Title: Molecular mechanisms of neurogenesis and neural stem cell expansion

Abstract

Organ size is regulated by balancing stem cell self-renewal versus the generation of differentiated progeny or transit-amplifying progenitors to enlarge the progeny number. This is of particular relevance in brain development as the evolution of the mammalian brain encompassed a remarkable increase in size of specific brain regions, such as the cerebral cortex. This process encompasses expansion in the tangential (larger brain area) and radial (higher number of neurons per brain area) dimension. However, the mechanisms underlying these key features are still largely unknown. I will discuss the novel DNA associated protein Trnp1, which is highly conserved only in mammals, as a regulator of neural stem cell self-renewal and mammalian cerebral cortex expansion. Its dynamic regulation during brain development together with gain and loss of function experiments in the mouse cerebral cortex in vivo demonstrate that higher Trnp1 levels promote neural stem cell self-renewal and tangential expansion. In contrast, lower levels promote radial expansion with a potent increase of the number of intermediate progenitors and basal radial glial cells leading to folding of the otherwise smooth murine cerebral cortex. Remarkably, TRNP1 expression levels exhibit regional differences in the cerebral cortex of human fetuses anticipating radial or tangential expansion. Thus, the dynamic regulation of Trnp1 is critical to regulate tangential expansion by promoting neural stem cell self-renewal while its reduction results in rapid amplification of transient progenitor lineages causing a fast increase in neuron numbers and their appropriate guiding structures. I will end the presentation by discussing Trnp1 function more globally in neurogenesis and comparing mechanisms of embryonic and adult neurogenesis.

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