CDB SEMINAR

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14:00~15:00 A7F Seminar Room

A Matter of Commitment: TGFβ Signaling in the Regulation of Neural Stem/Progenitor Cells

Summary

Brain traumas caused by various damaging conditions, such as stroke and brain tumors, pose imminent health and social burden to patients and survivors. With the knowledge that mammalian central nervous system has some, albeit very low, regenerative capability, together with recent remarkable developments in the field of stem cell biology, understanding the mechanisms underlying the regulation of neural stem/progenitor cell behaviors is of considerable relevance to brain injury and disease, as well as regenerative medicine.

We are interested in elucidating the mechanisms by which the transforming growth factor-β (TGFβ) super-family (TGFβ/BMP) signaling pathways regulate neural stem/progenitor cells. Our recent preliminary studies using mutant mice have revealed that a key component of the TGFβ/BMP signaling pathways, Smad4, is essential to control proper behaviors of neural stem/progenitor cells in the postnatal brain. Genetic loss of Smad4 function in nascent neural progenitor cells in the subventricular zone (SVZ), one of the major sites of neurogenesis in the adult brain, causes an increase in neural stem cell-like properties, suggestive of reversion of progenitors to a stem-like state. Smad4 conditional mutants also exhibit a marked decrease in neuronal lineage differentiation in the adult brain that, in turn, leads to a deficit in olfactory bulb neurons. In vitro, SVZ-derived cells from the Smad4 mutant brains yield increased growth of neurospheres, associated with elevated self-renewal capacity and resistance to differentiation. These results strongly suggest that Smad4 plays an important role within the nascent neural progenitor cell population during establishment of a committed progenitor state and subsequent neuronal differentiation in the postnatal mouse brain. Current studies are aimed at gaining further insights into molecular mechanisms underlying these processes. A summary of these results will be followed by discussion of our more recent studies to address a possible contribution of TGFβ/BMP signaling pathways to the development of brain tumors.

Host:

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