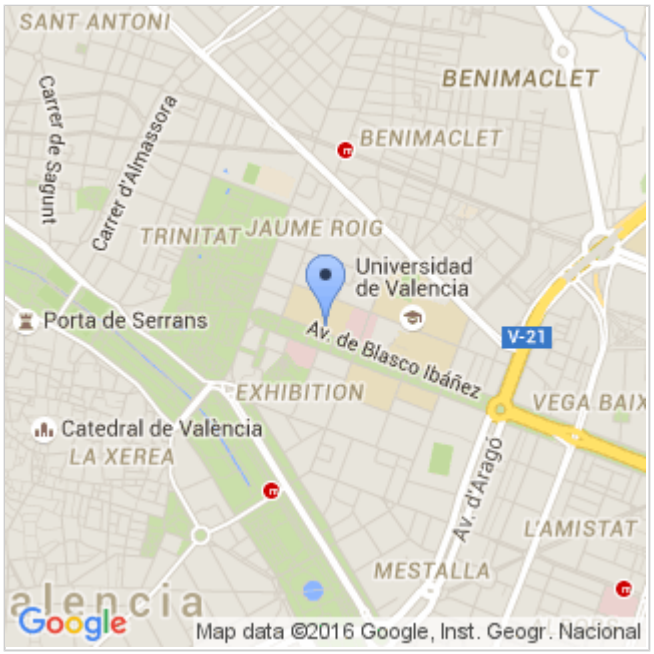
Expression of Interest



Contact Person/Scientist in Charge

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Centro de Investigación Biomédica en Red (CIBER)

Department / Institute / Centre

- **Name:** Department of Phisiology/Faculty of Medicine and Odontology/University of Valencia/CIBERER
- **Address:** Av. Blasco Ibáñez, 15. 46010 Valencia
- **Province:** Valencia

Research Area

- Life Sciences (LIF)

Brief description of the institution:

The Centro de Investigación Biomédica en Red (CIBER) is a Public Research Consortium created in 2006 under the leadership of the Instituto de Salud Carlos III (ISCIII, the main Public Research Entity responsible of funding, managing and carrying out biomedical research in Spain), to promote research excellence and build a critical mass of researchers in the field of Biomedicine and Health Sciences. Organized in 8 research areas including Bioengineering, Biomaterials and Nanomedicine (CIBERBBN), Mental Health (CIBERSAM), Hepatic Diseases (CIBEREHD), Diabetes and Metabolic Diseases (CIBERDEM), Rare Diseases (CIBERER), Respiratory Diseases (CIBERES), Public Health and Epidemiology (CIBERESP) and, Obesity and Metabolic Diseases (CIBEROBN), CIBER is the largest Research Network in Spain.
CIBER counts with more than 830 dedicated employees and 4,000 associated researchers integrated in 399 leading-edge research groups. Thanks to its network structure, CIBER is capable of bringing together more than 92 different associated institutions including Hospitals, Research Centers, Technology Centers, Private Institutions and Universities selected to join CIBER consortium on the basis of their excellence.

Brief description of the Centre/Research Group (including URL if applicable):

Dr. González-Cabo belongs to the Center for Biomedical Network Research on Rare diseases (CIBERER) a research center from the Spanish National Institute of Health ISCIII, the Department of Physiology at the School of Medicine and Dentistry (University of Valencia, and the research institute of the Valencia Clinical hospital (INCLIVA, Spain). Dr. González-Cabo's group is a junior research group. The research programme is focused on understanding the cell mechanisms of axonal degeneration by studying the molecular mechanism that causes axonal neurophaties, paying attention in Friedreich ataxia. The development of new therapies, mainly pharmacological is our ultimate goal.The present aims are:

- Confirm biomarkers associated with frataxin deficiency in Friedreich ataxia samples (serum and fibroblast) which may useful for clinical trials.

- Proof-of-concept that ablating the GAA triplet expansion of cells from Fridreich ataxia patients by means of RNA-guided nucleases (CRISPR/Cas9) is feasible.

- Investigate the role of mitochondrial-associated membranes (MAMs) in celular pathophysiology of axonal neuropathy.

Project description:

Our goal is to investigate the role of mitochondrial-associated membranes (MAMs) in celular pathophysiology of axonal neuropathy, initially working in Friedreich ataxia (FRDA) disease but as part of a broader programme to know the relevance of axonal mitocondria and biology and its interaction with endoplasmic reticulum (ER) at MAM domain in neurological disease. We postulate that MAMs play a role in the pathogenesis of neurodegeneration and such a functional defect may involve cell domains and mechanisms that relate pathways in different neurodegenerative disorders. To address this hypothesis we propose to investigate MAM biology and consequences on axonal biology in neurogenetic disorders that affect mitochondria and have different axonal targets in peripheral nerves, central sensory or pyramidal tracts or involving axons from CNS structures. We work with cellular and mouse models of GDAP1-related Charcot-Marie-Tooth involving motor and sensory peripheral nerves, Friedreich ataxia as sensory axonal neuropathy that also affects posterior columns in the spinal cord, hereditary spastic paraglegia type 7 to modeled large pyramidal tracts from cortical neurons, and Huntington's disease that offers the opportunity to compare axonal defects in the striatum. The general aim is to determine the role of MAMs in the cellular pathophysiology in neurodegeneration and its relevance as a therapeutic target domain by focusing the experimental work in 4 specific objectives: (i) to define the mechanisms of MAM defects in axonal biology and neurodegeneration; (ii) to evaluate MAM protein profiles and protein interactions in celular models of neurodegenerative diseases; and (iii) to study drug modulation approaches to improve neurodegeneration by targeting MAM function or integrity.

Applications

- Brief introductory cover letter
- Curriculum Vitae
- Names and contact details of three academic referees

Description of past research activities, technical skills and main accomplishments (up to 2 pages)