

ERA-Net NEURON

ERA-Net NEURON Successful Projects, Call of 2008

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ERMCC-NDEG: The activity-driven ER-mitochondria Calcium Cycle (ERMCC) and protein misfolding in neurodegenerative diseases: finding targets for therapy

Project Description




Neurodegenerative diseases like Amyotrophic Lateral sclerosis and Alzheimer's disease occur mostly without identifiable cause, and are as yet incurable. The project aims to develop a new strategy of neuroprotection by moderation of the endoplasmic-reticulum-mitochondria-calcium cycle (ERMCC) which links functional and structural metabolism in neurons and plays a central role in neuronal development and survival. We will identify the key pathways of the ERMCC in models of ALS and Alzheimer's disease which collates different features of neurodegenerative processes into manifest ERMCC dysfunction. In a series of collaborative experiments in neuron-like cell and neuron cultures, and tissues of animal models of neurodegenerative diseases we use patch-clamp, fluorescent and photoluminescent imaging, neurogenetic and neuroproteomic approaches to identify neurotoxic and neuroprotective properties of the ERMCC. A pathogenic imbalance of the ERMCC function will be reported by mitochondrial calcium overload, ER calcium depletion, fluorescent protein misfolding and activation of cell death pathways. In the established neuronal systems we will identify molecular targets for serial testing of neuroprotective ERMCC modulators which can then be carried on to preclinical testing in follow-up studies. Drugs stabilizing ERMCC function may thus provide neuroprotection for a range of neurodegenerative diseases of different causes.



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