RUHR-UNIVERSITÄT BOCHUM

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IGSN - SYMPOSIUM

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Human Brain Development and the Use of Cerebral Organoids to Decipher Cellular and Molecular Mechanisms

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Epigenetic and cellular regulation of cortex expansion and folding

One of the most prominent features of the human brain is the fabulous size of the cerebral cortex and its intricate folding, both of which emerge during development. Over the last few years we have shown that cortex folding depends on high rates of neurogenesis and abundance of a particular type of basal progenitor, basal Radial Glia Cells (bRGCs). bRGCs profusely populate the Outer Subventricular Zone (OSVZ), and modify the organization of the radial fiber scaffold used by migrating neurons, hence driving cortex folding. The formation of the OSVZ along development, and of the highly stereotyped patterns of cortex folding, are linked to spatial-temporal patterns of progenitor cell proliferation, which are defined by a spatial-temporal protomap of gene expression within germinal layers. I will present recent findings from my laboratory revealing novel cellular and genetic mechanisms that regulate cortex expansion and folding. We have uncovered the contribution of epigenetic regulation to the establishment of the cortex folding protomap, modulating the expression levels of key transcription factors that control progenitor cell proliferation and cortex folding. At the single cell level, we have identified an unprecedented diversity of cortical progenitor cell classes in the ferret and human embryonic cortex. These are differentially enriched in gyrus versus sulcus regions and establish parallel cell lineages, not observed in mouse. Neurons born in gyrus versus sulcus are also transcriptomically distinct, especially related to human cortical malformation genes. Our findings show that genetic and epigenetic mechanisms in gyrencephalic species diversify cortical progenitor cell types and implement parallel cell linages, driving the expansion of neurogenesis and patterning cerebral cortex folds.

Host:

ASISA MUCHAMEDIN

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