Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Deciphering the protein fingerprint of brain mitochondria

Synopsis:

Neurons are morphologically polarized cells and mitochondria have been observed in all neuronal sub-compartments. However, this distribution has been shown to be heterogeneous, with presynaptic and postsynaptic terminals containing more mitochondria than other neuronal domains. Additionally, these neuronal compartment-specific mitochondria appear to have different dynamics and morphological features, raising the question of whether these are functionally similar or actually have specialized functions adapted to the environment where they reside. Therefore, defining the intrinsic properties preferentially used by synaptic mitochondria to maintain their overall health is of particular relevance in the context of neuron function.

Mitochondria homeostasis is a process involving an intimate crosstalk between energy production, quality control and mitophagy. Perturbances of this intricate system are widely speculated to contribute to neurodegeneration. Our work focuses on elucidating these mitochondrial mechanisms crucial for brain function, and how a dysregulation in these processes can be fatal for the mitochondria itself or for the neuron.

To achieve this and in order to decipher the molecular mechanisms that regulate synaptic mitochondrial, this project will build on a previously obtained proteomic dataset from the host laboratory where protein abundance from synaptic mitochondria was directly compared to non-synaptic mitochondria. Bioinformatics analysis revealed several top candidate proteins significantly upregulated in the synaptic pool that are connected to mitochondrial bioenergetics, dynamics and turnover pathways. Therefore, this research project aims to validate these top candidate proteins and to further understand their role within regulating synaptic mitochondria's unique fingerprint. This project will use mouse models and their derived primary neuronal cultures to perform cell biology, imaging, biochemical and bioenergetics approaches.

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Webpage of the group

Remunerated or volunteer training: Volunteer training