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Development of glial cells
~Regulation of oligodendrocyte development in the forebrain~

Oligodendrocyte precursor cells (OPCs) appear in the late embryonic brain, mature to become oligodendrocytes (OLs) and form myelin in the postnatal brain. Recently, it has been proposed that early-born OPCs derived from the ventral forebrain are eradicated postnatally and that late-born Gsh2- and Emx1-lineage OLs predominate in the cortex of the adult mouse brain. However, the types of intrinsic and extrinsic factors that specify the ability of self-renewing multipotent neural stem cells (NSCs) in the ventricular zone/sub-ventricular zone (VZ/SVZ) of the embryonic brain to generate cortical OL-lineage cells remain unknown. To examine this subject, it is essential to identify the temporally and spatially restricted niche in which OL-producing NSCs are harbored. We clarified that Olig2 is not expressed by self-renewing NSCs but is expressed by more committed cell populations, while Nestin is expressed by both the self-renewing and committed populations. Identification of this difference enabled birth-dating analysis of forebrain OLs. Using an inducible Cre-loxP system to permanently label Nestin- and Olig2-lineage cells, we revealed that cortical OL-lineage cells start differentiating from neural stem cells within a restricted temporal window just prior to E16.5 through P10. We then showed, by means of electroporation of a Cre expression plasmid into the VZ/SVZ of E15.5 reporter mouse brains, that neural precursor cells in the dorsal VZ/SVZ are inhibited by Wnt signaling from contributing to cortical OLs in the adult brain. In contrast, neural precursor cells present in the dorsoventral boundary VZ/SVZ produce a significant amount of OLs in the adult cortex. Our results suggest that neural stem cells at this boundary are uniquely specialized to produce myelin-forming OLs in the cortex.

References

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CV

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