémico y creación de un score clínico-genético de predicCIÓN de riesgo)**
IP: Israel Fernández Cadenas (Vall d'Hebron Institut de Recerca i Mútua de Terrassa)
Estado: Financiado. Pendiente iniciar

Para solicitar más información sobre los proyectos podéis contactar conmigo



Marina Mola
(mmola@imim.es)

NOVEDADES SOBRE GENÉTICA EN EL ICTUS:

COX-2 rs20417 Polymorphism Is Associated with Stroke and White Matter Disease.
Oliveira-Filho J, Ornellas AC, Zhang CR, Oliveira LM, Araújo-Santos T, Borges VM, Ventura LM, Reis FJ, Aras R, Fernandes AM, Rosand J, Greenberg SM, Furie KL, Rost NS.
J Stroke Cerebrovasc Dis. 2015 Aug.

Abstract

BACKGROUND: To investigate the effect of COX-2 polymorphism and its product, prostaglandin E2 (PGE2), on stroke risk in an endemic area for Chagas disease. In a separate cohort, to investigate the effect of COX-2 polymorphisms on the total burden of cerebral white matter disease.

METHODS: Cases were outpatients with ischemic stroke; controls were stroke-free subjects from 2 outpatient clinics (heart failure and caregivers of a movement disorders clinic). We extracted DNA from total blood to investigate the rs20417 COX-2 polymorphism. Serologic tests (Enzime-linked immunosorbent assay) were performed to confirm Trypanosoma cruzi infection and to quantify PGE2 levels. In the Boston cohort, white matter hyperintensity volume (WMHv) was quantified on the admission brain magnetic resonance images of subjects with ischemic stroke, who also donated DNA for the COX-2 gene region analysis.

RESULTS: We studied 44 patients with stroke and 96 controls (46 with heart failure and 50 caregivers) in the Brazilian cohort; and 788 stroke patients (302 cardioembolic and 486 noncardioembolic) in the Boston cohort. In the Brazilian cohort, rs20417 polymorphism was associated with both stroke (P = 5 × 10(-6)) and decreased PGE2 levels (P = 4 × 10(-5)); similarly, Chagas was associated with stroke (P = 4 × 10(-3)) and decreased PGE2 levels (P = 7 × 10(-3)). In the Boston cohort, rs20417 polymorphism was associated with increased WMHv among noncardioembolic (P = .037), but not among cardioembolic stroke patients.

CONCLUSIONS: Variation in COX-2 gene is associated with both symptomatic and silent brain cerebrovascular disease. This candidate gene region should be tested in population-based samples.

Rare Coding Variation and Risk of Intracerebral Hemorrhage.

Radmanesh F, Falcone GJ, Anderson CD, McWilliams D, Devan WJ, Brown WM, Battey TW, Ayres AM, Raffeld MR, Schwab K, Sun G, Deka R, Viswanathan A, Goldstein JN, Greenberg SM, Tirschwell DL, Silliman SL, Selim M, Meschia JF, Brown DL, Worrall BB, Langefeld CD, Woo D,Rosand J.
Stroke. 2015 Aug.

Abstract

BACKGROUND AND PURPOSE: Intracerebral hemorrhage has a substantial genetic component. We performed a preliminary search for rare coding variants associated with intracerebral hemorrhage.

METHODS: A total of 757 cases and 795 controls were genotyped using the Illumina HumanExome Beadchip (Illumina, Inc, San Diego, CA). Meta-analyses of single-variant and gene-based association were computed.

RESULTS: No rare coding variants were associated with intracerebral hemorrhage. Three common variants on chromosome 19q13 at an established susceptibility locus, encompassing TOMM40, APOE, and APOC1, met genome-wide significance (P<5e-08). After adjusting for the APOE epsilon alleles, this locus was no longer convincingly associated with intracerebral hemorrhage. No gene reached genome-wide significance level in gene-based association testing.

