It is now relatively well accepted that adult brains possess regenerative properties to some extent. There are several kinds of progenitor (or stem) cells in adult brain, and they are thought to play important roles in endogenous repair mechanisms after stroke. However, the precise mechanisms as to how residual progenitor cells mature in adult brain still remain unknown. Three recent articles describe novel roles of those immature cells in neurogenesis under aged conditions, oligodendrogenesis after demyelination, and neurogenesis/angiogenesis after ischemic stroke in adult brain.

**Kang and Hebert** (FGF signaling is necessary for neurogenesis in young mice and sufficient to reverse its decline in old mice. *J Neurosci*. 2015;35:10217–10223. doi: 10.1523/JNEUROSCI.1469-15.2015.) examined the signaling pathway of fibroblast growth factors (FGFs) for adult hippocampal neurogenesis in vivo. This study used Nestin-CreER mice to target adult neural stem and progenitor cells (NSPCs). For loss of function experiments, all 3 FGF receptor genes (FGfr1, FGfr2, and FGfr3) were conditionally deleted in nestin-positive cells by injecting tamoxifen to Nestin-CreER;FGfr1flox/flox;FGfr2flox/flox;FGfr3flox/-. deleted in nestin-positive cells by injecting tamoxifen to Nestin-CreER;FGfr1flox/flox;FGfr2flox/flox;FGfr3flox/-. transgenic mice. The FGF receptor–deficient mutants (2–3 months old) exhibited low numbers of immature neurons and newly generated mature neurons in the subgranular zone in hippocampus. On the contrary, mice with constitutively active FGF receptor (2–3 months old) showed larger numbers of immature and newly generated mature neurons. Adult neurogenesis in rodent hippocampus declines by age. However, aged mutants with constitutively active FGF receptor (12–14 months old) showed 3× higher number of neuroblasts in hippocampus than age-matched controls. These results show that FGF signaling is a critical regulator of hippocampal neurogenesis in adult brain and that enhancing FGF signaling in NSPCs can be used to reverse age-related declined in adult neurogenesis.

Besides neurons, NSPCs can differentiate into oligodendrocytes under some conditions. **Braun et al** (Programming hippocampal neural stem/progenitor cells into oligodendrocytes enhances remyelination in the adult brain after injury. *Cell Rep*. 2015;11:1679–1685. doi: 10.1016/j.celrep.2015.05.024.) evaluated the remyelination capacity of hippocampal NSPCs in a mouse model of demyelinating disease. This study focused on the roles of transcription factor Ascl1 as it is known to convert hippocampal NSPCs into oligodendrocytes in vivo. In fact, when the authors injected Ascl1-expressing retrovirus directly into the dentate gyrus of adult mice, the NSPC differentiation into oligodendrocytes was significantly enhanced. Then this study tested whether Ascl1-induced–directed differentiation of NSPCs into oligodendrocytes would enhance remyelination in the hippocampus in a mouse model of demyelination. For this purpose, the authors developed a novel mouse model of focal ablation of oligodendrocyte/myelin by injecting diphtheria toxin into the dentate gyrus of adult *MOG-Cre:diphtheria-toxin-receptor* transgenic mice. After demyelination in this model, the majority of hippocampal NSPCs still differentiated into neurons, suggesting that demyelination was not sufficient to change the fate of NSPCs. However, when Ascl1 was overexpressed in hippocampal NSPCs, they differentiated into mature oligodendrocytes to enhance remyelination after injury. These findings propose a novel therapeutic approach that harnesses endogenous NSPCs for remyelination by reprogramming the cell fate.

Cellular reprogramming may occur in other cell types than NSPCs. **Nakagomi et al** (Brain vascular pericytes following ischemia have multipotent stem cell activity to differentiate into neural and vascular lineage cells. *Stem Cells*. 2015;33:1962–1974. doi: 10.1002/stem.1977.) demonstrated that brain vascular pericytes acquired multipotential stem cell activity after ischemic stress. The authors extracted pericytes from mouse brains with ischemic damage (eg, distal middle cerebral artery occlusion) and maintained them in in vitro cell culture conditions. These pericytes from ischemic region developed stemness in vitro over time and differentiated into neural and vascular lineage cells by modulating cell culture conditions. This study also confirmed the reprogramming in pericytes after ischemic stress in human brain pericytes cultured under oxygen-glucose deprivation (in vitro ischemia model). These data suggest that pericytes may contribute to neurogenesis and angiogenesis at the site of ischemic brain injury.

These 3 studies demonstrate novel mechanisms as to how residual progenitor (or stem) cells differentiate in adult brains under aged or pathological conditions. Further investigations into signaling pathways for the differentiation/maturation processes would be important to pursue the therapeutic approach of brain repair after stroke.
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