DEVELOPMENT

Retinoids expand their repertoire

Retinoids are involved in a plethora of events during vertebrate neural development, including various aspects of neural tube patterning and neurogenesis. Three papers in *Neuron* provide some interesting new additions for their functional repertoire.

Diez del Corral *et al.* investigated caudal extension of the spinal cord in chick embryos. Previous work has shown that spinal cord progenitor cells reside in a 'stem zone', and fibroblast growth factor (FGF) signalling keeps them in an undifferentiated state. Unidentified signals from the somites that counteract FGF signalling cause these cells to differentiate and contribute to the growing spinal cord. Diez del Corral *et al.* now show that retinoic acid (RA) is one such signal. They present a model in which the balance between stem zone maintenance and neuronal differentiation is maintained by opposing gradients of Fgf8 and RA. As the Fgf8-expressing primitive streak regresses caudally, RA synthesis is activated, and this causes further repression of FGF signalling.

Novitch *et al.* show that retinoid signalling is also required for the specification of motor neurons in the ventral neural tube. Most of the signals that control ventral neuronal cell fate seem to be transcriptional repressors, but the authors found that activated retinoid receptors act as transcriptional activators for the homeodomain genes that specify the motor neuron progenitor domain. In addition, RA signalling promotes the adoption of a neuronal fate by activating the proneural gene *Olig2*.

Last, as Sockanathan *et al.* demonstrate, retinoids are also involved in postmitotic events in motor neurons. Although all motor neurons derive from a single domain along the dorsoventral axis of the neural tube, postmitotic motor neurons diversify along the anteroposterior axis to generate a series of motor columns. The authors show that RA is required for the specification of lateral motor column (LMC) neurons at the brachial level of the spinal cord, and that it also has a more general role in specifying LMC identity. Retinoid signalling also seems to control the acquisition of other motor neuron characteristics, including their positioning within the spinal cord and their axonal projection patterns.

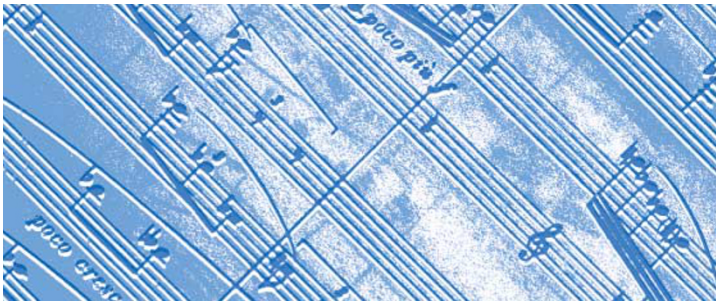
These findings reveal crucial roles for retinoids in the extension of the spinal cord and the specification and differentiation of motor neurons, thereby sealing their reputation as key regulators of neural development.

Heather Wood

References and links

ORIGINAL RESEARCH PAPERS Diez del Corral, R. *et al.* Opposing FGF and retinoid pathways control ventral neural pattern, neuronal differentiation, and segmentation during body axis extension. *Neuron* **40**, 65–79 (2003) | Novitch, B. G. *et al.* A requirement for retinoic acid-mediated transcriptional activation in ventral neural patterning and motor neuron specification. *Neuron* **40**, 81–95 (2003) | Sockanathan, S. *et al.* Retinoid receptor signaling in postmitotic motor neurons regulates rostrocaudal positional identity and axonal projection pattern. *Neuron* **40**, 97–111 (2003)

FURTHER READING Maden, M. Retinoid signalling in the development of the nervous system. *Nature Rev. Neurosci.* **3**, 843–853 (2003)



AXON GUIDANCE

The end of the branch

During neuronal development, axons form branches that allow a neuron to project to many targets. Colavita and Tessier-Lavigne have identified a signal in the worm *Caenorhabditis elegans* that acts as a branch-specific stop signal, giving new insight into how axonal branches are specified.

In *C. elegans*, a group of identified neurons — the VC neurons — form axonal branches at the vulva that travel a short way from the ventral nerve cord along the vulval epithelium before stopping. In the new study, Colavita and Tessier-Lavigne found that mutations in a particular gene, *bam-2*, cause the branches to overshoot so that they continue to extend across the vulval midline. *bam-2* is expressed in a number of cells, including the vulval VulF cell, but not in the VC neurons.

The phenotype of *bam-2* mutants could be rescued by expression of *bam-2* in the VulF cell but not by expression in the VC neurons. The cytoplasmic domain of BAM-2 seems not to be needed for its branch-termination role, as a truncated *bam-2* gene that lacked this domain could also rescue the phenotype. The sequence of the BAM-2 protein indicates that it is a cell-surface protein and is related to the neurexin family, members of which have been implicated in synaptogenesis.

Ectopic expression of *bam-2* in the VC neurons of *bam-2*-null worms caused an interesting additional phenotype: in 43% of cases, one branch fascicle failed to form completely. Ectopic expression in a wild-type background did not have this effect. The authors propose that BAM-2 acts as a positive signal that attracts axon branches to the appropriate termination point: in the wild type, the normally expressed BAM-2 on the VulF cell overrides the effects of the transgene, but in the *bam-2*-null worms, ectopic expression in the neurons themselves interferes with branch extension.

The results of the study support the proposal that BAM-2 acts as a branch-termination signal for the VC axons. Surprisingly, it does not seem to influence termination of the primary axons; rather, it acts only on their branches. It seems likely that BAM-2 on the VulF cell acts as a ligand for a receptor that is localized to the VC axonal branches.

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References and links

ORIGINAL RESEARCH PAPER Colavita, A. & Tessier-Lavigne, M. A neurexin-related protein, BAM-2, terminates axonal branches in *C. elegans*. *Science* **302**, 293–296 (2003)

WEB SITES

Tessier-Lavigne laboratory: http://www.ucsf.edu/pibs/faculty/tessier_lavigne.html

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