The Ups and Downs of Wnt Signaling

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During development, neurons are best regarded as master navigators. At the tips of their extending axons are motile structures, called growth cones, endowed with the capacity to recognize specific cues in the extracellular environment that help to guide them to distant target cells. One particularly well-studied class of neurons, the commissural neurons within the spinal cord, project their axons over long distances across the midline to the opposite side of the developing nervous system. As commissural growth cones set course for the floor plate at the ventral midline, they encounter sloping concentrations of guidance molecules (1-3). Those released by roof plate cells at the dorsal midline are perceived by the growth cones as repulsive, forcing them to take a ventral heading into regions where the number of molecules gradually taper off. At the same time, the growth cones encounter an ever-increasing concentration of guidance molecules secreted by cells at the floor plate. Because these are perceived as attractive, the growth cones continue their ventral migration toward the source, eventually crossing it. In order for these growth cones to complete their task of finding and connecting with their target neurons, they must change direction the moment they emerge from the floor plate on the opposite side (4). It is this act—an abrupt and invariant change in course to an anterior heading toward the brain—that captured the interest of Lyukysytova et al. (5). These investigators report on page 1984 of this issue their identification of a rather unlikely candidate that influences the decision to “go anterior.”

Borrowing from what was already known about the ventral guidance of commissural growth cones, the authors reasoned that a “go anterior” signal might also exist as a gradient. However, it was not clear whether the “go anterior” signal is secreted or remains firmly embedded within the membranes of the cells that produce it. Because gradients formed by both types of signaling molecule (secreted and anchored) exist within the nervous system (6), distinguishing between these two possibilities would help to narrow the search for possible candidates.

A clue to the nature of the “go anterior” signal came when the authors examined the projections of commissural axons in cultured spinal cord explants. They reasoned that a gradient of secreted molecules might dissipate as molecules slowly leach out of the explant near its cut edges. Should this occur at the low end of the gradient, only its slope would be changed. If, on the other hand, molecular cues escape from the opposite cut end of the spinal cord where the gradient is at its peak, the gradient might be locally reversed, creating a situation where growth cones in the vicinity of the cut end could lose their bearings or even turn in the opposite direction. This is precisely what Lyukysytova et al. (5) observed. Near the anterior cut end of cultured spinal cord explants, commissural axons either stall or project randomly along the anterior-posterior axis after crossing the floor plate. Such behavior implicates an increasing posterior-to-anterior gradient of an attractive guidance molecule controlling the postcrossing trajectory of commissural axons.

To identify candidates for this attractive cue, the authors tested the effects of different molecules on the behavior of commissural growth cones in spinal cord explants. Of those tested, several members of the Wnt family of secreted signaling molecules were able to affect the growth of commissural axons after they crossed the floor plate. Might one or more of these Wnts represent the elusive...
Heading due north. Guidance of commissural axons in the spinal cord. Gradients of diffusible molecules secreted by the roof plate and floor plate guide commissural axons to the ventral midline (1–3). After crossing the floor plate, growth cones turn anteriorly in response to an increasing gradient of Wnt4 (red) secreted by floor plate cells. In cultured “open-book” explants, Wnt protein escapes from the cut edges, changing the slope of the gradient near the posterior end and reversing the gradient near the anterior end. The gradient is restored by cells secreting Wnt4 protein, thus allowing growth cones to assume their normal anterior course.

Polymers Get Organized

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Polymers often behave like tangled spaghetti, but sometimes the sheer size of polymer molecules can make them organize into regular nanometer-scale structures. Chemists are increasingly looking for ways to understand and manipulate such self-organization, with potential applications from solar cells to drug delivery.

Three key factors affect the macroscopic behavior of polymers: chemical composition, molecular architecture (the way in which the monomer building blocks are together bound in the polymer chain), and supramolecular architecture (the organization of the chains relative to each other). The combination of these factors leads to a hierarchy of architectures over a range of length scales, similar to the primary, secondary, and tertiary structures found in DNA and proteins.

The simplest polymers are isolated linear chains, which tend to form random coils. More complex polymers include branched polymers, block copolymers, polymer networks, cyclic polymers, and tree-like structures (such as dendrimers). Recent advances in polymer synthesis have extended the range of molecular architectures dramatically (1).

The weak, noncovalent interactions of the monomer units along a polymer chain tend to add up cooperatively, amplifying supramolecular effects. Thus, polymers are naturally predisposed to self-organize.

References