This Week in The Journal

● Cellular/Molecular

Actin-Branching Protein Localization in Spines

Bence Rácz and Richard J. Weinberg

(see pages 5654–5659)

Dendritic spines start as thin filaments, but as their synapses strengthen, they evolve into short mushroom-shaped structures, presumably due to changes in the actin cytoskeleton. Actin dynamics are regulated by actin-binding proteins, some of which are concentrated in discrete domains of the spine. This week, Rácz and Weinberg describe the localization of a protein involved in actin branching, based on immunoelectron microscopy. By averaging data from many spines, the authors found that ARPC-2, a part of the Arp2/3 protein complex, is concentrated in a ring at a fixed distance from the plasma membrane, about halfway between the spine neck and the postsynaptic density. This region was previously defined as an endocytic zone, rich in proteins involved in activity-dependent endocytosis and receptor trafficking. This is consistent with previous evidence that Arp2/3 is involved in clathrin-coated vesicle formation and movement. The localization also suggests that Arp2/3 as a potential mediator of synaptic plasticity.

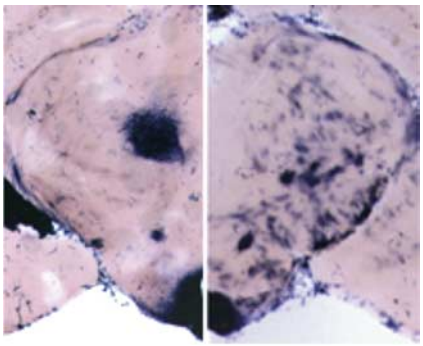
▲ Development/Plasticity/Repair

Role for Frizzled in Neuron Survival

Chunqiao Liu, Yanshu Wang, Philip M. Smallwood, and Jeremy Nathans

(see pages 5641–5653)

Secreted proteins of the Wnt family bind to receptor proteins of the Frizzled family, activating signaling pathways important throughout development. In this issue, Liu et al. add to mounting evidence that Wnt–Frizzled signaling is also essential for survival of adult neurons. Frizzled 5 (Fz5) is expressed throughout life in mouse retina, hypothalamus, and parafascicular nucleus (PFN) of the thalamus. Fz5 knock-out in embryonic tissues did not appear to hinder nervous system development (presumably because other Frizzleds compensate for the loss); but after birth, knock-out mice had progressive retinal degeneration and loss of Fz5-expressing neurons in the PFN. Neuron loss in the PFN was preceded by down-regulation of several genes, including Wnt9b and β-catenin, which are likely to be involved in Fz5 signaling. Knocking out Fz5 in a subset of adult PFN neurons resulted in their death, indicating that Fz5 is required cell-autonomously: PFN neurons must express Fz5 to survive.



PFN neurons (purple) survive in adult control mice (left) but are lost after conditional knock-out of Fz5 (right). See the article by Liu et al. for details.

■ Behavioral/Systems/Cognitive

Horizontal-Cell Feedback to Rods

Wallace B. Thoreson, Norbert Babai, and Theodore M. Bartoletti

(see pages 5691–5695)

Until now, it was thought that rods, unlike cones, do not receive feedback from horizontal cells. But by using a voltage-ramping protocol to measure calcium currents in salamander rods, Thoreson et al. have demonstrated that rods do receive such feedback. Hyperpolarizing horizontal cells with voltage steps or light increased the amplitude of I_{Ca} in synaptically coupled rods and caused I_{Ca} to activate at more negative potentials. These changes were blocked by adding a pH buffer, suggesting that like feedback to cones, feedback to rods may be mediated by a decrease in protons in the synaptic cleft. Horizontal-cell feedback to cones is thought to help generate center-surround receptive fields, but the role of feedback to rods is unclear. Bright light causes rods to hyperpolarize, which would reduce I_{Ca}; because the feedback from horizontal cells is sufficient to counteract this reduction, it may help to restore light sensitivity.

♦ Neurobiology of Disease

MARK2 Kinase in Migration

Tamar Sapir, Sivan Sapoznik, Talia Levy, Danit Finkelshtein, Anat Shmueli, Thomas Timm, Eva-Maria Mandelkow, and Orly Reiner

(see pages 5710–5720)

The kinase MARK2 regulates interactions between microtubule-associated proteins and tubulin, and it functions in the development of neuronal polarity. One might therefore expect MARK2 to be involved in neuronal migration, but such a role was not reported before this week. Sapir et al. used *in utero* electroporation to introduce short hairpin RNAs (shRNAs) targeting MARK2, as well as shRNA-resistant *MARK2* cDNA, into developing mouse cortex. After MARK2 knockdown, neurons failed to migrate beyond the intermediate zone, and they failed to acquire a normal bipolar morphology. Elevating MARK2 levels also blocked migration from the intermediate zone, suggesting that kinase activity must be within a set range for migration to occur. The effects of MARK2 knockdown may have been due to disruption of microtubule dynamics, because staining for stabilized microtubules increased, protein turnover at the tips of microtubules decreased, and polymerization slowed. MARK2 knockdown also abolished the continual forward movement of centrosomes that normally accompanies neuronal migration.