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NR2F1 MODULATES ACTIVATION DYNAMICS AND MAINTENANCE OF THE ADULT MURINE HIPPOCAMPAL NEURAL STEM CELL POOL

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Neural stem cells (NSCs) in the adult mammalian brain generate new neurons supporting critical sensory and cognitive functions. In rodents, these NSCs are located in the subventricular zone (SVZ) and the subgranular zone (SGZ) of the hippocampus. Most adult NSCs exist in a reversible quiescent state, capable of exiting quiescence to enter an activated, proliferative phase. This transition is tightly regulated by a combination of extrinsic factors and cell-intrinsic mechanisms to ensure continuous neurogenesis and prevent premature stem cell exhaustion.

In this study, we investigate the role of the transcriptional regulator NR2F1 (COUP-TFI) in modulating adult NSC behavior. We have previously demonstrated that Nr2f1 expression is maintained in adult neurogenic zones and that its conditional loss impairs differentiation and neuronal lineage progression in the SGZ1, as well as functional integration and survival of adult-born hippocampal neurons in association with mitochondrial alterations2.

Using Glast and Ascl1-lineage mouse genetics, we show that Nr2f1-deficient NSCs exhibit reduced activation, resulting in slower depletion of the NSC pool over time in vivo. Accordingly, in vivo clonal analyses confirmed that Nr2f1 loss leads to altered expansion of NSC-derived clones, further substantiating its role in maintaining the equilibrium of the NSC pool. Ongoing analyses aim to identify direct NR2F1-dependent transcriptional programs, revealing candidate targets that play a pivotal role in regulating NSC behavior and fate in the adult SGZ neurogenic niche.

Our findings position NR2F1 as a key regulator of NSC dynamics, ensuring the long-term maintenance of the hippocampal neurogenic potential.

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References

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