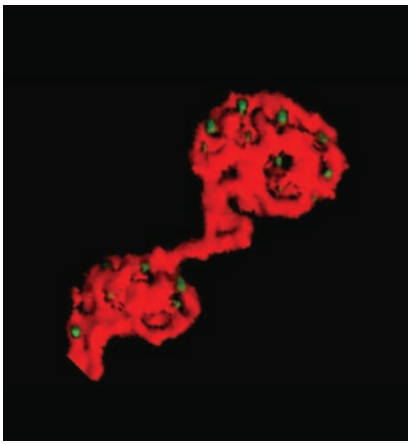
# *This Week in The Journal*

## ● Cellular/Molecular

### *Seeing Presynaptic Calcium Channels*

Fumiko Kawasaki, Beiyan Zou, Xia Xu, and Richard W. Ordway
(see pages 282–285)

The *Drosophila* gene *cacophony* (*cac*) encodes the $\alpha$1 subunit of a presynaptic voltage-gated calcium channel. This gene locus was first identified, and named, because of a role in the male courtship song. These channels, activated during an action potential, trigger neurotransmitter release at the fly neuromuscular junction. To visualize their location in live animals, Kawasaki et al. created a transgenic fly in which $\alpha$1 subunits were tagged with enhanced green fluorescent protein (EGFP). Deletion of the *cac* gene is embryonic lethal, but flies rescued with the transgene had normal viability and EPSCs, confirming that the transgene was functional. CAC1-EGFP was expressed on synaptic boutons at larval neuromuscular junctions in register with postsynaptic active zones. In the adult fly, CAC1-EGFP marked synaptic axonal swellings of 1–2 $\mu$m that were spaced at 1–2 $\mu$m intervals. The new protein will allow live imaging of calcium channels as well as colocalization of other presynaptic proteins.



The fly neuromuscular junction was labeled with an EGFP-tagged presynaptic calcium channel. See the article by Kawasaki et al. for details.

## ▲ Development/Plasticity/Repair

### *Branding Neurons by their Birthdate*

Mitsuhiro Hashimoto and Katsuhiko Mikoshiba
(see pages 286–296)

The "inside-out" organization of the developing cerebral cortex makes for a birthdate-specific set of layers. First-born neurons end up in internal layers, whereas younger cells migrate to outer layers. Thus progenitor cells that divide on a given day are expected to give rise to distinct neuronal populations. Studies of the function and morphology of these cohorts requires a time-sensitive labeling method. In this issue, Hashimoto and Mikoshiba used single ventricular injections of a nonreplicating adenoviral vector carrying the *LacZ* gene to pulse-label progenitors in the subventricular zone. Colabeling with bromodeoxyuridine demonstrated that virus could infect and label cells within a 4 hr time window. Distinct cohorts were observed after different injection times. For example, injection on embryonic day 11.5 (E11.5) preferentially labeled subplate and Cajal-Retzius cells, whereas injection on E12.5 labeled neurons in the cortical plate. This approach provides another strategy to examine the molecular processes that determine neuronal fate.

## ■ Behavioral/Systems/Cognitive

### *A Cyclic Nucleotide Channelopathy in Two Sisters*

Dimitri Tränkner, Herbert Jägle, Susanne Kohl, Eckart Apfelstedt-Sylla, Lindsay T. Sharpe, U. Benjamin Kaupp, Eberhart Zrenner, Reinhard Seifert, and Bernd Wissinger
(see pages 138–147)

Imagine living in a blurry, black-and-white world. Such is the case for those with achromatopsia, a family of disorders that arises from gene mutations in cones. This week, Tränkner et al. describe two sisters with incomplete achromatopsia. They carry two heterozygous mutations of the *CNGA3* gene that encodes the A3 subunit of the cyclic nucleotide-gated channel. The girls showed increased sensitivity to light (photophobia), reduced visual acuity, and color-discrimination defects. One mutation was within an intracellular loop, whereas the other was within the pore region of the channel subunit. When homomeric A3 channels were expressed in HEK293 cells, one mutant was nonfunctional, whereas the pore mutation dramatically altered channel activity. However, coexpression of the pore mutant with the B3 subunit, the expected subunit mixture in intact cells, restored wild-type channel properties except for altered calcium permeability. Thus this channelopathy appears to result from a relatively subtle change in ion flux through the channel.

## ♦ Neurobiology of Disease

### *Huntingtin and Vesicle Trafficking*

Zheng-Hong Qin, Yumei Wang, Ellen Sapp, Benjamin Cuiffo, Erich Wanker, Michael R. Hayden, Kimberly B. Kegel, Neil Aronin, and Marian DiFiglia
(see pages 269–281)

In Huntington's disease, the huntingtin protein (htt) contains a polyglutamine expansion at its N terminus, leading to selective neuronal dysfunction and death. Expression of mutant htt in mice, or in cells *in vitro*, results in marked neuronal accumulation of insoluble protein aggregates, although their relationship to cell death is disputed. In this week's *Journal*, Qin et al. examined the so-called huntingtin bodies in search of alternate forms of htt. The htt bodies contained an insoluble core with fibrillar htt, but also a shell with soluble htt and several cytosolic proteins including heat shock protein 70 and dynamin. Cells containing htt bodies had impaired internalization of membrane proteins, suggesting that the soluble htt sequestered proteins involved in vesicular trafficking. Deletion of a polyproline region adjacent to the polyglutamate expansion reduced htt bodies and prevented redistribution of cytosolic proteins. Thus abnormal protein interactions might allow soluble forms of mutant htt to deprive the neuron of critical cytoplasmic proteins.