Isabel Salas

Laboratory for the Research of Neurodegenerative Diseases
VIB Center for the Biology of Disease
Center of Human Genetics
University of Leuven (K.U.Leuven)

BSc Biomedical Science, Universidad Autonoma of Madrid, 2012
MSc Biomedical Science, Universidad Autonoma of Madrid, 2013

Current Position

PhD student at Laboratory for the Research of Neurodegenerative Diseases
VIB Center for the Biology of Disease

E-mail: isabel.salas@cme.vib-kuleuven.be
Phone: +32 1 637 91 06

Current Project Members

Post-doctoral scientist: Francesc Guix

Lab technician: Jarl Bastianen

PI: Bart de Strooper, Carlos Dotti.

Keywords
Late onset Alzheimer's disease (LOAD) - risk factors - metabolic syndrome - ApoJ/CLU.

Science

Alzheimer's disease (AD) is the most common cause of dementia and is characterized by memory loss and impaired cognition. Neuronal dysfunction in AD is related to extracellular aggregation of amyloid-beta peptides, and intracellular neurofibrillary tangles composed of aggregations of hyperphosphorylated Tau. The etiology of most cases of AD is unknown and they are termed sporadic Azheimer disease, or late-onset AD (LOAD). Very little is known about the definitive triggering factors of the disease, although the combination of a genetically predisposed background and environmental risk factors are thought to determine the occurrence of LOAD.

Metabolic syndrome is a strong risk factor for LOAD. Type II Diabetes *mellitus* (insulin resistance) is one of the diseases in metabolic syndrome patients which is thought to be a major determinant of increased vulnerability to LOAD. However, metabolic syndrome is not *per se* sufficient to induce LOAD. The second, and perhaps more relevant, risk factor for LOAD is genetic predisposition. Pathway analysis derived from recent genome wide associated studies (GWAS), identified a number of single nucleotide polymorphisms (SNPs) in a number of genes, of which those involved in cholesterol metabolism and inflammation are highly represented. One of the LOAD risk genes with a putative role in both types of pathway, already identified in early familial association studies and confirmed in the recent GWAS studies, is ApoJ/Clusterin (CLU). Several of the SNPs for ApoJ/Clu identified in the GWAS maps have been associated with changes in expression, which can be relevant for a disease like LOAD. In fact, a series of in vitro and in vivo studies show that ApoJ/Clu is a protective molecule and consequently a genetic defect in expression could predispose to a low protection state. Nevertheless, as is the case for environmental insults, the existence of SNPs is not determing disease, which suggests

that, even with a strong genetic risk factor like mutations in ApoJ/CLU, environmental distress might be needed to determine LOAD.

In this project we will analyze the structural, biochemical and functional consequences of metabolic stress on a genetic background that could predispose to LOAD. ApoJ/Clu heterozygous mice will be our model for genetic predisposition to LOAD. Metabolic stress through high fat diet will be our model of metabolic syndrome.

Recent Research Projects

Master's thesis at the Centre of Molecular Biology Severo-Ochoa (CBMSO).
Period: 01.10.2012 - 31.08.2013
Tittle: "The role of membrane cholesterol loss in synaptic plasticity".
Role: Master student

Recent Fellowships

2012-2013: "Ayudas para el inicio de estudios en programas de Posgrado" from the Universidad Autónoma de Madrid.
2011-2012: Beca de Colaboración of the Ministry of Education in Madrid for the research during the final year project.
2011: Summer Research Project with Christoph Baumann, University of York.
2010-2011: Universidad Autónoma de Madrid, Erasmus-Mundus for 9 months