

# This Week in The Journal

## ● Cellular/Molecular

### *Drosophila Vap Is Required for Axonal Trafficking of Dscam1*

Zhen Yang, Sung Un Huh,  
J. Michelle Drennan, Hitesh Kathuria,  
Juan S. Martinez, et al.

(see pages 17241–17250)

Down syndrome cell adhesion molecule (DSCAM) mediates homophilic repulsion between neurites, thus increasing the coverage of dendritic and axonal fields. *Drosophila Dscam1*, unlike its vertebrate homolog, undergoes alternative splicing in its ectodomain, which generates thousands of variants with distinct binding affinities, and in its transmembrane domain, which produces one isoform (TM1) that is excluded from axons, and another (TM2) that is not. Yang et al. have identified two proteins that interact with Dscam1: ubiquitin and Vap. Vap interacted preferentially with the Dscam1-TM2 isoform, and loss of Vap reduced axonal levels of Dscam1-TM2. As a result, homophilic repulsion of axons was reduced. Interestingly, Vap is the *Drosophila* homolog of human VAPB, a transmembrane protein that is highly expressed in the endoplasmic reticulum and Golgi and is mutated in some forms of amyotrophic lateral sclerosis (ALS). Whether VAPB is involved in axonal trafficking of DSCAM or other human proteins, and whether disrupting this function contributes to VAPB-linked ALS, remain unknown.

## ▲ Development/Plasticity/Repair

### *Numb Regulates Cell Cycle Progression and Terminal Division*

Amel Kechad, Christine Jolicoeur,  
Adele Tufford, Pierre Mattar,  
Renee W. Y. Chow, et al.

(see pages 17197–17210)

Asymmetric cell division, in which cell fate determinants are unequally distributed between daughter cells, is an important mechanism for generating diverse cell types during development. Two types of asymmetric divisions occur in the nervous system: self-renewing divisions that generate one progenitor and one post-

mitotic neuron, and terminal divisions that produce two postmitotic cell types. Numb is a cytoplasmic protein that can associate with the plasma membrane and become differentially distributed during cell division, but it does not appear to specify cell fate directly. Instead it may help determine cell fate by regulating expression of receptors for extracellular cues. Because such cues change over time, Numb can have different effects at different stages of development. Kechad et al. report that early in retinal development, Numb was required for retinal progenitor cells to progress through the cell cycle at a normal rate, but later it was required for asymmetric terminal divisions that produced one photoreceptor and one amacrine, bipolar, or Müller cell.

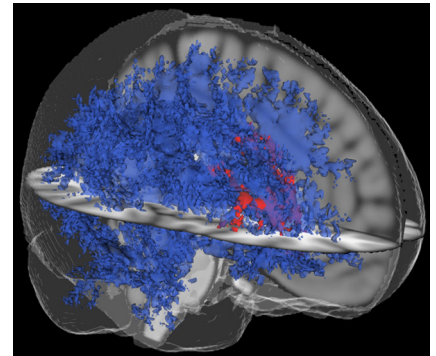
## ■ Behavioral/Systems/Cognitive

### *Taste-Selective Cells Are Present in Olfactory Cortex*

Joost X. Maier, Matt Wachowiak,  
and Donald B. Katz

(see pages 17037–17047)

The smell and taste of food combine to form a unitary perception of flavor. The orbitofrontal cortex—which contains neurons that respond preferentially to odor, taste, or oral somatosensory stimuli, as well as neurons that respond best to multimodal stimuli—has been proposed as the primary site of flavor integration. But similar unimodal and multimodal neurons have been identified in primary taste cortex, and the primary olfactory (piriform) cortex receives projections from gustatory cortex. While recording single neurons in rat posterior piriform cortex, Maier et al. discovered cells whose firing increased or decreased when specific tastants were applied to the intraoral cavity. These cells did not respond to odors, and whereas anesthetizing the tongue prevented the neurons' responses, blocking the nasal epithelium did not. Multimodal gustatory–olfactory neurons were also found in piriform cortex, suggesting that sensory integration for flavor perception occurs in primary olfactory cortex in addition to primary gustatory cortex and higher-level association areas.



DTI analysis reveals that free-water diffusion (blue) increases globally early in schizophrenia, whereas anisotropy resulting from disruption of fiber tracts (red) is limited to a small area in the frontal lobes. See the article by Pasternak et al. for details.

## ◆ Neurobiology of Disease

### *Neuroinflammation May Contribute to Schizophrenia*

Ofer Pasternak, Carl-Fredrik Westin,  
Sylvain Bouix, Larry J. Seidman,  
Jill M. Goldstein, et al.

(see pages 17365–17372)

In diffusion tensor imaging (DTI), parameters for acquiring magnetic resonance images are optimized to detect water movement in the brain. Because cell membranes block diffusion, water moves along processes, resulting in diffusion anisotropy. When many axons are oriented in the same direction, as they are in white matter, the average diffusion anisotropy in the area is high. In gray matter, where axons and dendrites are oriented in all directions, average anisotropy is low. Similarly, when axon tracts degenerate, diffusion anisotropy within them decreases. Therefore, DTI is valuable for investigating the integrity of white matter tracts. Diffusion anisotropy decreases in schizophrenia, suggesting that the disease stems from disruption of fiber tracts that connect brain areas. But anisotropy also decreases when extracellular volume increases, letting water diffuse more freely. This occurs during inflammation. Using a recently developed technique that estimates free-water diffusion, Pasternak et al. found that increased extracellular fluid is the primary abnormality in early-stage schizophrenia. They therefore conclude that neuroinflammation contributes to the disease.