

Just Another Notch on the Clock during Neurogenesis in the V-SVZ

The Notch intracellular domain (NICD) is more active in the type B1 cell than in the other cells of the V-SVZ niche, and it functions with other transcription factors to repress gene expression associated with both proliferation and differentiation, thereby promoting quiescence and maintaining the number of neural stem cells (NSCs) (Ables et al. 2011; Pierfelice et al. 2011; Giachino and Taylor 2014; Urbán and Guillemot 2014). Notch1 is actually expressed in all major cell types in the V-SVZ niche (B cells, progenitor [transit-amplifying] cells, and type A migrating neuroblasts; Basak et al. 2012), which raises the question, how can differentiation begin in the presence of Notch? An important part of the Notch regulatory mechanism of neurogenesis lies in the downstream transcriptional targets, namely the Hairy and Enhancer of Split (Hes)-related genes. Hes genes primarily function to repress proneural gene expression. As will be seen in Chapter 17, Notch-Delta signaling and its Hes targets can show temporally oscillating patterns of gene expression established through negative feedback loops in which upregulation of Hes by Notch leads to Hes-mediated repression of Notch. A growing hypothesis is that constant activity of Notch signaling promotes quiescence, whereas the oscillating expression of Hes genes—and, consequently, the anti-oscillation periods of proneural genes (such as *Ascl1/Mash1*)—supports proliferative states until proneural gene expression is sustained and the cell differentiates (see Figure 5.12; Imayoshi et al. 2013).

Literature Cited

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