This Week in The Journal

● Cellular/Molecular

An Axon-to-Glial Damage Signal

Amy D. Guertin, Dan P. Zhang, Kimberley S. Mak, John A. Alberta, and Haesun A. Kim
(see pages 3478–3487)

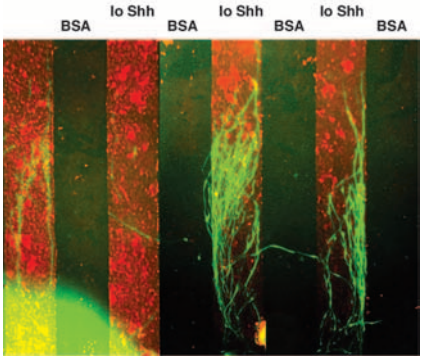
This week, Guertin et al. follow up on a story reported in the Edinburgh Medical and Surgical Journal 154 years ago. Wallerian degeneration includes a characteristic demyelinating response of Schwann cells surrounding the distal stump of an injured peripheral nerve. This degeneration requires close contact of the distal axon with Schwann cells, but what is the signal? The authors think it's neuregulin/erbB2. Neuregulin expressed by neurons binds the receptor tyrosine kinase erbB2 on Schwann cell microvilli that directly contact the axon. Although erbB2 activation previously had been seen days after injury, the authors saw a transient spike in erbB2 activation within minutes after injury. Phospho-specific erbB2 antibodies detected activated erbB2 at nodal and paranodal regions of myelinating Schwann cells. This signaling pathway appears necessary and sufficient because the erbB2 antagonist PKI166 blocked myelin degeneration; it also blocked neuregulin-induced demyelination of Schwann cells *in vitro* when added to the glial compartment of a cell culture chamber.

▲ Development/Plasticity/Repair

Sonic Hedgehog and Retinal Ganglion Cell Axons

Adrianne Kolpak, Jinhua Zhang, and Zheng-Zheng Bao
(see pages 3432–3441)

Retinal ganglion cells (RGCs) develop in waves, starting at the central retina and then progressing outward toward the periphery. As a result, growing RGC axons must backtrack to the center before entering the optic nerve. Kolpak et al. cultured retinal segments in agar blocks to examine a role for the morphogen Sonic hedgehog (Shh) on retinal axonogenesis. Central retinal explants from embryonic day 5 (E5) chicks, but not periphery explants, promoted RGC axon growth from adjacent "test" explants. The reverse was true of E8 explants, suggesting that a growth-promoting factor was expressed first at the center and later in the periphery. Retinal expression of Shh corresponded to the differentiation wave and the pattern of the secreted factor. An *in vitro* "stripe" assay of alternating low and high Shh provoked growth and retraction, respectively. Cyclopamine, which inhibits the Shh coreceptor Smoothened, blocked both effects, consistent with a direct and concentration-dependent effect of Shh on axonal growth.



RGC axons preferred to grow on 0.5 μg/ml Shh-coated stripes (lo Shh) rather than bovine serum albumin-coated stripes (BSA). See the article by Kolpak et al. for details.

■ Behavioral/Systems/Cognitive

Color Processing in the Human Brain

Junjie Liu and Brian A. Wandell
(see pages 3459–3468)

Retinal cones detect color, but the perception of color resides in the cortex. This week, Liu and Wandell set out to find regions of the human cortical visual field map that are "computationally specialized" for color processing (i.e., they respond not only to color but also to additional stimulus properties, such as frequency). Using functional magnetic resonance imaging, the authors measured blood oxygen level-dependent contrast responses to colors presented at various frequencies (1.5–10 Hz). The primary visual cortex (V1) responded to luminance and red–green across frequencies, but blue–yellow responses decreased at higher frequencies. The ventral occipital cortex (VO) responded strongly to all colors, but all responses decreased at high frequencies. The dorsal occipital regions V3 and MT+, in contrast, responded to high-frequency modulations of luminance and red–green stimuli but not to blue–yellow stimuli. The authors conclude that color perception is based on comparing signals in multiple pathways and that the comparison is optimized when luminance and color signals are temporally matched.

♦ Neurobiology of Disease

Backcrossing Epilepsy

Wayne N. Frankel, Barbara Beyer, Christina R. Maxwell, Stephanie Pretel, Verity A. Letts, and Steven J. Siegel
(see pages 3452–3458)

Absence or petit-mal epilepsy, the prototypic human genetic epilepsy, causes seizures with characteristic spike-wave discharges (SWDs). Several spontaneous mutations in mice (i.e., a monogenic inheritance pattern) also cause absence seizures associated with SWDs, but the human disorder has complex inheritance. This week Frankel et al. take advantage of their discovery of SWDs in C3H/He mice to begin a search for SWD susceptibility genes. SWDs were absent in F_1 hybrids of C3H/HeJ and C57BL/6J mice, consistent with recessive inheritance. Unlike the prediction for single-gene inheritance, almost all of the N_2 mice (backcrosses of the F_1 hybrids to C3H/HeJ) showed SWDs, and at a higher frequency than the C3H/HeJ parents. A genome scan revealed a high correlation of the phenotype with markers on chromosome 9. The locus, *spkw1* for spike wave 1, accounted for 40% of the phenotypic variance. Although multiple loci and thus multiple susceptibility genes are involved in SWDs in these mice, the *spkw1* locus warrants a close look.