This Week in The Journal

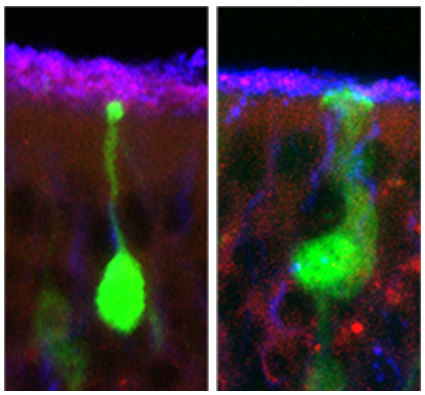
● Cellular/Molecular

Localization of Ciliary Proteins Requires PACS-1

Paul M. Jenkins, Lian Zhang, Gary Thomas, and Jeffrey R. Martens

(see pages 10541–10551)

Proper subcellular localization of proteins is essential for neuronal function. In olfactory sensory neurons, olfactory receptors, and their downstream effectors—G-proteins, adenylyl cyclase, and cyclic-nucleotide-gated (CNG) channels—are expressed predominantly in the apical cilia that project from the olfactory epithelium. Mislocalization of these proteins causes anosmia. Jenkins et al. report that proper targeting of one of these components, the CNG channel, requires the trafficking protein phosphofurin acidic cluster-sorting protein 1 (PACS-1), which specifically binds CNG channel subunit CNGB1b. PACS-1 and CNGB1b were phosphorylated by CK2, and inhibiting CK2 caused loss of CNG channels from cilia and reduced odor-evoked responses in olfactory sensory neurons. Furthermore, in kidney cells, RNA-mediated silencing of PACS-1 disrupted ciliary trafficking of transfected CNG channels. Interestingly, although PACS-1 was expressed in the dendritic knob from which olfactory cilia emanate, it was not present within the cilia, suggesting that the knob is a hub for trafficking of proteins into the cilia.



CNG channels (red) are present in the apical cilia (visualized with tubulin staining, blue) in olfactory sensory neurons infected with GFP (green, left). Localization is disrupted in neurons infected with GFP + inactive PACS-1 (right). See the article by Jenkins et al. for details.

▲ Development/Plasticity/Repair

Growth Cone Collapse Is Associated With Macropinocytosis

Adrianne L. Kolpak, Jun Jiang, Daorong Guo, Clive Standley, Karl Bellve, et al.

(see pages 10488–10498)

Macropinocytosis is an actin-driven endocytic process that can be induced by growth factors. In non-neural cells, macropinosomes are produced by actin-supported plasma membrane extensions called ruffles, which fold back on themselves, forming large fluid-filled compartments. A similar, but not identical, process is associated with growth cone collapse in neurons. Like ruffles, growth cones are actin-based structures; localized extracellular guidance cues cause them to extend or retract, sometimes folding back on themselves. Kolpak et al. report that repulsive guidance cues increased the number of dextran-labeled macropinosomes in cultured chick retinal ganglion neurons. Inhibiting either dynamin, a protein involved in endocytosis, or the actin motor myosin II blocked dextran uptake and prevented induction of growth cone collapse and turning by repulsive guidance molecules. In contrast, enhancing myosin II activity increased growth cone collapse. These results support the hypothesis that membrane trafficking and recycling is intimately linked to guided neurite extension.

■ Behavioral/Systems/Cognitive

Microbands of Purkinje Cells Are Activated Synchronously

Ilker Ozden, Megan R. Sullivan, H. Megan Lee, and Samuel S.-H. Wang

(see pages 10463–10473)

Climbing fibers from circumscribed regions of the inferior olive innervate Purkinje cells within specific zones of the cerebellar cortex, and these in turn project to a defined region of deep cerebellar nuclei, forming modules that regulate motor output. Climbing fibers convey motor error signals based on sensory input, and they transmit reinforcement information during classical conditioning. But because the fibers typically fire only about once per second, how they reliably convey information on the time scale required for motor control is not clear. Using *in vivo* calcium imaging to visualize climbing-fiber-induced spikes in Purkinje cells of anesthetized rodents, Ozden et al. found that spontaneous activity in climbing fibers induced correlated activity in "microbands" of Purkinje cells. Air puffs to the face, which are expected to increase climbing fiber firing, increased the frequency and synchrony of Purkinje cell spiking. Synchrony of evoked responses was reduced by gap junction blockers applied to the olive.

♦ Neurobiology of Disease

Tau Hyperphosphorylation Alters Synaptic Function

Manuela Polydoro, Christopher M. Acker, Karen Duff, Pablo E. Castillo, and Peter Davies

(see pages 10741–10749)

Hyperphosphorylation and conformational changes of the microtubule-associated protein tau lead to intracellular aggregation of the protein in paired helical filaments and neurofibrillary tangles. These aggregates characterize several forms of dementia, including Alzheimer's disease (AD). The role of tau aggregates in disease progression is not clear, but Polydoro et al. report that tau aggregates can alter synaptic function before neurodegeneration becomes widespread. Mice that express normal human tau protein instead of mouse tau gradually developed aggregates of hyperphosphorylated tau in forebrain structures similar to those affected in AD. Year-old mice had moderate tau pathology but little neuronal degeneration. These mice showed deficits in object recognition and spatial memory tasks. Electrophysiological recordings from hippocampal slices showed an increase in paired pulse facilitation, suggestive of a decreased probability of neurotransmitter release. In addition, high-frequency stimulation was not sufficient to induce long-term potentiation in hippocampal neurons, possibly because charge transfer during bursts was reduced.