# This Week in The Journal

## Cellular/Molecular

### *Astrocyte dnSNARE Transgenic Mouse Called into Question*

Takumi Fujita, Michael J. Chen, Baoman Li, Nathan A. Smith, Weiguo Peng, et al.

(see pages 16594–16604)

Recent research has revolutionized our understanding of neuron–glia signaling, implicating astrocytes as key players in brain activities from sleep to thought. But now some of that research has been thrown into question by the revelation that a critical tool may be flawed. Transgenic dnSNARE mice were engineered to overexpress a dominant-negative peptide that mimics a cytosolic piece of vesicle-associated membrane protein 2 (VAMP2), part of the SNARE protein complex required for vesicle fusion and transmitter release. Conditional expression of the transgene can be reversibly halted by administration of doxycycline, and mice are typically raised on the drug so that exocytosis functions normally during development. The dnSNARE transgene lies under control of the promoter for glial-fibrillary acidic protein (GFAP), which should have relegated the dominant-negative protein specifically to astrocytes. But now Fujita et al. show that cortical neurons, too, express the dnSNARE protein in dnSNARE mice—with far-reaching consequences—and they call on scientists to re-examine some of the conclusions drawn from dnSNARE mouse studies.

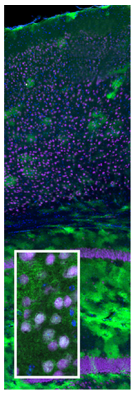
## Development/Plasticity/Repair

### *Diffusible Messengers Modulate Presynaptic Kainate Receptors*

Vernon R.J. Clarke, Svetlana Molchanova, Teemu Hirvonen, Tomi Taira, and Sari E. Lauri

(see pages 16902–16916)

Presynaptic kainate-type glutamate receptors (KAR) play a role in dynamically modulating synaptic transmission, but they also contribute to the long-term synaptic architecture of the system, because synapses may be either strengthened by synchronous activity or pruned by asynchronous activity.



EGFP (green) controlled by the GFAP promoter is expressed at low to moderate levels in neurons (purple) in mouse cortex and hippocampus. See the article by Fujita et al. for details.

At developing hippocampal CA1–CA3 synapses, ambient extracellular glutamate tonically activates high-affinity presynaptic KARs to lower the release probability of glutamate. In response to stimulation that induces long-term potentiation, activation of postsynaptic NMDA-type glutamate receptors causes calcium influx that leads to release of brain-derived neurotrophic factor (BDNF), which in turn downregulates presynaptic high-affinity KARs. Now Clark et al. demonstrate a role for presynaptic KARs in long-term depression (LTD) as well. After induction of LTD, presynaptic inhibitory KAR activity increased; upregulation of KAR activity required activation of postsynaptic nitric oxide synthetase, which produces the diffusible messenger nitric oxide. LTD induction only modulated KAR signaling in immature synapses or in synapses that received chronic BDNF to suppress maturation.

## Systems/Circuits

### *Olfactory Network Responds to Dynamic Changes in Odorants*

Terufumi Fujiwara, Tomoki Kazawa, Takeshi Sakurai, Ryota Fukushima, Keiro Uchino, et al.

(see pages 16581–16593)

In a laboratory setting, neurons in the olfactory network respond to single pulses of odorants with concentration-dependent firing. But experimental conditions do not mimic the natural world, where animals are constantly bombarded with odors that fluctuate across time and space, signaling food or a potential mate. To recreate a stimulus profile more evocative of a naturalistic setting, Fujiwara et al. presented male *Bombyx mori* silkmoths with repeated puffs of bombykol, the major sex pheromone used by the female silkmoth. Olfactory receptor neurons (ORN) and their upstream projection neurons (PN) in the antennal lobe made concentration-dependent responses to single puffs of bombykol as expected, but repetitive puffs evoked sustained PN responses that were independent of odor strength. Instead, PNs responded to fluctuations in bombykol concentration, providing greater sensitivity to a dynamic odorant landscape. The adaptation depended not on ORNs but on local inhibitory interneurons in the antennal lobe, reminiscent of other sensory systems.

## Behavioral/Cognitive

### *Amygdala Central Nucleus Narrows, Intensifies Motivation*

Mike J.F. Robinson, Shelley M. Warlow, and Kent C. Berridge

(see pages 16567–16580)

With addiction, motivation to seek out a singular activity at the expense of other rewarding experiences can lead to dangerous compulsive behaviors like binge drinking, eating, or gambling. Robinson et al. used optogenetics to dissect microcircuitry in the amygdala underlying this maladaptive reward-seeking. Without laser stimulation, transgenic rats expressing channel rhodopsin (ChR2) in the central nucleus of the amygdala (CeA) randomly pressed each of two levers that both delivered a sucrose reward. But when the researchers used the laser to activate CeA neurons when the rats pressed and earned a pellet from one of the levers, over several days the rats intensely narrowed their focus and magnified their effort, compulsively pressing the laser-associated lever at the expense of pressing the other, equally rewarding lever. In contrast, rats that expressed ChR2 in the basolateral amygdala did not develop a preference for the laser-paired lever, indicating a specific role for the CeA in narrowing and intensification of wanting.