

## Gli3 repressor governs the proper establishment of postnatal neurogenic niche

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Postnatal neural stem cells (NSCs) reside in the subventricular zone (SVZ) neurogenic niche and produce new neurons throughout the life of an animal. NSCs and ependymal cells both originate from embryonic radial glial cells (RGCs) and are arranged in a pinwheel-like structure in the SVZ. However, little is known about mechanisms underlying the cell fate specification and formation of the SVZ cytoarchitecture. Here, we show that Gli3 repressor (Gli3R), a negative regulator of Shh pathway, is critical for the initial establishment of the postnatal neurogenic niche. We first demonstrate that RGCs require Gli3R to correctly specify postnatal ependymal cells. In the absence of Gli3, NSC marker GFAP is ectopically induced during ependymal cell development. We identified *il6st*, a gene encoding the cytokine co-receptor gp130, as a direct transcriptional target of Gli3R. gp130 overexpression in the absence of Gli3R resulted in persistent activation of STAT3 signaling to induce widespread GFAP expression in the SVZ. In addition, we found that the disrupted cytoarchitecture of the SVZ in the Gli3 conditional mutants was due to the altered distribution of cell adhesion molecule, VCAM1. Interestingly, Numb, one of the important players regulating cell-cell adhesion, was greatly down-regulated in the absence of Gli3. We further identified that Lnx1, an E3 ubiquitin-protein ligase responsible for Numb degradation, as a direct downstream transcription target of Gli3R. Our findings highlight the critical role of Gli3R in the initial establishment of SVZ neurogenic niche through its transcriptional repression of key genes in cell fate determination and cell adhesion.

### Biography

Hui Wang has completed her Ph.D. in 2007 from University of Virginia and has been a postdoc in NIH since then. She worked on embryonic neural development during her PhD study and has been working on mammalian adult neural stem cell for her postdoc training. She graduated from the Medical School of Shanghai Tongji University in 1998.

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