

# This Week in The Journal

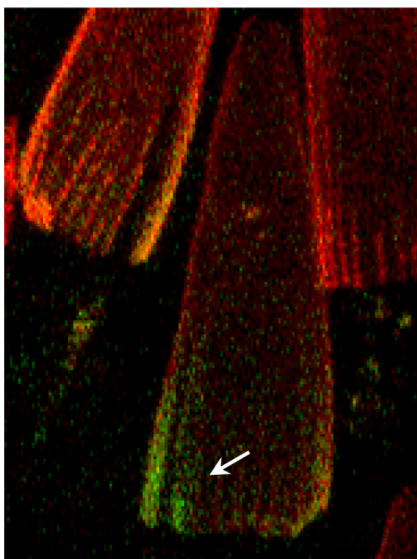
## ● Cellular/Molecular

### *Barrier Likely Keeps Plasma Membrane Proteins from Rod Disks*

Ina Nemet, Guilian Tian, and Yoshikazu Imanishi

(see pages 8164–8174)

The outer segments (OS) of rod photoreceptors contain stacks of membranous disks enclosed within the plasma membrane (PM). The disks and PM contain different sets of proteins: for example, disks house components of the phototransduction machinery, whereas the PM contains the cyclic nucleotide-gated channels (CNGs) that close in response to light. How disks form and how proteins are segregated between PM and disks are poorly understood. To address these questions, Nemet et al. expressed CNG $\alpha$  subunits tagged with a photoconvertible fluorescent protein in frog rods. CNG $\alpha$  was concentrated in vertical stripes in the OS PM, but it was absent at the base of the OS where disk formation occurs. After photoconversion of previously expressed CNG $\alpha$ , newly synthesized CNG $\alpha$  first appeared at the lateral portion of the OS base. Most CNG $\alpha$  was immobile, but some diffused vertically. This mobile fraction did not enter



Newly synthesized CNG $\alpha$  (green) is inserted near the lateral base of rod OS, but it ultimately is concentrated in vertical bands (red) in the distal portion of the OS. See the article by Nemet et al. for details.

the bottom of the OS, however, suggesting a diffusion barrier prevents PM proteins from entering the disk-forming region.

## ● Development/Plasticity/Repair

### *Increasing Astrocytic BDNF Secretion May Boost Remyelination*

Clifton G. Fulmer, Melissa W. VonDran, Althea A. Stillman, Yangyang Huang, Barbara L. Hempstead, et al.

(see pages 8186–8196)

Brain-derived neurotrophic factor (BDNF) supports differentiation, maturation, and survival of both neurons and glia. BDNF levels are reduced in several neurodegenerative disorders and in patients with relapsing-remitting multiple sclerosis (MS). Loss of BDNF exacerbates myelin loss after cuprizone treatment (a mouse model of MS). Although implanting BDNF-producing stem cells has been shown to promote oligodendrocyte differentiation after demyelination, promoting endogenous production might be a more viable treatment option. A possible source of endogenous BDNF is astrocytes, which upregulate BDNF expression after injury. Because the metabotropic glutamate receptor agonist ACPD stimulates BDNF production by astrocytes *in vitro*, Fulmer et al. asked whether ACPD would promote remyelination *in vivo*. Indeed, a single injection of ACPD into mouse corpus callosum increased the number of astrocytes expressing BDNF after cuprizone treatment and at least partially reversed cuprizone-induced reductions in levels of two myelin-associated proteins. The latter effect was blocked by either inhibiting the BDNF receptor or knocking out BDNF expression selectively in astrocytes.

## ● Systems/Circuits

### *Dendritic Arbor Size Influences Encoding Capabilities*

Guy Eyal, Huibert D. Mansvelder, Christiaan P.J. de Kock, and Idan Segev

(see pages 8063–8071)

Action potential shapes affect not only the time course of neurotransmitter release, but also how fast a neuron can fire, and thus its encoding ability. In particular, the speed of spike onset at the spike initiating zone (SIZ)

determines how well the neuron can encode changes in synaptic input: faster onset allows better encoding. Although spike onset rapidness is determined largely by local voltage-gated Na<sup>+</sup> channels, Eyal et al. have discovered a hitherto unrecognized contributor: the size of the dendritic arbor. In computational models, increasing the dendritic arbor size and thus its impedance load (i.e., the ratio of somatodendritic to axonal conductance) decreased the effective time constant at the SIZ, which increased spike onset rapidness. The significance of this effect was revealed by comparing the encoding capabilities of reconstructed models of rat and human cortical pyramidal neurons: the larger dendritic arbor of human neurons allowed these neurons to track input modulations approximately threefold faster than those tracked by rat neurons.

## ● Neurobiology of Disease

### *Auditory Hallucinations Are Linked to Weak Prediction Errors*

Guillermo Horga, Kelly C. Schatz, Anissa Abi-Dargham, and Bradley S. Peterson

(see pages 8072–8082)

Throughout our lives, we use associations between events to create internal models of the world. Each moment's sensory input is compared to these internal models to generate predictions about what will happen next. Expectations feed back to primary cortical areas and shape perception of subsequent sensory input by priming neural circuits that encode the predicted stimulus; this boosts recognition of expected stimuli in noisy environments. When sensory inputs cannot be reconciled with expectations, however, sensory cortex is thought to generate prediction errors that tell higher brain areas to update expectations. Deficits in generating prediction errors and/or updating predictions have been proposed to underlie several features of schizophrenia, including hallucinations. Horga et al. support this hypothesis with analyses of functional magnetic resonance imaging data, which indicate that prediction error signals in auditory cortex during an auditory speech–nonspeech decision task were weaker in schizophrenic patients than in controls. The deficit was correlated with increased auditory cortical activity during silence, which was associated with auditory hallucinations.