**Research Roundup**

**Old and unattracted**

With a limited number of guidance molecules in the nervous system, the same molecules get used in multiple places. Now Derryck Shewan, Christine Holt, and colleagues (University of Cambridge, Cambridge, UK) have shown that an intrinsic timing mechanism allows netrin to be used as both an attractant and repellent for the same set of growth cones during different periods of their outgrowth.

Holt had already shown that, at the beginning of the pathway traversed by frog retinal axons, netrin leads the axons out of the eye. To study the rest of the pathway, Shewan achieved the finicky feat of culturing the entire pathway. He confirmed that netrin could later act as a repellent that probably helps to prevent overshoot of the axons’ final target.

That was a nice result. But the surprise was yet to come. When the team cultured a chunk of retina, which lacked the rest of the optic pathway and had not yet initiated axon outgrowth, they saw that after two days there was the same switch from netrin attraction to netrin repulsion. Thus, the switch appears to be intrinsic.

“It was when we did the control experiment that we realized [that the switch to repulsion] was happening even without the pathway experience,” says Holt. “It was one of those strange twists.”

The initial, acute switch during outgrowth may still be influenced by pathway cues—possibly a combination of laminin, which Holt’s group has shown can flip the netrin switch, and another guidance molecule called Robo, whose receptor in the spinal cord can silence the netrin receptor. But the more long-lasting switch in netrin responsiveness may be a result of dropping levels of cyclic AMP (cAMP), which Holt’s group shows is correlated with the aging of the retinal neurons. Boosting cAMP can restore the youthful attraction to netrin, but the ultimate cause of the age-dependent dip in cAMP is not yet known.

Reference: Shewan, D., et al. 2002. Nat. Neurosci. 10.1038/nn919.

**Electrical healing**

Electrical fields (EFs) present at wound sites can orient and promote cell divisions, according to work by Bing Song, Colin McCaig, and colleagues (University of Aberdeen, Aberdeen, Scotland).

The EFs arise because channels shuttle ions between the tear fluid on the outside of the eye and the extracellular fluid bathing the underlying tissue layers. Before the surface of an eye is damaged, channels actively pump out Cl\(^-\)/H\(^+\) ions and pump in Na\(^+\)/H\(^+\) and K\(^+\)/H\(^+\) ions. That gradient is destroyed by wounding, leaving an EF in the extracellular fluid that runs from positive (far from the wound) to neutral or less positive (at the wound site). The authors directly measured the decline of this EF near wound sites. Various drugs changed the EF by activating or inhibiting the ion pumps.

The authors then provided the first in vivo correlation of EF magnitude with cellular behavior. Proximity to the wound and some of the drugs led to both higher EFs and greater orientation of mitotic spindles parallel to the EF. This orientation may help cells feed into the wound area—a process that is also promoted by EGF-directed cell migration. McCaig and others have shown in earlier work that EGF receptors, which have charged extracellular domains, redistribute in an EF and are necessary for directed cell migration.

The high level of migration may suppress cell division nearest the wound, but further from the wound the authors again found a correlation: this time between a higher EF and increased cell division. This may also be driven by the clustering of EGF receptors on the cell surface nearest the wound. Similar EFs may operate during neural development, so should prospective mothers be worried about the effects of high voltage power lines? McCaig says that the high electrical resistance of skin would render such voltages “vanishingly small” for an embryo, and that the power lines generate AC rather than DC electrical fields. But individuals recovering from laser eye surgery might think twice before basking in the sun under a major electrical supply.

Reference: Song, B., et al. 2002. Proc. Natl. Acad. Sci. USA. 10.1073/pnas.202235299.