

**PhD Position: Program INPhINIT Fundació La Caixa**

**“EPIGENESIS project: EPIgenetic and GENETic study combined with integromics and functional analysis to find genes associated with neurological deterioration after ISchemic stroke”**

**(Dr. Israel Fernández Cadenas)**

**CENTRE: IIB SANT PAU - Fundació Institut de Recerca de l’Hospital de la Santa Creu i Sant Pau**

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**CENTRE DESCRIPTION:** The Research Institute of the Hospital de la Santa Creu i Sant Pau (HSCSP-IR) was created on 4 June 1992 as a private scientific foundation. Its mission is to promote basic, clinical, epidemiological and healthcare research in the health science and biomedical fields, with the ultimate aim of improving the health of the population. On 10 December 2003, the Autonomous Government of Catalonia approved affiliation of the HSCSP-IR as a University Research Institute attached to the Autonomous University of Barcelona (UAB).

The HSCSP-IR has as its mission to improve the health and quality of life of the population through the production and dissemination of scientific knowledge, the training of researchers to an international standard, innovation in health and the incorporation of medical advances in clinical practice and in healthcare policies.

The HSCSP-IR is currently one of the most active research centres in Catalonia, especially in relation to translational research and the application of new discoveries to clinical practice. Since 2011 it has been part of the Catalan System of Research Centres (CERCA).

On 17 May 2009, the HSCSP-IR and nine other organizations created the Sant Pau Biomedical Research Institute (IIB Sant Pau), with the aim of strengthening collaborative translational research and bridging the gap between basic research and clinical practice so as to ultimately improve patient care.

**AREA OF KNOWLEDGE:** Life Sciences Panel

**GROUP OF DISCIPLINES:** Human Biology, Microbiology, Molecular Biology, Genetics, Cell Biology, Genomics and Proteomics, Biochemistry

**GROUP LEADER:** Dr. Israel Fernández Cadenas / [israelcadenas@yahoo.es](mailto:israelcadenas@yahoo.es)

## RESEARCH PROJECT/RESEARCH GROUP:

The web of the Spanish stroke genetics consortium, we are the coordinators of this consortium and the webmaster of the website. Here is possible to find a description of the project and a brief description of the group

[www.genestroke.com](http://www.genestroke.com)

## POSITION DESCRIPTION

-Research Project / Research Group Description:

Background.

Stroke is the second cause of death and the first cause of disability in adults. Currently there are not neuroprotective drugs to improve the neurological deterioration after a stroke.

Our objective is to find new drug targets and improve neurological deterioration after stroke.

Methods.

PHASE-1: We will analyze strokes with neurological outcome data, measured using NIHSS score. We will perform an Epigenome-wide Association Study (EWAS) to analyze the methylation pattern of 850,000 CpG sites using the EPIC-Infinium BeadChip in 1.000 strokes. We will perform a Genome-Wide Association Study (GWAS) in 4,000 strokes using a Human-Exon BeadChip to detect more than 3,000,000 polymorphisms.

PHASE-2: Replication of the significant results (EWAS:  $pvalue < 10^{-7}$ ; GWAS:  $pvalue < 10^{-8}$ ) in a new cohort of patients ( $n=2,000$ ). We will perform integromics analysis with mixOmics platform and pathway analysis.

PHASE-3: We will use the GTEX platform to determine the genes altered due to the significant CpG sites or polymorphisms from Phase-2. We will determine the association with the size of the brain infarct (animal models) and the response to ischemia (in vitro models).

Finally, the interesting genes from Phase-2 and Phase-3 and the key proteins in the integromics and pathway analysis, will be included in the Anaxomics platform to find currently used drugs that could modulate those risk factor genes.

### Group description.

The group is composed by seven members and takes part in four international genetic consortiums (ISGC, MEGASTROKE, CADISP and ICPC) coordinating the Spanish stroke genetics consortium (Genestroke).

Our experience is reflected in the publication of more than 90 articles including Nature Genetics, Lancet Neurology or Circulation research. We are a young and motivated group that works hard but at the same time we try to have fun, we will be glad to wellcome a new member if you select our group

**-Job position description:**

The candidate that would work in the EPIGENESIS project will be the responsible of the project. The candidate would do the genetics and epigenetics analysis and in addition the candidate will work with in vitro and animal models of stroke, as a consequence the candidate will acquire strong skills in bioinformatics, genetics and epigenetics, but also will acquire skills in molecular biology. The objective of our project is to find drug targets and/or new treatments to improve neurological deterioration after stroke. The project has been funded by several grants (Marató TV3, Carlos III Institute and NIH) and the samples has been already recruited we need to start with the genetic and epigenetic analysis.

THE TASKS OF THE CANDIDATE:

**PHASE-1.** Discovery EWAs and GWAs.

1-The candidate will learn how to do analysis of EWAs, GWAs, integromics and functional studies. The members of the group (Natalia Cullell, Caty Carrera and Nuria Torres) will teach the candidate.

2- Assistance to Genestroke bioinformatic courses and King's college Epigenetics course.

3-Analysis of EWAS (n=1.000) and GWAS (n=4.000). SNPtest, IMPUTE, HRC, R, Bioconductor packages, Methyumi will be used for the analysis.

**PHASE-2:** Replication of epigenetics and genetics analyses. Integromics

4-Replication of the top CpG sites and SNPs in a new cohort of 2.000 patients (Sequenom IPLEX or pyrosequencing).

5-Integromics and pathway analysis. Analysis using Mixomics, Ingenuity Pathways, Panther and David platforms

**PHASE-3:** Functional studies and treatment.

6- GTEX platform and eQTL, pQTL analysis.

7-Functional studies in animal models and in vitro models.

8-Transcriptomic and proteomic experiments in brain necrotic samples of ischemic stroke patients (n=6).

9-Drug repurposing analysis. To find commercial drugs currently used in the clinical practice, which can modulate the genes associated with neurological outcome.

10-Redaction of the manuscripts.

11-Assistance to the European Stroke Congress and the ISGC Workshop

#### **OTHER RELEVANT WEBSITES:**

Is a specific website focus on a rare genetic disease that causes stroke episodes. In this web is possible to find a description of the group and the activities performed with this rare disease. Is a webpage for researchers and for CADASIL patients.[www.cadasil.com](http://www.cadasil.com)

Website from the International Stroke Genetics Consortium. The group is member of this consortium. Next year the PI of the group will be member of the steering committee of the ISGC, he will be the only Spaniard in this committee. <https://strokegenetics.org/>

