

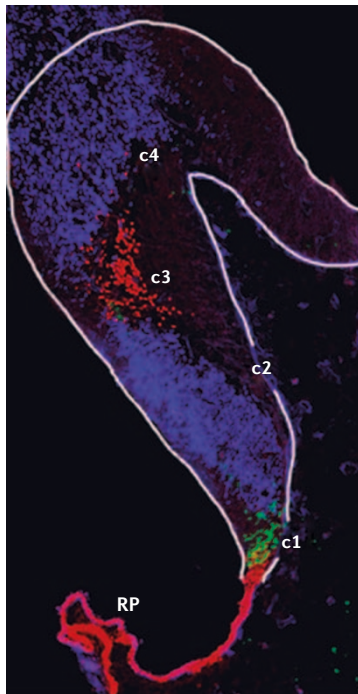
DEVELOPMENT

Mapping cerebellar development

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Sagittal section of mouse cerebellar anlage at embryonic day 12.5, stained with anti-LMX1a (red), anti-MATH1 (green) and anti-LHX1/5 (blue) antibodies. Roof plate (RP), c1, c2, c3 and c4 cells are labelled. Image courtesy of V. Chizhikov and K. Millen, University of Chicago, USA.

The cerebellum, with its complex structure and diverse cell types, follows a complicated developmental

course. We know that the isthmic organizer, a signalling centre at the junction of the midbrain and hindbrain, is crucial for regulating cerebellar development along the anterior–posterior axis, but the mechanisms that specify the distinct cell types in the early cerebellar anlage are far less clear. Reporting in *Development*, Chizhikov and colleagues highlight a previously unappreciated role for the roof plate in regulating cell type specification and proliferation during development of the cerebellar anlage.

The spinal cord roof plate is a signalling centre that resides in the dorsal midline of the developing neural tube that produces numerous bone morphogenetic protein (BMP)-related molecules and is responsible for patterning the specification and differentiation of the dorsal neural tube. The cerebellum develops from rhombomere 1 (r1), a segment of the hindbrain that lies alongside the fourth ventricle. Interestingly, there is considerable overlap in the molecules expressed in dorsal r1 and in the spinal cord roof plate. So, is it possible that the r1 roof plate regulates the development of the cerebellar anlage

and cerebellar cell types?

Chizhikov and co-workers tested this possibility first by creating a gene expression map of the early developing cerebellar anlage, showing that it is divided into several distinct cell populations (c1–c4) that express different genetic markers. Through gain- and loss-of-function studies to disrupt the BMP pathways that mediate r1 roof plate signalling in mice, they revealed an essential role for the roof plate in the specification of the cerebellar rhombic lip and adjacent c1 cells. The more distant c2 and c3 cells were still generated in these mutant mice, although intact roof plate signalling was necessary to regulate their proliferation and positioning.

This work offers valuable insights into the complex processes of cerebellar development. Moreover, the comprehensive molecular map of the entire early cerebellar anlage provides a useful new tool for elucidating the intricacies of cerebellar development.

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ORIGINAL RESEARCH PAPER Chizhikov, V. V. et al. The roof plate regulates cerebellar cell-type specification and proliferation. *Development* **133**, 2793–2804 (2006)