GFP expression in retinal ganglion cells of a transgenic zebrafish. Courtesy of Ava Udvadia, Duke University Medical Center, Durham, North Carolina, USA.

AXON GROWTH

A GAP between development and repair

In spite of the supposed superiority of higher vertebrates, so-called primitive organisms have many 'talents' that we seem to have lost, not least of which is the capacity for self-repair. Some examples, such as the regeneration of whole limbs in salamanders, can be quite spectacular. However, less visible but equally important is the ability to repair damage to the nervous system. The question remains as to how and why such a useful mechanism has been lost in higher vertebrates. According to a paper published in *Development* by Udvadia *et al.*, part of the answer might lie in a 1-kb fragment of DNA.

Certain common signalling pathways are activated in axons during developmental growth and nerve regeneration. For example, both processes are accompanied by upregulation of genes that encode growth-associated proteins (GAPs). Udvadia *et al.* used a 1-kb fragment of the rat *GAP-43* promoter to drive expression of green fluorescent protein (GFP) in transgenic zebrafish, and they analysed transgene expression in retinal ganglion cells (RGCs) during development and repair. The 1-kb fragment is highly conserved between species and is sufficient to drive neuronal *GAP-43* expression *in vitro*. The authors showed that the onset of developmental axon growth in RGCs coincided with upregulation of both the transgene and the endogenous zebrafish *GAP-43* gene. Similarly, both were downregulated at the onset of neuronal maturation. However, unlike the endogenous gene, the transgene was not activated during axonal regeneration following a crush injury to the optic nerve. This implies that the sequences required to drive *GAP-43* expression during regeneration have either diverged during evo-

lution or lie outside the 1-kb region. Both interpretations lead to the conclusion that the signalling components involved in regeneration differ from the highly conserved factors that drive developmental *GAP-43* expression. This might explain how mammals lost the ability to re-activate GAPs for regeneration without disrupting the precise regulation of axon growth during normal development. It would now be interesting to find out whether the 1-kb fragment from the zebrafish gene can drive transgene expression during zebrafish axonal regeneration.

Whereas previous studies have shown that molecules extrinsic to neurons, such as Nogo, can inhibit axon growth after injury, this new study suggests that intrinsic factors might also be differentially regulated during development and regeneration. If the differences between these two processes can indeed be attributed to divergence within the 1-kb region of the *GAP-43* gene, this could provide a key to understanding the evolutionary basis for the differing regenerative capacities of the nervous system in lower and higher vertebrates. More importantly, it could provide us with a new lead in the development of strategies to treat people with nerve injuries.

Heather Wood

References and links

ORIGINAL RESEARCH PAPER Udvadia, A. J. *et al.* *GAP-43* promoter elements in transgenic zebrafish reveal a difference in signals for axon growth during CNS development and regeneration. *Development* **128**, 1175–1182 (2001)
FURTHER READING Benowitz, L. I. & Routtenberg, A. *GAP-43: an intrinsic determinant of neuronal development and plasticity. Trends Neurosci.* **20**, 84–91 (1997) | Raineteau, O. & Schwab, M. E. Plasticity of the motor systems after incomplete spinal cord injury. *Nature Rev. Neurosci.* **2**, 263–273 (2001)
WEB SITE Pate Skene's lab
ENCYCLOPEDIA OF LIFE SCIENCES Nerve regeneration: mammalian | Axon growth

IN BRIEF

COGNITIVE NEUROSCIENCE

Cortical mechanisms specific to explicit visual object recognition.

Bar, M. *et al.* *Neuron* **29**, 529–535 (2001)

The authors explored the neural correlates of object recognition by asking subjects to identify pictures of masked objects, which were presented several times for brief periods. Using functional magnetic resonance imaging, they compared brain activity between trials in which recognition actually occurred and trials in which objects were 'almost' recognized. They found that activity in the fusiform gyrus was linearly correlated with the awareness of object identity. So, although recognition of an object is an abrupt experience, awareness of its identity might be associated with gradual increases in cortical activity.

DEVELOPMENT

PLC- β 1, activated via mGluRs, mediates activity-dependent differentiation in cerebral cortex.

Hannan, A. J. *et al.* *Nature Neurosci.* **4**, 282–288 (2001)

The formation of somatosensory barrels in the cortex was disrupted in mice that lacked PLC- β 1 or mGluR5, despite the ability of thalamic afferents to segregate in an appropriate manner. This observation helps to outline the signalling pathway involved in the development of cortical cytoarchitecture and indicates that it is possible to dissociate its thalamic and cortical determinants.

SYNAPTIC PLASTICITY

Inducible and reversible enhancement of learning, memory, and long-term potentiation by genetic inhibition of calcineurin.

Malleret, G. *et al.* *Cell* **104**, 675–686 (2001)

The regulated expression of a calcineurin inhibitor was found to facilitate long-term potentiation in mouse hippocampus. This facilitation was accompanied by enhanced learning and memory in several hippocampus-dependent tasks and was reversed by suppressing expression of the inhibitor. These findings indicate that calcineurin, a Ca^{2+} /calmodulin-dependent phosphatase, is likely to act as an inhibitory constraint on synaptic plasticity and memory.

NEUROPATHOLOGY

A novel erythroid-specific marker of transmissible spongiform encephalopathies.

Miele, G. *et al.* *Nature Med.* **7**, 361–364 (2001)

By performing differential-display analysis of cDNAs from spleen, the authors found that the expression of erythroid differentiation-related factor (EDRF) was reduced in scrapie-infected mice. Furthermore, EDRF expression was also reduced in cows and sheep with signs of spongiform encephalopathy. As EDRF transcripts can be readily detected in haematopoietic tissues and blood, this finding raises the possibility of developing a diagnostic test for prion-related diseases.