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MEPIcephaly

Metabolic and epigenetic interplay in neural progenitor cells: investigating neurodevelopmental disorders associated with impaired neural progenitor cell expansion

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The size of the brain matters for its functional capability. Having an abnormally small brain, referred to as microcephaly, may lead to mental impairments and motor disabilities. An abnormally small brain may result from insufficient numbers of neurons produced during fetal brain development, often caused by the inadequate expansion of neural progenitor cells. Currently, our knowledge about the mechanistic causes of microcephaly is far from complete, leaving a large proportion of microcephaly patients without a genetic diagnosis. Lack of early diagnosis limits the options for early intervention and counseling of affected families.

We have recently discovered that metabolic regulations are important for the adequate expansion of neural progenitor cells during fetal development. Based on our findings, this project aims to further explore the metabolism of progenitor cells in normal and diseased conditions, seeking to better understand the causal relationship between abnormal neural progenitor cell metabolism and microcephaly. This project will investigate important metabolic pathways and their link with epigenetics – a layer of information on top of our genome that affects which genes are expressed by a given cell type. We will study how the metabolic-epigenetic interplay regulates gene expression during neural progenitor cell expansion. Finally, we aim to identify novel causative metabolic genes of microcephaly. This project will provide new insights into the causes of microcephaly, which is key for the development of improved diagnostic tools, treatment options and preventive care.