HIGHLIGHTS

DEVELOPMENT

Taking orders from above

Just as Sonic hedgehog signalling is required for the specification of ventral neuronal subtypes, so the bone morphogenetic protein (Bmp) signalling pathway is emerging as a key regulator of patterning in the dorsal neural tube. Reporting in *Development*, Liu and colleagues present evidence that the transcription factors Msx1 and Msx3, which are believed to be downstream targets of Bmp signalling, regulate distinct phases of development in the dorsal neural tube.

It was previously shown that neural plate explants from chick embryos at Hamburger–Hamilton (HH) stage 10–12 generate neural crest cells in response to Bmp treatment, whereas explants from HH15 embryos generate dorsal interneurons. Liu *et al.* used a gain-of-function approach in whole chick embryos to compare the effects of *Msx1* and *Msx3* overexpression with the effects of Bmp signalling during and after neural tube closure (HH10–12 and HH14–16, respectively). They used *in ovo* electroporation to transfect one side of the neural tube with an expression vector for the mouse *Msx1* or *Msx3* gene, or for a constitutively active Bmp receptor.

The authors found that at HH10–12, both Bmp signalling and overexpression of *Msx1* induced ectopic expression of roof plate markers and increased production of neural crest. Also, in both cases, neuronal differentiation was suppressed throughout the neural tube, as indicated by the failure to establish a normal pattern of marker-gene expression for neuronal progenitor domains along the dorsoventral axis. At HH14–16, the effects of Bmp signalling were mimicked by the overexpression of *Msx3*, with both manipulations causing an expansion of the dorsal interneuron progenitor domain at the expense of more ventral cell types.

Interestingly, the effects of *Msx1* and *Msx3* gain-of-function in the chick are consistent with the normal expression patterns of these genes in the mouse. Although both genes are initially expressed throughout the dorsal neural tube, *Msx1* expression becomes confined to the roof plate, whereas *Msx3* expression is maintained in the dorsal third of the neural tube, but is absent from the roof plate. Therefore, evidence is accumulating that the Msx factors mediate specific aspects of Bmp signalling in the dorsal neural tube. The findings of Liu *et al.* provide a good indication of the stages at which the neuroepithelium is competent to respond to Msx1 and Msx3 during development, and it should now be possible to test their predictions in the mouse using a conditional loss-of-function approach.

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References and links

ORIGINAL RESEARCH PAPER Liu, Y. *et al.* Distinct activities of Msx1 and Msx3 in dorsal neural tube development. *Development* **131**, 1017–1028 (2004)

FURTHER READING Caspary, T. & Anderson, K. V. Patterning cell types in the dorsal spinal cord: what the mouse mutants say. *Nature Rev. Neurosci.* **4**, 290–298 (2003) | Gammill, L. S. & Bronner-Fraser, M. Neural crest specification: migrating into genomics. *Nature Rev. Neurosci.* **4**, 795–805 (2003)