# *This Week in The Journal*

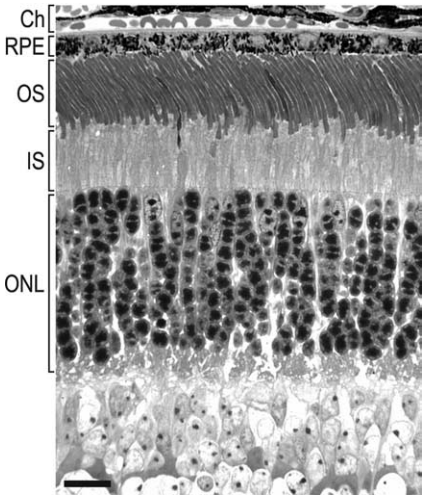
## ● Cellular/Molecular

### *IRBP* Is *Required for Retinaldehyde Transport*

Minghao Jin, Songhua Li, Steven Nusinowitz, Marcia Lloyd, Jane Hu, Roxana A. Radu, Dean Bok, and Gabriel H. Travis

(see pages 1486–1495)

In photoreceptors, absorption of a photon by an opsin-associated chromophore causes isomerization of 11-*cis* to all-*trans* retinaldehyde, which activates the opsin. Before the chromophore can absorb another photon, the all-*trans* isomer must be converted back to the 11-*cis* form. Because part of this recycling process occurs in the retinal pigment epithelium (RPE), retinaldehyde isoforms must be shuttled between the retina and RPE. Interphotoreceptor retinoid-binding protein (IRBP) was thought to mediate this shuttling until IRBP knock-out was found not to affect retinaldehyde movement. More recently, however, it was discovered that the mouse strain in which the IRBP-null mice were generated also harbored a deleterious mutation in another critical visual cycle protein. Jin et al. have now created a new IRBP knock-out line that expresses the wild-type form of the second protein. In these mice, transport of retinaldehyde isoforms was impaired, indicating that IRBP is indeed required for this process.




Light microscopic image of retina showing the choroid (Ch), RPE, photoreceptor outer segments (OS), inner segments (IS), and outer nuclear layers (ONL). In IRBP knock-out mice, the outer segments are shorter, wider, and irregularly dispersed, and fewer nuclei are present in the ONL. Scale bar, 20 $\mu$m. See the article by Jin et al. for details.

## ▲ Development/Plasticity/Repair

### *FRMP Is Expressed in Some Axons During Synaptogenesis*

Sean B. Christie, Michael R. Akins, James E. Schwob, and Justin R. Fallon

(see pages 1514-1524)

Fragile X mental retardation protein (FMRP) is an RNA-binding protein expressed in neuronal somata and dendrites throughout the brain. FMRP is thought to function in neuronal plasticity, and its loss causes mental retardation and autism. This week, Christie et al. report that, in addition to somatodendritic compartments, FMRP and its homologs FXR1P and FXR2P are present in granular particles in the presynaptic terminals and axons of a subset of neurons in cortex, hippocampus, and olfactory bulb. These "fragile X granules" are seen during defined developmental epochs corresponding to periods of synaptic development, and their numbers increase during reinnervation in the olfactory bulb. FXR2P is required for fragile X granule formation, because its knock-out eliminates granules. In contrast, FMRP appears to restrict granule formation, because its knock-out increases the number of granules in neurons that normally express them. These data raise the possibility that increases in fragile X granules might contribute to mental retardation or autism.

## ■ Behavioral/Systems/Cognitive

### *Adenosine Receptor Is Required for Increased Slow-Wave Activity*

Theresa E. Bjorness, Christine L. Kelly, Tianshu Gao, Virginia Poffenberger, and Robert W. Greene

(see pages 1267–1276)

Sleep deprivation impairs attention, working memory, and other cognitive functions. Recovery from sleep deprivation involves increases not only in sleep duration, but also in sleep intensity, as reflected in increases in the amplitude of synchronized slow-wave activity (SWA) during non-REM sleep. Enhancement of SWA is correlated with increased performance on working memory tests, suggesting that SWA may contribute to maintaining cognitive function. Much evidence suggests that adenosine is involved in modulating SWA. To examine this hypothesis, Bjorness et al. recorded electroencephalographic activity in mice in which adenosine $A_1$ receptors ($AdoA_1Rs$) were conditionally deleted. $AdoA_1R$ knock-out reduced the magnitude of SWA during non-REM sleep without affecting sleep duration, and mice without $AdoA_1R$ did not display the normal enhancement of SWA after sleep deprivation. Additionally, many $AdoA_1R$–knock-out mice performed poorly on a working memory task after sleep deprivation, supporting the hypothesis that modulation of SWA is linked to cognitive function.

## ♦ Neurobiology of Disease

### *Disrupting Huntingtin–Ins$P_3$R1 Interactions Reduces Pathology*

Tie-Shan Tang, Caixia Guo, Hongyu Wang, Xi Chen, and Ilya Bezprozvanny

(see pages 1257–1266)

Huntington's disease is caused by a polyglutamine expansion in huntingtin protein. The mutation leads to apoptosis specifically of striatal medium spiny neurons (MSNs), causing motor impairments and eventual death of affected individuals. Mutant huntingtin has an increased affinity for the cytoplasmic tail of type 1 inositol 1,4,5-trisphosphate receptor ($InsP_3R1$), which releases calcium from internal stores. Binding of mutant huntingtin to $InsP_3R1$ increases receptor activity, which is hypothesized to cause calcium toxicity. To disrupt the interaction between huntingtin and $InsP_3R1$, Tang et al. have overexpressed the cytoplasmic tail peptide of $InsP_3R1$ in MSNs from mice expressing mutant huntingtin. Expression of the $InsP_3R1$ peptide normalized calcium elevation following glutamate application and prevented glutamate-induced apoptosis in cultured neurons. Remarkably, viral-mediated expression of the peptide in the striatum *in vivo* reduced shrinkage and death of MSNs and improved motor function. Therefore, expression of $InsP_3R1$ peptides may be an effective treatment for Huntington's disease.