

Identification and validation of cerebral KCa3.1/KCa2.3 potassium channels a drug targets for the prevention and treatment of cerebral ischemia associated with diabetes and Alzheimers disease

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Name of Fellow

Institution

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Contact information of fellow

Country

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Identification and validation of cerebral KCa3.1/KCa2.3 potassium channels a drug targets for the prevention and treatment of cerebral ischemia associated with diabetes and Alzheimers disease

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The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

cerebral ischemia | neurodegenerative disorders | Alzheimers disease | diabetes | endothelium | microglia | potassium channel | neuroprotection | animal models | small molecule

Research Abstract

The objectives of the project are to identify and evaluate potassium channels of the KCa3.1/KCa2.X type as novel drug targets for the prevention and treatment of cerebrovascular ischemia and neuroprotection in metabolic disease and neurodegenerative disorders associated with vascular pathologies, as a new pathophysiological concept and treatment strategy.

To reach these aims, the proponent employs genetic models of ion channel deficiency and experimental models of human disease for pharmacological interventions with highly selective small molecule modulators and performs target identification studies on human material. The project will be conducted within the research frame of the Aragonese Institute of Health Sciences and in collaboration with clinical departments of the University Hospital Miguel Servet in Zaragoza, Spain, and the University Hospital Odense, Denmark, and with neuroscientists and pharmacologists at the University of Southern Denmark and the University of California, Davis, United States, for optimal scientific synergy and use of resources.

The 1st and 2nd work packages consist of electrophysiological, molecular biological, and imaging studies using genetic and pharmacological tools for “target identification” in cerebrovasculature from murine and human diabetes mellitus type 2 (DM-2), Alzheimer disease (AD), and Morbus Fabry. The 3rd of work package consists of intervention trials and the testing the efficacy of recently developed small molecule modulators in mice models of DM-2 and AD for “target validation”. The 4th work package consists of epidemiological studies in which we define the genetic variability and polymorphisms in KCa3.1/KCa2.3 genes in Aragon Workers Health Study (AWHS)-cohort and evaluate their potential predictive value for disease.

Our conceptually new approach and the outcome of our study may provide the rationale to develop small molecule modulators of KCa3.1/KCa2.X for the treatment of cerebrovascular and neurological disease.

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