CONCLUSIONS: Although no coding variants of large effect were detected, this study further underscores a major challenge for the study of genetic susceptibility loci; large sample sizes are required for sufficient power except for loci with large effects.

Heritability of young- and old-onset ischaemic stroke.

Bluher A, Devan WJ, Holliday EG, Nalls M, Parolo S, Bione S, Giese AK, Boncoraglio GB, Maguire JM, Müller-Nurasyid M, Gieger C, Meschia JF, Rosand J, Rolfs A, Kittner SJ, Mitchell BD, O'Connell JR, Cheng YC.
Eur J Neurol. 2015 Sep 2.

Abstract

BACKGROUND AND PURPOSE: Although the genetic contribution to stroke risk is well known, it remains unclear if young-onset stroke has a stronger genetic contribution than old-onset stroke. This study aims to compare the heritability of ischaemic stroke risk between young and old, using common genetic variants from whole-genome array data in population-based samples.

METHODS: This analysis included 4050 ischaemic stroke cases and 5765 controls from six study populations of European ancestry; 47% of cases were young-onset stroke (age < 55 years). To quantify the heritability for stroke risk in these unrelated individuals, the pairwise genetic relatedness was estimated between individuals based on their whole-genome array data using a mixed linear model. Heritability was estimated separately for young-onset stroke and old-onset stroke (age ≥ 55 years).

RESULTS: Heritabilities for young-onset stroke and old-onset stroke were estimated at 42% (±8%, P < 0.001) and 34% (±10%, P < 0.001), respectively.

CONCLUSIONS: Our data suggest that the genetic contribution to the risk of stroke may be higher in young-onset ischaemic stroke, although the difference was not statistically significant.

review

Ischemic Stroke: From Next Generation Sequencing and GWAS to Community Genomics?

Black M, Wang W, Wang W.
OMICS. 2015 Aug

Abstract

Stroke is a major cause of mortality and morbidity in both the developed and developing world. Next generation sequencing (NGS) and multi-omics integrative biology research offer new opportunities in the way we research and understand stroke. These biotechnologies also signal a shift fromgenetics to genomics of stroke, which is highlighted in this review. Stroke is a focal neurological deficit resulting from disruption of the cerebral blood supply. There are two main types of common stroke, ischemic stroke (IS), which comprises 80% of cases, and hemorrhagic stroke (HS) that accounts for about 20% of cases. IS is a complex multi-factorial disease with multiple environmental and genomic determinants. We discuss here IS from genomics and bioinformatics perspectives, including the highlights of the genome wide association studies (GWAS), NGS progress to date, and exome studies. While both 'common variant, common disease' and 'rare variant, common disease' approaches need to be assessed in tandem, future studies into IS omics should also consider pedigree and/or community based sampling to take account of the complex diversity of ISgenetics. We conclude by presenting an example of such community genomics research from China in an extended pedigree sample, and the ways in which the intersection of genomics and global society can usefully inform our understanding of IS pathophysiology and potential preventive medicine interventions in the future.

An Inflammatory Polymorphisms Risk Scoring System for the Differentiation of Ischemic Stroke Subtypes.

Muiño E, Krupinski J, Carrera C, Gallego-Fabrega C, Montaner J, Fernández-Cadenas I.
Mediators Inflamm. 2015 Aug.

Abstract

Inflammation has been associated with atherothrombotic stroke and recently with cardioembolic stroke. Different genetic risk factors have been specifically associated with the subtypes of ischemic stroke (cardioembolic, atherothrombotic, and lacunar). However, there are no studies that have generated genetic risk scores for the different subtypes of ischemic stroke using polymorphisms associated with inflammation. Methods. We have analyzed 68 polymorphisms of 30 inflammatory mediator genes in 2,685 subjects: 1,987 stroke cases and 698 controls. We generated a genetic scoring system with the most significant polymorphisms weighted by the odds ratio of every polymorphism and taken into consideration the strokesubtype. Results. Three polymorphisms, rs1205 (CRP gene), rs1800779, and rs2257073 (NOS3 gene), were associated with cardioembolic stroke (p value <0.05). The score generated was only associated with the cardioembolic stroke subtype (p value: 0.001) and was replicated in an independent cohort (p value: 0.017). The subjects with the highest score presented a cardioembolic stroke in 92.2% of the cases (p value: 0.002). Conclusion. The genetics of inflammatory markers is more closely associated with cardioembolic strokes than with atherothrombotic or lacunar strokes. The genetic risk scoring system could be useful in the prediction and differentiation of ischemic stroke; however, it might be specific to particularischemic stroke subtypes.

