

halo of the intervening galaxy dominates the lensing. Sometimes, strong lensing results in anomalous intensity ratios among the multiple images of distant galaxies. The anomalies are probably generated by substructure in the dark halos of the intervening galaxies.

When the line of sight passes at larger distances from the intervening galaxy, the lensing generates only weak distortions in the observed shapes of the distant galaxies. Despite its weakness, this effect can be detected statistically from the huge samples of galaxy images that are becoming available from surveys. Weak lensing is an important tool for studying the properties of dark matter halos and for estimating the total mass of dark halos in the universe.

Combining the latest weak lensing data for dark halos with results from the WMAP cosmic microwave background mission (5) and the 2dF Galaxy Redshift Survey (6) yields a census of the different forms of mass in the universe. Stars and cold gas provide just 0.4% of the mass of the universe. When gas in all forms is included, this percentage increases to 4% for all baryons. Dark halos alone contribute about

11%. All types of matter (dark matter plus baryons) add up to 27%. The remaining 73% comes in the form of a currently poorly understood “dark energy.” The mass ratio of dark halos to stars and cold gas, 11 to 0.4, is close to the independent dynamical estimate of about 20 for the Milky Way (7).

The largest galaxies have dark halos with masses of up to  $\sim 10^{13}$  solar masses. At the other end of the scale are the dwarf spheroidal neighbors of the Milky Way and M31 (Andromeda). These very small and extremely faint galaxies have dark halos of  $\sim 10^7$  solar masses. Their dark halos may represent the smallest quantum of galactic dark matter that could condense from the expanding universe.

Only a few percent of the mass of these galaxies is in the form of stars. In principle, galaxies with dark halos but no baryons could also exist, as could galaxies with dark halos and gas but no stars. However, deep neutral hydrogen surveys like the recent all-sky HI survey at Parkes (8) have found no examples of dark galaxies with gas but no stars. Current weak lensing surveys have not yet detected

any indication of entirely dark galaxies.

Early in the evolution of the universe, theory predicts that the first objects to detach from the expanding universe were small and dense. We would expect to find correlations between the size and density of dark halos and the brightness of the galaxies that inhabit them. A careful reassessment of dark halo densities and sizes shows that these correlations are indeed present with the expected slope (9). This is another indication that the basic current paradigm of galaxy formation is correct.

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## NEUROSCIENCE

# The Ups and Downs of Wnt Signaling

Ralph Imondi and John B. Thomas

**D**uring 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 tapers 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 Lyuksytova *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.”

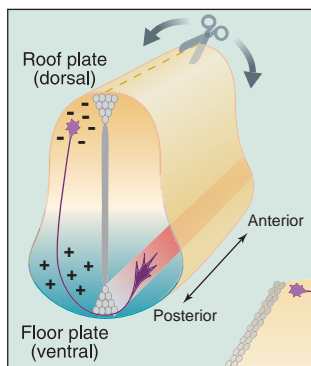
Borrowing from what was already known about the ventral guidance of commissural growth cones, the authors reasoned that a “go anterior” signal might also exist as a gradient. However, it was not clear whether the “go anterior” signal is secreted or remains firmly embedded within the membranes of the 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 pos-

sibilities would help to narrow the search for possible candidates.

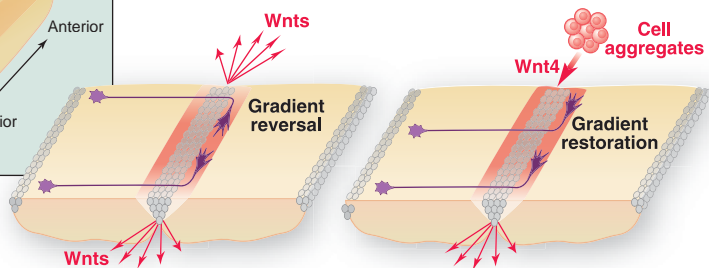
A clue to the nature of the “go anterior” signal came when the authors examined the projections of commissural axons in cultured spinal cord explants. They reasoned that a gradient of secreted molecules might dissipate as molecules slowly leach out of the explant near its cut edges. Should this occur 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 Lyuksytova *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 elu-

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**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.



sive “go anterior” signal? Of the several Wnt family members expressed in the spinal cord, the authors found Wnt4 to have an increasing posterior-to-anterior gradient of RNA expression. This is just what one might expect for a “go anterior” cue if levels of Wnt4 RNA reflect the amount of protein released. A noteworthy finding was that Wnt4, when expressed by cell aggregates positioned at the anterior cut end of spinal cord explants, could redirect commissural axons anteriorly, thereby rescuing the projection defects near the cut end (see the figure).

Further support for a Wnt protein being the “go anterior” signal came when the authors examined commissural axon trajectories in mice lacking *Frizzled3*, one member of a family of Wnt receptors expressed by commissural neurons. In such mice, growth cones emerge from the floor plate and project randomly along the anterior-posterior axis of the spinal cord, seemingly oblivious to any anterior guidance cue.

Wnt proteins are best known as secreted morphogens that specify the fates of responding cells by activating *Frizzled* receptors. Activated *Frizzled* receptors then engage a well-studied canonical signaling pathway that terminates in the nucleus, resulting in altered gene expression (7). However, if Wnts are acting directly on growth cones to guide them, they must initiate a signaling cascade that leads to rearrangement of the cytoskeleton, the major structural apparatus controlling growth cone movement. Lyuksyutova *et al.* provide evidence that the canonical Wnt signaling pathway is not involved in the guidance of commissural axons. What then might the actual signaling pathway be? At present, it is unknown, but finding its components should provide key insights into the poorly understood process of how growth cones translate discrete extracellular signals into changes in the direction of growth.

The present study raises several questions. Although Wnt4 is sufficient to redi-

rect axons in explants, is it the main player during normal development? Do other Wnts, or perhaps other classes of molecules altogether, cooperate with Wnt4? How might commissural growth cones bearing *Frizzled3* receptors delay their response to a gradient of Wnt protein until after they have crossed the floor plate? Do other classes of neurons that normally project posteriorly along the floor plate deploy receptors that interpret a Wnt gradient as repulsive? In *Drosophila*, axons bearing *Derailed*, another Wnt receptor, are repelled by Wnt5 protein during their guidance (8). By analogy, could growth cones equipped with the vertebrate homolog of *Derailed* or another receptor be capable of traveling down a Wnt4 gradient?

Within the past year, studies have revealed that several members of protein

families best known as morphogens are shaping up to be important axon guidance molecules. For example, opposing gradients of bone morphogenetic proteins and Sonic hedgehog act early in development to dictate the numbers and types of cells in the spinal cord (9), but later direct the ventral migration of commissural growth cones (1, 3). In addition, *Drosophila* Wnt5 ensures the correct passage of commissural growth cones across the fly equivalent of the floor plate (8). The study by Lyuksyutova *et al.* (5) implicates a new role for a morphogen family member in a fundamental guidance decision faced by many developing neurons: whether to “go anterior” or “go posterior.”

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#### CHEMISTRY

## Polymers Get Organized

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**P**olymers 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 bound together in the polymer chain), and supramolecular architecture (the organiza-

tion 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.

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