Cerebellar granule cell

Cerebellar granule cells form the thick granular layer of the cerebellar cortex and are among the smallest neurons in the brain. (The term granule cell is used for several unrelated types of small neurons in various parts of the brain.) Cerebellar granule cells are also the most numerous neurons in the brain: in humans, estimates of their total number average around 50 billion, which means that they constitute about 3/4 of the brain's neurons.

Cerebellar granule neurons are the most abundant neurons in the brain, and a critical element of the circuitry that controls motor coordination and learning. In addition, granule neuron precursors (GNPs) are thought to represent cells of origin for medulloblastoma, the most common malignant brain tumor in children. Thus, understanding the signals that control the growth and differentiation of these cells has important implications for neurobiology and neurooncology. Our previous studies have shown that proliferation of GNPs is regulated by Sonic hedgehog (Shh), and that aberrant activation of the Shh pathway can lead to medulloblastoma. Moreover, we have demonstrated that Shh-dependent proliferation of GNPs and medulloblastoma cells can be blocked by basic fibroblast growth factor (bFGF). But while the mitogenic effects of Shh signaling have been confirmed in vivo, the inhibitory effects of bFGF have primarily been studied in culture. Here, we demonstrate that mice lacking FGF signaling in GNPs exhibit no discernable changes in GNP proliferation or differentiation. In contrast, activation of FGF signaling has a potent effect on tumor growth: treatment of medulloblastoma cells with bFGF prevents them from forming tumors following transplantation, and inoculation of tumor-bearing mice with bFGF markedly inhibits tumor growth in vivo. These results suggest that activators of FGF signaling may be useful for targeting medulloblastoma and other Shh-dependent tumors [1].

1)
Emmenegger BA, Hwang EI, Moore C, Markant SL, Brun SN, Dutton JW, Read TA, Fogarty MP, Singh AR, Durden DL, Yang C, McKeehan WL, Wechsler-Reya RJ. Distinct roles for fibroblast growth factor signaling in cerebellar development and medulloblastoma. Oncogene. 2013 Aug 29;32(35):4181-8. doi: 10.1038/onc.2012.440. Epub 2012 Oct 8. PubMed PMID: 23045271; PubMed Central PMCID: PMC3808889.