This Week in The Journal

● Cellular/Molecular

Myelin Rides a WAVE

Hyun-Ju Kim, Allitia B. DiBernardo, Jacob A. Sloane, Matthew N. Rasband, David Solomon, Bela Kosaras, Seung P. Kwak, and Timothy K. Vartanian

(see pages 5849–5859)

When one thinks of lamellopodia, the image is usually of a neuronal growth cone, but the leading edge of myelin-forming oligodendrocyte processes can be considered to be giant lamellopodia. This week, Kim et al. identify a role for WAVE1 in oligodendrocyte process formation. WASP (Wiskott-Aldrich syndrome proteins) and WAVE (WASP family verprolin homologous) proteins alter actin dynamics and lamellopodia formation by linking small Rho GTPases to Arp2/3, the controller of *de novo* actin nucleation. The authors report that WAVE1 was expressed by oligodendrocytes and neurons, but a dominant-negative WAVE1 decreased process formation only in oligodendrocyte precursor cells (OPCs). In cultured oligodendrocytes, WAVE1 was concentrated at the edges of processes. In rat optic nerve, WAVE1 expression increased at postnatal day 9, when myelination begins. In WAVE1-deficient mice, the number of nodes of Ranvier was decreased, and the mice had hypomyelination in the corpus callosum and optic nerve, consistent with a defect in myelin formation.

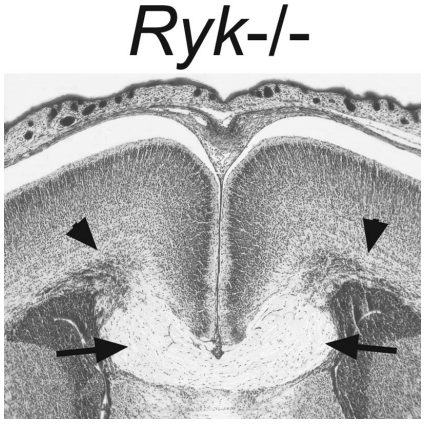
▲ Development/Plasticity/Repair

The Wnt Receptor Ryk and the Corpus Callosum

Thomas R. Keeble, Michael M. Halford, Clare Seaman, Nigel Kee, Maria Macheda, Richard B. Anderson, Steven A. Stacker, and Helen M. Cooper

(see pages 5840–5848)

For axons seeking to get to the other hemisphere, it is good idea to pack along some Ryk (receptor related to tyrosine kinase) according to work by Keeble et al. this week. Signaling by Wnt ligands directs many developmental processes, each coupled to specific receptor interactions. In general, Wnt–Ryk interactions are chemorepulsive, whereas Wnt–Frizzled are chemoattractive. The authors examined Wnt signaling associated with Ryk. In mice lacking Ryk, the corpus callosum was abnormally wide, and loosely fasciculated axons accumulated on either side of the midline. Although $Ryk^{-/-}$ neurons successfully crossed the midline, they were unable to escape into the contralateral hemisphere and even made turns back toward the midline. The precise temporal and spatial pattern of Wnt5a expression suggested that it drives callosal axons beyond the midline by a chemorepulsive mechanism. Coimmunoprecipitation showed that Wnt5a binds the extracellular domain of Ryk.



The panel shows a coronal section of embryonic day 18 forebrain in Ryk $^{-/-}$ mice. Nissl stains show that callosal axons cross the midline but then form axon bundles rather than entering the contralateral hemisphere. See the article by Keeble et al. for details.

■ Behavioral/Systems/Cognitive

Estrogen Levels and μ-Opioid Neurotransmission

Yolanda R. Smith, Christian S. Stohler, Thomas E. Nichols, Joshua A. Bueller, Robert A. Koeppe, and Jon-Kar Zubieta

(see pages 5777–5785)

The rating of pain differs between men and women, and fluctuates in women with their estrous cycle. In this week's *Journal*, Smith et al. examined whether these differences might be attributable to estrogen regulation of endogenous opioid neurotransmission. Women subjects were treated for 1 week with estradiol via transdermal patches. Treatment was given at the follicular phase of the cycle when endogenous gonadal steroids are low. Using positron emission tomography (PET) of a μ-opioid receptor-selective tracer, the authors measured receptor binding of the PET ligand. In pain processing areas previously associated with sex differences (thalamus, hypothalamus, nucleus accumbens, amygdala), estradiol increased baseline receptor levels by 15–32%. During a sustained painful stimulus—hypertonic saline delivered to a jaw muscle—treated subjects displayed regional activation of opioid neurotransmission as measured by reduced *in vivo* receptor availability. In a test of recall, estrogen-treated subjects also underestimated the pain.

♦ Neurobiology of Disease

Strain-Dependent Regeneration without Nogo-A

Leda Dimou, Lisa Schnell, Laura Montani, Carri Duncan, Marjo Simonen, Regula Schneider, Thomas Liebscher, Miriam Gullo, and Martin E. Schwab

(see pages 5591–5603)

Nogo-A means what it says. This molecule acts as one of the barriers against neurite outgrowth and regeneration after injury in the CNS. However, Dimou et al. report that the impact of the no-go signal in part depends on your background. The authors compared the regenerative potential of two commonly used mouse strains, 129X1/SvJ and C57BL/6. Sv129 mice had lower endogenous levels of Nogo-A and Nogo-B. Two weeks after a partial spinal cord transection, regeneration of the corticospinal tract was enhanced in Nogo-A-deficient mice of both strains, but knockouts on the Sv129 background had two to four times more regenerating fibers caudal to the lesion than BL/6 mice. Dorsal root ganglia explants from wild-type Sv129 mice also displayed more neurite outgrowth than those from BL/6 mice. The two strains also displayed a dizzying array of differences in mRNA expression patterns in intact and injured spinal cord.