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## AYUDAS RAMÓN Y CAJAL CONVOCATORIA 2020

### Turno de acceso general

**Nombre:** LOPEZ HERNANDEZ, TANIA  
**Referencia:** RYC2020-030096-I  
**Área Temática:** **Biomedicina**  
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#### Título:

Protein membrane trafficking in the regulation of ion homeostasis in health and disease

#### Resumen de la Memoria:

Who I am Working at the interface between cell biology and disease mechanisms

My primary research is to study how ion homeostasis in the endo-lysosomal system modulates protein turnover in physiological but also pathological conditions, such as neurological diseases, with an especial focus in the bidirectional communication between neurons and glial cells.

During my PhD at the University of Barcelona (granted with a FPI Fellowship), I shed light in the pathophysiology of a very rare leukodystrophy by understanding the molecular determinants involved in the disease. On a cellular and functional level I managed to disentangle that defective protein trafficking and altered ion transport were responsible for explaining the accumulation of water in the brain and the subsequent spongiform degeneration of the myelin. My scientific performance during this time is reflected by the award of the Extraordinary doctor's degree prize given by the University of Barcelona.

Then, I moved to the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP), in Berlin (Germany), where I was granted with a Postdoctoral Research Fellowship. Here I broadened my knowledge in basic cell biology by focusing on the study of the molecular and cellular mechanisms of endocytosis, and especially how dysregulation of the endo-lysosomal system can impact on brain function, leading to neurological disorders, ranging from epilepsy to lysosomal diseases. In addition I have established important collaborations to in-depth understand the cargo sorting mechanisms to form new and release-competent synaptic vesicles, what has significantly boosted my expertise in synapse biology.

I have also established my own research lines in the lab focused on i) the study of the close crosstalk between glial cells and neurons to unravel non-cell autonomous mechanisms of neurodegeneration, and ii) the regulation of ion fluxes across the endo-lysosomal membranes as a key to improve our knowledge about endosomal/lysosomal function and the mechanisms underlying both protein degradation and neurodegeneration. I really believe that exploring these mechanistic rules of biology will shed light to understand diseases, which will have medical implications.

In summary, after 13 years of scientific career I have published 19 scientific articles (11 as first author and 3 as corresponding author); I have supervised several bachelor and master students as well as co-directed one Master thesis and I have established an active network of collaborators that has allowed me to establish new projects in different fields which support my enthusiasm about advancing in my scientific career.

Altogether, I trust that my broad methodological portfolio and my conceptual and scientific achievements, position me optimally as a candidate for the Ramón y Cajal Program to establish and lead a future research group in Spain in order to make ground-breaking contributions in the field of cell biology and pathobiology.

#### Resumen del Currículum Vitae:

My primary research interest is to unravel molecular mechanism underlying human diseases, with especial focus in the functional relationship between glia and neurons.

During my scientific career I have combined molecular, biochemistry and cell biology approaches to study fundamental processes for brain physiology to disentangle key mechanisms subjacent to several neurological disorders such as a rare leukodystrophy called megalencephalic leukoencephalopathy with subcortical cysts (MLC), a group of heterogeneous disorders encompassing the developmental and epileptic encephalopathies as well as the molecular mechanisms underlying lysosomal diseases.

During my PhD at the University of Barcelona in the laboratory of Prof. Raúl Estévez, I published twelve research articles (six as first author). My studies shed light on the pathogenesis of MLC by discovering not only the second gene involved in the disease but also the molecular and cellular impact of the MLC-related mutations. My scientific performance during this time was awarded with the Extraordinary doctor's degree prize given by the University of Barcelona.

Then, I moved to the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP), in Berlin (Germany), where I was granted with a Postdoctoral Research Fellowship from the Leibniz DAAD Research Fellowship programme. During my postdoctoral period with Prof. Volker Haucke, I have substantially expanded my conceptual and methodology portfolio on the molecular and cellular mechanisms of endocytosis, especially in its role in normal brain function and disease. Taking together my knowledge in pathological mechanisms and



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endocytosis, I successfully elucidated a novel link between dysfunction of endocytosis and epileptic encephalopathies that has been published as first author research article in a prominent journal. In parallel, I have established an important collaboration with leaders in the field of endocytosis to in-depth understand the cargo sorting mechanisms to form new, release-competent synaptic vesicles to sustain proper neurotransmission, what has significantly boosted my expertise in synapse biology.

In addition, I have established my own research line in the lab focused on the study of the endocytic regulation of ion homeostasis to control lysosome biogenesis and function which will further shed light on the comprehension of pathologies caused by lysosomal dysfunction. These findings have been recently published in a research article as a first- and corresponding-author in a prestigious top-rated journal. Furthermore, by combining my expertise in astrocyte physiology and endocytosis I have focused my attention in better understanding the close crosstalk between glial cells and neurons, highlighting how glial cells fine-tune the glutamatergic system to control synaptic transmission, being of especial relevance under excitotoxicity.

In summary, after 13 years of scientific career I have published 16 scientific articles and 3 reviews; I have supervised several bachelor and master students as well as co-directed one Master thesis and I have established an active network of collaborators that has allowed me to stablish new projects in different fields which support my enthusiasm about advancing in my scientific career.

I would really believe that the Ramón y Cajal program is the best qualified opportunity for the next stage of my academic career in order to confirm my leadership role and establish my ow