Progressive changes in hippocampal stem cell properties ensure lifelong neurogenesis

Lachlan Harris, Piero Rigo, Francois Guillemot

The Francis Crick Institute, 1 Midland Road, London NW1 1AT, UK

Neuronal production occurs during embryonic development and ceases around birth in most regions of the mammalian brain, but it continues throughout life in two brain regions, the hippocampus and the subventricular zone. In the hippocampus, the transition from developmental to adult neurogenesis occurs in juvenile mice and involves a rapid reduction of the neural stem cell pool, reaching small but stable stem cell numbers during adulthood. We found that the transition from developmental to adult neurogenesis involves multiple coordinated changes in stem cell behaviour. In particular, while active neural stem cells differentiate rapidly in juveniles, they increasingly return to a state of shallow quiescence, and undergo additional self-renewing divisions in adults. These changes in stem cell behaviour result from a progressive reduction in expression of the pro-activation protein ASCL1 due to increased post-translational degradation. These findings help reconcile current contradictory models of hippocampal stem cell dynamics and may contribute to the different timings of transition from developmental to adult neurogenesis and different rates of decline of hippocampal neurogenesis in mammalian species including humans.