I CURSO DE FORMACIÓN Y ACTUALIZACIÓN EN GENÉTICA DE LAS ENFERMEDADES COMPLEJAS

SOCIEDAD ESPAÑOLA DE NEUROLOGIA

Societat Catalana de Neurologia

8:30 Acreditación

9:00 Introducción y bienvenida

9:30 BASES GENÉTICA HUMANA
Modera: Kelly Rabionet. Tòfol Vives-Bauzà

Bases Biológicas de la Genética. *Tòfol Vives-Bauzà, Investigador Principal, Research Unit, Son Espases University Hospital, IdISPa, Palma de Mallorca.*

Genética Mendeliana y Enfermedades Neurológicas. *Raquel Rabionet, Genomics and Disease group, Centro de regulación genómica, Barcelona.*

10:30 ESTUDIOS DE ASOCIACIÓN DE GENOTIPADO MASIVO
Modera: Jordi Jiménez-Conde. Caty Carrera

Epidemiología genética. *Roberto Elosúa, Grup d'Epidemiologia i Genètica Cardiovascular, IMIM-Hospital del Mar, Barcelona.*

Claros y oscuros de la era GWAs. *Jordi Jiménez-Conde, Coordinator Neurovascular Genetics, Department of Neurology, Neurovascular Research Group, IMIM-Hospital del Mar, Barcelona.*

11:45 EPIGENÉTICA Y EXPRESIÓN GÉNICA
Modera: Carolina Soriano. Tòfol Vives-Bauzà

Epigenética, más allá de la genética. *Carolina Soriano, Department of Neurology, Neurovascular Research Group, IMIM-Hospital del Mar, Barcelona.*

Estudios de expresión génica y su utilidad en la práctica clínica. *Tòfol Vives-Bauzà, Investigador Principal, Research Unit, Son Espases University Hospital, IdISPa, Palma de Mallorca.*

12:45 APLICABILIDAD Y FUTURO
Modera: Israel Fernández, Jerzy Krupinski

Farmacogenética. ¿Es aplicable o es ciencia ficción? *Israel Fernández. Investigador Principal Laboratorio Farmacogenómica y Genética Neurovascular. Fundació Mutua Terrassa.*

Biomarcadores. ¿Cómo, cuándo y por qué? *Joan Montaner. Investigador Principal Laboratorio de Investigación Neurovascular. Hospital Vall d'Hebron, Barcelona.*

Barcelona, 20 de octubre

http://info262230.wix.com/i-curso-genestroke

Boehringer Ingelheim

PRELIMINARY PROGRAMME

Thursday 22 October

7:30 – 8:15 Registration

8:15 – 8:30 Introduction and welcome
Chair: **Israel Fernández** *(Barcelona, Spain)*, **Jordi Jiménez** *(Barcelona, Spain)*

8:30 – 9:15 Outcome Panel
Chair: **Arne Lindgren** *(Lund, Sweden)*

Arne Lindgren *(Lund, Sweden)*. Update on the GISCOME project
Israel Fernández *(Barcelona, Spain)*. Update Acute endophenotypes group
Michèle M. Sale *(Charlottesville, USA)* Elevated von Willebrand Factor (vWF) levels and genetic determinants of vWF levels are associated with recurrent stroke risk in the Vitamin Intervention for Stroke Prevention (VISP) trial

