DEVELOPMENT

Mirror images of asymmetry

The vertebrate nervous system contains numerous striking asymmetries of structure and function. Two recent reports shed light on the mechanisms that underlie left–right organization and their place in evolution.

Laterality of the nervous system is intimately associated with asymmetry of the viscera, a fact that is highlighted by the reversals of some brain structures in people with *situs inversus totalis*, in which the positioning of internal organs is inverted. But individuals with this condition retain left-sided language processing, which indicates that functional laterality of the nervous system does not always follow asymmetry of the viscera.

Barth and colleagues explored the relationship between visceral, neuroanatomical and behavioural asymmetries in *frequent situs inversus* (*fsi*) zebrafish, which often show reversed laterality of the brain and viscera. In reversed *fsi* mutants, the main left–right body asymmetries were coupled to certain brain asymmetries and lateralized behaviours. But some behavioural asymmetries did not reverse, which suggests that more than one mechanism underlies lateralization in the zebrafish CNS.

Left-sided expression of genes functioning in the Nodal signalling pathway is associated with CNS and visceral laterality in wild-type zebrafish. Importantly, Barth *et al.* found a correlation between asymmetrical gene expression, asymmetrical brain structure and lateralized behaviour, showing that right-sided *nodal* expression precedes the abnormal, right-sided placement of forebrain structures in *fsi* mutants.

The evolutionary origins of mechanisms that control the asymmetrical positioning of internal organs are not known. However, unilateral Nodal signalling seems to be a conserved feature in vertebrates, and a new study by Duboc *et al.* shows that this mechanism is also present in the sea urchin, an echinoderm. Intriguingly, the researchers found that *nodal* expression in sea urchins is reversed such that signals on the right side, not the left, drive the establishment of asymmetry, restricting formation of the imaginal rudiment, from which most adult tissues are formed, to the left.

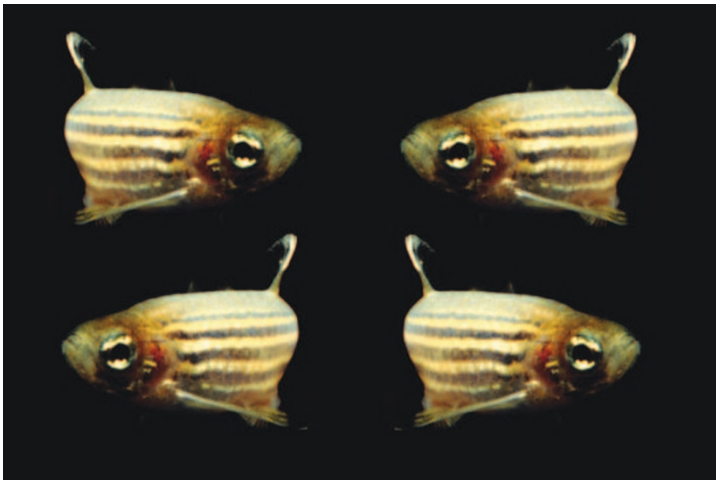
This work shows that one of the regulatory cascades responsible for left–right organization of the nervous system and other tissues was present before the separation of chordates and echinoderms more than 500 million years ago. But the notable findings of Duboc, Barth and colleagues highlight the fact that we still know relatively little about the nature and evolutionary origins of the multiple molecular pathways that influence neuroanatomical, behavioural and cognitive asymmetries in vertebrates.

Rebecca Craven

References and links

ORIGINAL RESEARCH PAPERS Barth, K. A. *et al.* *fsi* zebrafish with *situs inversus* show concordant reversal of laterality of viscera, neuroanatomy, and a subset of behavioral responses. *Curr. Biol.* **15**, 844–850 (2005) | Duboc, V. *et al.* Left–right asymmetry in the sea urchin embryo is regulated by Nodal signalling on the right side. *Dev. Cell* **9**, 147–158 (2005)

FURTHER READING Toga, A. W. & Thompson, P. M. Mapping brain asymmetry. *Nature Rev. Neurosci.* **4**, 37–48 (2003)



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