Project title: Dissection of common mechanisms in genetic primary microcephaly

Acronym: MIND (MIcrocephaly Neurodevelopmental Dissection)

Partners:

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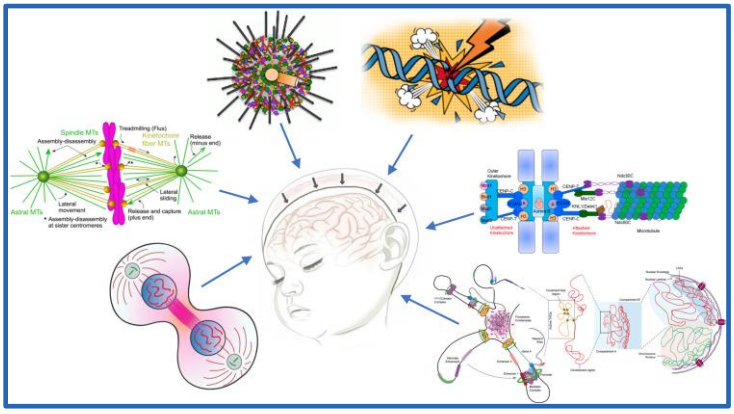

Description:

Primary microcephaly (MCPH) is an invalidating condition characterized by a reduced brain size, resulting from alteration of the balance between proliferation, differentiation and death during brain development. We will explore possible common mechanisms of MCPH, using Drosophila and mammalian mutants as well as in vitro models, including human brain organoids. Our working hypothesis is that, in the developing brain, the proteins encoded by MCPH genes are required for maintaining genome stability, for ensuring a precise temporal order of gene expression to achieve a correct balance in cell fate commitment. We expected to improve mechanistic knowledge, to identify new prognostic markers and to highlight possible therapeutic strategies.

Aims:

We propose 4 aims, whose implementation is expected to improve mechanistic knowledge, to identify new prognostic markers and to highlight possible therapeutic strategies. 1. Assessment of DNA/chromosome integrity maintenance as a common mechanism of MCPH syndromes. 2. Identification of novel candidate MCPH genes. 3. Assessment of MCPH genes in establishing and maintaining proper chromatin conformation. 4. Identification and functional characterization of Asp/Aspm and Dck/CIT interactomes.

Expected results:

By increasing our knowledge of pathogenetic MCPH mechanisms, our project has the potential to improve diagnostic and prognostic accuracy. First, it will provide information about the cellular processes underlying microcephaly. This knowledge will shed light on unknown genetic factors that can modify the penetrance and expressivity of phenotypes. Second, it will contribute to the identification of new MCPH genes, which could help in the interpretation of sequence variants identified in patients.

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