Regulation of radial glial cells in the mouse brain by the Pax6-Sox2-EGFR pathway

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Homozygous null mice for Pax6 exhibit severe abnormality in the cerebral cortex and die immediately after birth. The cellular and molecular mechanisms underlying these phenomena are still largely unknown. In the present study, we examined the consequence of inactivating Pax6 using N-ethyl-N-nitrosourea (ENU) mutagen in the mouse brain. While the population of neural stem cells (NSCs) at E16.5 appeared to be normal as measured by their expression of Sox2, EGF receptor (EGFR) and incorporation of BrdU, their numbers were significantly reduced in the subventricular zone (SVZ) both at age E18.5 and at birth in homozygous Pax6 null mice. This decrease in the NSC population coincides with the switch from predominant neurogenesis, which normally occurs from E12.5 to E18.5, to gliogenesis. Based on the chromatin immuno-precipitation assay, luciferase gene-reporter analysis and western blot, we provide evidence indicating that Pax6 regulates the expression of Sox2, which in turn regulates EGFR expression in NSCs. We also demonstrate that blockage of any one of three factors, Pax6, Sox2 and EGFR *in vitro* leads to a decrease in proliferation of NSCs. We therefore propose that the Pax6-Sox2-EGFR pathway is required for the maintenance of NSCs in the SVZ at the late stage of embryonic development.

Keywords: neuro stem cells, radial glial cells, neurogenesis, Pax6, Sox2, EGFR

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