9:15 - 10:00 CHARGE session
Chair: **Stéphanie Debette** *(Bordeaux, France)*

Ganesh Chauhan *(Bordeaux, France)* / **Stéphanie Debette** *(Bordeaux, France)*. Vascular genetic risk score and risk of dementia / dementia-endophenotypes
Ganesh Chauhan *(Bordeaux, France)* Genetic risk score of vascular risk factors and vascular comorbidities in association with MRI defined brain infarcts
Myriam Fornage *(Houston, USA)* / **Stéphanie Debette** *(Bordeaux, France)* Update and plans of WES projects on MRI-markers of cerebrovascular disease

ISGC

Barcelona, 22-23 de octubre

http://info262230.wix.com/stroke-barcelona#!scientific-program/c10g1

CONGRESOS Y REUNIONES DE INTERÉS 2015-2016

American Society of Human Genetics (ASHG), October 6-10, 2015. Baltimore, USA.

Society for Neuroscience (SFN) Annual Meeting. October 17-21, 2015. Chicago, Illinois.

XXII World Congress of Neurology, October 31- November 5, 2015. Santiago, Chile.

LXVII Reunión Anual de la Sociedad Española de Neurología, Noviembre 17-21, 2015. Valencia.

International Stroke Conference, February 17-19, 2016. Los Angeles, California.

25 European Stroke Conference, April 13-15, 2016. Venice, Italy.

American Academy of Neurology Annual Meeting (AAN), April 15-21, 2016. Vancouver, Canada.

European Stroke Organisation Conference, May 10-12, 2016. Barcelona, Spain.

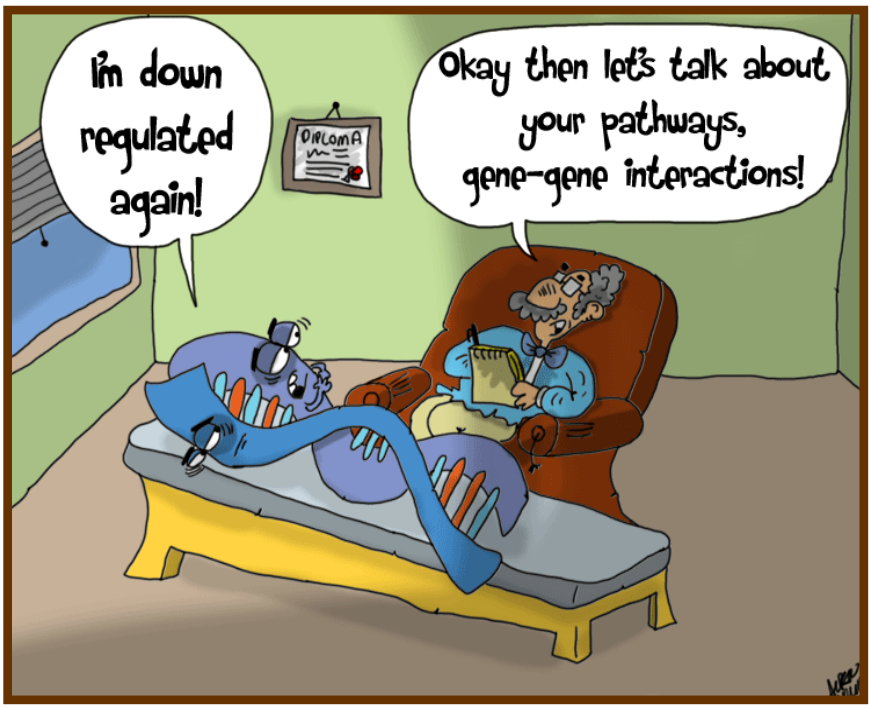
The European Human Genetics Conference, May 21-24, 2016. Barcelona, Spain.

10th FENS Forum of Neuroscience, July 2-6, 2016. Copenhagen, Denmark.

Canadian Stroke Congress, September 14-17, 2016. Québec City, Québec.

10th World Stroke Congress, October 26-29, 2016. Hyderabad, India.

GE, GE, GE...



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

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