This Week in The Journal

● Cellular/Molecular

Wnt Enhances NMDA Currents via Noncanonical Pathway

Waldo Cerpa, Abigail Gambrill, Nibaldo C. Inestrosa, and Andres Barria

(see pages 9466–9471)

Wnts are a large family of secreted proteins that regulate cell polarity and migration throughout development, from gastrulation to synaptogenesis. Wnt binds to Frizzled receptors along with different coreceptors, leading to activation of Disheveled. Depending on which coreceptor is involved and whether Disheveled is localized to the membrane, Wnt signaling either leads to accumulation of cytoplasmic β-catenin, which then enters the nucleus and activates transcription of specific genes (the canonical pathway), or it activates Rho GTPases, calcium influx, protein kinase C (PKC), and/or JNK signaling (noncanonical pathways). Expression of Wnts and their downstream effectors persists in adult CNS and is involved in synaptic plasticity. Cerpa et al. report that Wnt-5a regulates NMDA receptor currents in mouse hippocampal slices. Wnt scavengers reduced NMDA currents, whereas exogenous Wnt-5a increased currents, apparently by increasing the proportion of NMDA receptors incorporating the NR2B subunit. The initial increase required calcium influx and PKC, but sustained increase required JNK signaling.

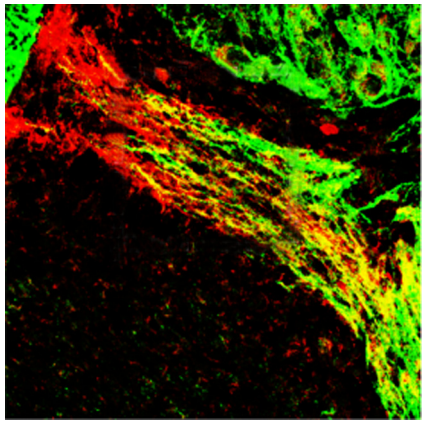
▲ Development/Plasticity/Repair

Schwann Cells Induce Axons to Secrete Schwann Cell Survival Factor

Zhenzhong Ma, Jiajing Wang, Fei Song, and Jeffrey A. Loeb

(see pages 9630–9640)

Alternatively spliced forms of neuregulin-1 (NRG1) are important at many stages of nervous system development, particularly in processes requiring neuron–glia communication. For example, expression of membrane-bound NRG1 on peripheral axons guides mature Schwann cells as they extend along axons during myelination. NRG1 is also required for survival of Schwann cell precursors, and Ma et al. suggest that, here, soluble NRG1 is required. Selectively disrupting soluble NRG1 signaling in chick motor axons at embryonic days 5–7 increased Schwann cell apoptosis and reduced differentiation of Schwann cell precursors into immature Schwann cells. Axonal release of soluble NRG1 was induced by brain-derived neurotrophic factor (BDNF) produced by Schwann cells. Thus, Schwann cell secretion of BDNF promotes axonal secretion of NRG1, which promotes Schwann cell survival and differentiation. This positive feedback loop might ensure that the number of myelinating Schwann cells precisely matches the number of axons that require myelination.



Matrix-bound soluble NRG1 (green) is colocalized with Schwann cells (red) in embryonic chick motor nerve. See the article by Ma et al. for details.

■ Behavioral/Systems/Cognitive

V1 and Prefrontal Cortical Volumes Are Inversely Correlated

Chen Song, Dietrich Samuel Schwarzkopf, Ryota Kanai, and Geraint Rees

(see pages 9472–9480)

Cerebral cortex has expanded over the course of hominid evolution, but not uniformly: anterior prefrontal cortex (aPFC), which is involved in problem-solving and complex planning, is especially enlarged in humans, whereas primary visual cortex (V1) has expanded less. The size of these and other brain areas varies greatly across individuals—up to threefold for V1. Most studies of interindividual differences have asked whether variations in the size of an area correlate with variation in performance on tasks associated with that area. Such correlations have been found. Song et al. asked whether expansion of one cortical area correlated with expansion of other areas in the same person. They found the opposite: V1 volume was inversely correlated with the volume of aPFC and of the gray matter of the entire brain. The volume of aPFC was positively correlated with whole-brain volume, however. Thus, the same volume correlations that occur across species also occur across individual humans.

♦ Neurobiology of Disease

BDNF–Akt-mTOR Pathway Is Hyperactive in Trisomic Mice

José Antonio Troca-Marín, Alexandra Alves-Sampaio, and María Luz Montesinos

(see pages 9445–9455)

Synaptic activity paired with postsynaptic spiking causes dendritic release of brain-derived neurotrophic factor (BDNF). BDNF binds to postsynaptic receptors, leading to activation of Akt. Akt activates the mammalian target of rapamycin (mTOR), which interacts with translational machinery to stimulate local synthesis of glutamate receptors and other proteins that mediate long-term potentiation (LTP). LTP increases the probability that synaptic activity will cause spiking. Thus, BDNF–mTOR pathways form a positive feedback loop. BDNF levels are elevated in Down's syndrome, and Troca-Marín et al. found that it was also elevated in hippocampal neurons from trisomic mice. Furthermore, Akt, mTOR, and translation initiators were hyperactivated, translation of AMPA receptor subunits was elevated, and these potentiated states could not be further potentiated by BDNF. Rapamycin reduced basal activation of mTOR and its targets to wild-type levels, after which BDNF could upregulate these pathways. Which step in the BDNF–mTOR signaling loop was initially disrupted remains unknown, however.