How do neural stem cells self-renew and generate neurons?
Confusions and unsolved problems

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In mammalian brain development, neuroepithelial cells function as neural stem cells. These cells initially proliferate and then subsequently produce postmitotic neurons and different types of progenitors. In the proliferative and neurogenic phases, neuroepithelial cells become highly elongated, and the nucleus undergoes dynamic cyclical movements. The way in which neural stem cells generate further differentiated cells such as neurons, remains an unresolved fundamental problem in neural development. Neural stem cells have been thought to undergo typical modes of asymmetric divisions to generate neurons; according to one compelling model, vertical divisions parallel to the apicobasal axis represent asymmetric divisions into a neuron and progenitor, while planar divisions within the epithelial plane are symmetric and proliferative. These models have been influential as they are consistent with the asymmetric divisions observed in invertebrate model systems such as Drosophila neuroblasts and C. elegans zygotes. Some studies, however, have argued that the mitotic orientation of neuroepithelial cells is planar and does not change throughout neural development. Regulatory molecules of Notch signaling have also been studied extensively as cell-fate-determinant candidates because of the signal’s importance in maintaining neural stem cells; however, knockout studies of Notch regulators, such as Numb, have produced inconsistent results. Thus, this fundamental issue in neural development has been in a state of confusion.

New views on mammalian neurogenesis are rapidly emerging, as researchers have acquired new cell biological and genetic tools by which the behavior of a single cell in developing brain tissues can be dissected. In this lecture, I view the history of studies on neurogenesis and progenitor diversity, and discuss recent advances and future directions of this field. The lecture will also throw light on related topics of neural stem cells.

1) Konno et al. Neuroepithelial progenitors undergo LGN-dependent planar divisions to maintain self-renewability during mammalian neurogenesis. 