AXON GUIDANCE

The worm that turned

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During nervous system development, new connections and networks are established by the growing neuronal axons and dendrites. In the case of the mechanosensory neurons of the nematode worm *Caenorhabditis elegans*, these neurite extensions advance along the anteroposterior body axis. However, two new papers report that, in worms with mutated WNT proteins, the anterior/posterior trajectories of these neurites can become completely reversed.

The WNT family of proteins are known to regulate various developmental processes, including asymmetrical cell division, cell fate determination and axon guidance. They are secreted proteins that act on target cells, over long distances, through interaction with their cell surface receptors. Both teams observed that in worms with mutations in one of these receptors (LIN-17), the polarity of the mechanosensory neuron PLM was often reversed such that the anterior process was short and unbranched, much like the posterior process of the wild type, and the posterior process was long and branched, like the anterior process of the wild type.

The inverted neuronal processes observed in LIN-17 mutants indicated that WNT proteins might be involved in mechanosensory neuron polarity in *C. elegans*. *C. elegans* has five WNT proteins: CWN-1, CWN-2, EGL-20, LIN-44 and MOM-2. The authors found that specific combinations of WNT mutations could indeed produce inverted PLM neurons, and also inverted ALM neurons (another class of mechanosensory neuron).

Interestingly, Prasad and Clark found that PLM and ALM neurons were also inverted in worms mutant for VPS-35, a component of the retromer complex that mediates endosome-to-Golgi trafficking. They went on to show that the VPS-35 mutation disrupted WNT signalling, and that the ALM and PLM polarity defect could be rescued in these mutants by specific expression of VPS-35 in WNT-expressing cells.

WNT signalling controls a large repertoire of developmental functions, including cell fate decisions and cell growth/migratory guidance. The WNT proteins are highly conserved from invertebrates to vertebrates, and it is therefore possible that WNT signalling could also influence neuronal polarity in mammalian development.

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ORIGINAL RESEARCH PAPERS Hilliard, M. A. & Bargmann, C. I. Wnt signals and Frizzled activity orient anterior-posterior axon outgrowth in *C. elegans*. *Dev. Cell* **10**, 379–390 (2006) | Prasad, B. C. & Clark, S. G. Wnt signalling establishes anteroposterior neuronal polarity and requires retromer in *C. elegans*. *Development* **133**, 1757–1766 (2006)