Finanziato dall'Unione europea NextGenerationEU | Ministero dell'Università e della Ricerca | Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA | Consiglio Nazionale delle Ricerche

Project title: Nr2f1-mediated regulation of Mitochondrial Function in Neural Development and Disease

Acronym: Nr2f1-MiNDev

Partners:

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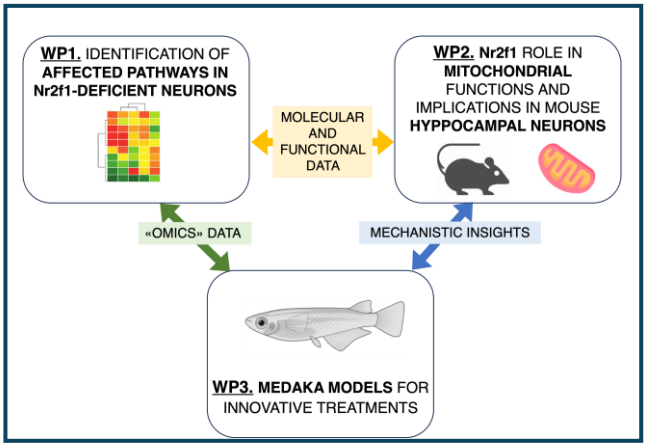

Description:

The transcriptional regulator Nr2f1 is expressed in neural stem/progenitor cells (NSPCs) and neurons of the mouse hippocampus, playing a key role in adult hippocampal neurogenesis. Nr2f1 regulates genes involved in mitochondrial dynamics and function. Nr2f1-deficient hippocampal neurons show reduced mitochondrial mass and increased fragmentation. Mutations in NR2F1 cause Boonstra-Bosch-Schaff optic atrophy syndrome (BBSOAS), characterized by optic atrophy, intellectual disability, and autistic traits, possibly linked to altered mitochondrial function. However, the impact of Nr2f1 deficiency on mitochondrial dynamics and metabolism in NSPCs and neurons remains unclear.

Aims:

To elucidate the role of the Nr2f1-dependent mitochondrial alterations on the physiopathology of neurons this project we will address the following open issues: Which Nr2f1 target genes are required to mediate different aspects of mitochondria function in neurogenesis and neuronal plasticity? Which specific aspects of mitochondria function are perturbed in BBSOAS and is it possible to identify novel therapeutic strategies for BBSOAS? How are the different mitochondria functions connected to neuronal maturation and plasticity?

Expected results:

We will characterize abnormal mitochondrial dynamics in neurons in mouse and will dissect how NR2F1 human mutations are causative of dysfunctional mitochondrial phenotype in neurons. We will identify evolutionarily common mitochondrial genes and pathways regulated by Nr2f1 that will contribute to decipher the pathological and molecular mechanisms underlying the onset and progression of BBSOAS disease in humans.

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