

# **Notch1 is Required for Adult Neural Stem Cell Maintenance and Continuous Neurogenesis**

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**Notch1 is a protein found on the surface** of most cell types in the dentate gyrus of the hippocampus, including adult **neural stem cells (NSCs)** also known as Type-1 cells. Through a process termed lateral inhibition, neighboring ligand-expressing neural progenitor cells (Type-2 cells) activate Notch1 in NSCs leading to release of the **intracellular domain of Notch1 (NICD)** and subsequent expression of genes that inhibit differentiation and promote the stem cell state and quiescence. The localization of Notch1 makes it uniquely situated to regulate the activity of NSCs depending on extrinsic cues from the local neurogenic niche, which is dynamically regulated by many stimuli, including chronic stress, exercise and antidepressants. Notch signaling is very rapid and transient, with no second messengers, ensuring adaptive responses and functional flexibility. While Notch1 has been shown to regulate cell proliferation, cell fate, neuronal maturation and stem-cell maintenance in the **subgranular zone (SGZ)** of the adult dentate gyrus, similar to its more established role in embryonic neurogenesis, **the long-term effects of altered Notch signaling in neuronally-restricted nestin+ NSCs and their progeny on continuous neurogenesis is unknown.** To address this question, we created nestin-creERT2/R26R-YFP/floxed Notch1 (Notch1 iKO) and nestin-creERT2/R26R-YFP/floxed stop Notch1 intracellular domain (NICD) triple-transgenic mice, which allow us to inducibly and irreversibly ablate or activate Notch1, respectively, in the NSCs and track the recombined population of cells and their progeny via yellow fluorescent protein (YFP).