

H2O2-MEDIATED SRC SIGNALING PATHWAYS IN GLUTAMATERGIC SYNAPSES IN ALZHEIMER'S DISEASE MODELS

<https://www.neurodegenerationresearch.eu/survey/h2o2-mediated-src-signaling-pathways-in-glutamatergic-synapses-in-alzheimers-disease-models/>

Name of Fellow

SANDRA ISABEL FREITAS MOTA

Institution

Funder

FCT

Contact information of fellow

Country

Portugal

Title of project/programme

H2O2-MEDIATED SRC SIGNALING PATHWAYS IN GLUTAMATERGIC SYNAPSES IN ALZHEIMER'S DISEASE MODELS

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FCT

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€ 107,640

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01/01/14

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6.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Research Abstract

Oxidative stress has been consistently associated to Alzheimer's disease (AD). Amyloid beta

peptide (A β) generates reactive oxygen species (ROS), which may result from interaction with mitochondria; A β also activates N-methyl-D-aspartate receptors (NMDARs), leading to intracellular Ca²⁺ dyshomeostasis. Importantly, NMDARs are positively regulated by Src Tyrosine-mediated phosphorylation. At the presynaptic terminal, Src may regulate neurotransmitter release. In mitochondria, Src phosphorylates respiratory chain components regulating cell survival. Importantly, Src activation is positively modulated by H₂O₂. Thus, in this project we will evaluate whether A β -induced H₂O₂ production regulates glutamate release and NMDARs through Src activation. We will also determine whether NMDAR activation triggers Src activation through Ca²⁺-induced H₂O₂ formation and the role of mitochondrial ROS in Src signaling, using hippocampal cultures and synaptosomes from 3xTg-AD and wild type (WT) mice, and GluN2B(-/-) hippocampal cultures. H₂O₂-induced activation of Src is expected to play an important role in the regulation of synaptic signaling in AD.

Types:

Fellowships

Member States:

Portugal

Diseases:

Alzheimer's disease & other dementias

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