

## Zinc-finger and helix-loop-helix transcription factors regulate Purkinje neuron neurogenesis and cerebellar corticogenesis

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Many regulatory genes have been pinpointed as orchestrators of cerebellar development, from the onset of neurogenesis to the patterning of the adult cerebellar cortex, with a special reference to the development of cerebellar Purkinje cells (PCs). PCs provide the sole output from cerebellar cortical circuits, where each PC integrates myriads of presynaptic inputs, both inhibitory and excitatory. In the murine cerebellar primordium PCs are generated from a pool of ventricular zone progenitors facing the fourth ventricle between embryonic day (E) 10.5 and 13.5. This progenitor pool expands in the ventricular zone (VZ) through symmetric cell division until E10.5, when a gradual switch to asymmetric cell division occurs, regulated by Notch1 (Lutolf et al., 2002) and its interactor (Masserdotti et al., 2010), the Zn-finger TF Zfp423 (Alcaraz et al., 2006; Warming et al., 2006; Croci et al., submitted). Zfp423 was recently implicated in Joubert syndrome and cerebellar vermis hypoplasia (Chaki et al., 2012). Allelic mutations of Zfp423 produce distinct alterations in PC development (Croci et al., submitted). PCs arise from a pool of progenitors positive for the basic-helix-loop-helix transcription factors (TFs) neurogenin (Ngn) 1 and 2 (Zordan et al., 2008; Lundell et al., 2009). Ngn2 regulates cell cycle progression and dendritic arbor generation in PC precursors (Florio et al., 2012). PCs also express HLH transcription factors of the Olf/EBF family. In *Ebf2* *-/-* mutants, PC migration and survival are affected (Croci et al., 2006). Neonatal PC death is due to local downregulation of *Igf1* gene expression (Croci et al., 2011). Finally, EBF2 regulates cortical patterning in the adult cerebellum, regulating its subdivision into alternate parasagittal stripes of distinct PC subtypes. Indeed, EBF2 is required to repress the zebrin II<sup>+</sup> phenotype in postnatal PCs (Croci et al., 2006; Chung et al., 2008).

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### Keywords

Cerebellar organogenesis; cerebellar neurogenesis; cerebellar cortical patterning; cell death; development; Purkinje neurons.