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DEVELOPMENT

Taking sides

MicroRNAs (miRNAs) are small non-coding RNA molecules, which have emerged in recent years as key regulators of gene expression at the post-transcriptional level. Numerous putative miRNAs have been identified in the developing and adult nervous systems of various species, although their functions are largely obscure. However, Johnston and Hobert have now identified a new miRNA in the nematode *Caenorhabditis elegans*, and have assigned it a specific role in the establishment of asymmetry in a pair of sensory neurons.

The *C. elegans* taste neurons ASEL and ASER are bilaterally symmetrical in terms of position, but show asymmetry with regard to gene expression profiles. ASEL expresses the chemoreceptor genes *gcy-6* and *gcy-7*, whereas ASER expresses *gcy-5*, and these discrepancies enable the two neurons to detect different ranges of chemosensory cues. The neurons are born identical, so Johnston and Hobert wanted to find out how they acquire their asymmetry during development.

The authors identified a mutant worm strain in which ASEL loses its characteristic gene expression profile and instead expresses ASER-specific chemoreceptors. They called the mutated locus *lsy-6* (*lsy* stands for laterally symmetrical). They found that *lsy-6* codes for an RNA with a palindromic sequence that can form a hairpin structure — a common hallmark of RNA molecules that are processed to generate miRNAs — and

that the ASEL gene expression profile could be restored with a 521-base pair fragment of the *lsy-6* locus that included the hairpin. The hairpin contains a 23-nucleotide sequence that shows considerable homology to a miRNA in the related species *C. briggsae*.

Next, Johnston and Hobert analysed the expression pattern of *lsy-6* by linking its regulatory sequences to a reporter gene. They found that the reporter was expressed in ASEL but not ASER, consistent with a role for *lsy-6* in conferring a specific chemoreceptor expression profile on ASEL. The *lsy-6* miRNA seems to work by repressing the homeobox gene *cog-1*, which has been shown to regulate differential *gcy* gene expression in ASEL and ASER.

Although these new findings take us one step upstream in the pathway that establishes asymmetry in the ASEL/ASER neurons, there is still the crucial question of how *lsy-6* expression becomes restricted to the ASEL neuron in the first place. It will also be interesting to find out whether miRNAs are involved in establishing any other aspects of nervous system asymmetry in *C. elegans*, and indeed in higher organisms.

Heather Wood

References and links

ORIGINAL RESEARCH PAPER Johnston, R. J. Jr & Hobert, O. A microRNA controlling left/right asymmetry in *Caenorhabditis elegans*. *Nature* **426**, 845–849 (2003)

FURTHER READING Hobert, O. et al. Left-right asymmetry in the nervous system: the *Caenorhabditis elegans* model. *Nature Rev. Neurosci.* **3**, 629–640 (2002)

Positions of neuronal nuclei (yellow; ASEL and ASER highlighted in green) in the head ganglia of an adult *Caenorhabditis elegans* worm. The animal is sliced open along the ventral midline and folded out.