

1: [Nature](#). 2007 Sep 20;449(7160):351-5. Epub 2007 Aug 26.

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## **Differential Notch signalling distinguishes neural stem cells from intermediate progenitors.**

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During brain development, neurons and glia are generated from a germinal zone containing both neural stem cells (NSCs) and more limited intermediate neural progenitors (INPs). The signalling events that distinguish between these two proliferative neural cell types remain poorly understood. The Notch signalling pathway is known to maintain NSC character and to inhibit neurogenesis, although little is known about the role of Notch signalling in INPs. Here we show that both NSCs and INPs respond to Notch receptor activation, but that NSCs signal through the canonical Notch effector C-promoter binding factor 1 (CBF1), whereas INPs have attenuated CBF1 signalling. Furthermore, whereas knockdown of CBF1 promotes the conversion of NSCs to INPs, activation of CBF1 is insufficient to convert INPs back to NSCs. Using both transgenic and transient in vivo reporter assays we show that NSCs and INPs coexist in the telencephalic ventricular zone and that they can be prospectively separated on the basis of CBF1 activity. Furthermore, using in vivo transplantation we show that whereas NSCs generate neurons, astrocytes and oligodendrocytes at similar frequencies, INPs are predominantly neurogenic. Together with previous work on haematopoietic stem cells, this study suggests that the use or blockade of the CBF1 cascade downstream of Notch is a general feature distinguishing stem cells from more limited progenitors in a variety of tissues.

PMID: 17721509 [PubMed - indexed for MEDLINE]