# *This Week in The Journal*

## ● Cellular/Molecular

### *Recruiting Secretory Vesicles with DAG and Munc13-1*

Claudia S. Bauer, Robert J. Woolley, Anja G. Teschemacher, and Elizabeth P. Seward

(see pages 212–219)

This week, Bauer et al. combined voltage-clamp recordings with membrane capacitance measurements to examine modulation of secretion in bovine chromaffin cells. Their goal was to determine whether $G_q$-protein-coupled receptors ($G_q$PCRs), specifically H1 histamine receptors, regulate Munc13–1, a protein that binds diacylglycerol (DAG) and facilitates the priming of vesicles for release. Histamine decreased current through voltage-gated calcium channels by a well described direct G-protein modulation, yet the capacitance associated with stimulus-evoked secretion increased markedly. Using a double pulse depolarization protocol, the authors found that histamine increased the size of the readily releasable pool (RRP) of vesicles, and specifically increased priming of the immediately releasable pool that are positioned near calcium channels. Expression of a DAG-insensitive mutant form of Munc13-1 abolished the histamine-induced potentiation of secretion. The results define a signaling pathway leading from $G_q$PCRs to DAG to Munc13–1 that can enhance vesicle priming and exocytosis.

## ▲ Development/Plasticity/Repair

### *DISC1 Complexes in Axonal Elongation*

Tomoyasu Shinoda, Shinichiro Taya, Daisuke Tsuboi, Takao Hikita, Reiko Matsuzawa, Setsuko Kuroda, Akihiro Iwamatsu, and Kozo Kaibuchi

(see pages 4–14)

Shinichiro Taya, Tomoyasu Shinoda, Daisuke Tsuboi, Junko Asaki, Kumiko Nagai, Takao Hikita, Setsuko Kuroda, Keisuke Kuroda, Mariko Shimizu, Shinji Hirotsune, Akihiro Iwamatsu, and Kozo Kaibuchi

(see pages 15–26)

This week, two papers from the same group investigated *Disrupted-In-Schizophrenia 1* (*DISC1*), a candidate gene in some cases of schizophrenia. The results suggest that DISC1 is in the cargo-hauling business. Taya et al. examined the association between DISC1 and the NUDEL (NudE-like)/lissencephaly-1 (LIS1)/14–3-3ε complex, which contributes to axonal elongation. DISC1 acted as a cargo receptor, linking the complex to the microtubule-dependent motor protein Kinesin-1 and thus sending the complexes down axons. In a complementary paper, Shinoda et al. identified another DISC1-binding protein, growth factor receptor-bound protein 2 (Grb2). Grb2 is an adaptor that is recruited to receptor tyrosine kinases (Trk) upon Trk activation and autophosphorylation, linking the receptors to downstream signaling cascades. DISC1 formed a ternary complex joining Grb2 to Kinesin-1, an association required for Grb2 transport to distal axon segments. The complex containing Grb2 participated in axonal elongation mediated by NT-3 (neurotrophin 3).

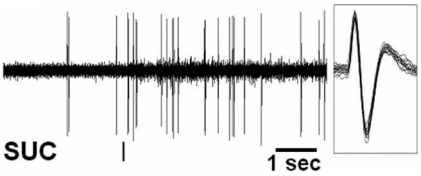
## ■ Behavioral/Systems/Cognitive

### *Sweet and Sweetener Units*

Stuart A. McCaughey

(see pages 35–45)

Having a "sweet tooth" might seem like a uniquely human characteristic, but it turns out that mice also show differences in their taste for sweets. B6 and 129 mice differ in their allelic expression of *TasIr3*, which encodes a component of the sweetener-binding receptor. McCaughey used single-unit recording of neurons in the nucleus of the solitary tract (NST), where peripheral taste fibers converge. In each strain, NST cells responded preferentially to sucrose, salt, or acid (S-, N-, and H-cells, respectively). B6 mice had more S-cells, and all neurons responded more strongly to sucrose than did neurons of 129 mice. The author deduced that strain differences likely arose from a reduced binding efficiency between sweeteners and their T1R2/T1R3 receptors in 129 mice. In response to saccharin, the response patterns suggested that B6s perceived the artificial sweetener as sweeter and less salty than 129s.




The trace shows single-unit responses in the nucleus of the solitary tract in a C57BL/6 mouse after exposure to sucrose (suc). The spike waveform is shown on an expanded time scale at the right. See the article by McCaughey for details.

## ◆ Neurobiology of Disease

### *Endocannabinoid Signaling and Febrile Seizures*

Kang Chen, Axel Neu, Allyson L. Howard, Csaba Földy, Julio Echegoyen, Lutz Hilgenberg, Martin Smith, Ken Mackie, and Ivan Soltesz

(see pages 46–58)

Although febrile seizures are common in childhood and often benign, prolonged febrile seizures can have long-term consequences. Prolonged febrile seizures paradoxically increase hippocampal GABA release and decrease seizure threshold. In this week's *Journal*, Chen et al. strengthen the case for depolarization-induced suppression of inhibition (DSI) as the underlying mechanism for these changes. DSI occurs when increases in postsynaptic calcium trigger production and release of endocannabinoids, which then bind at presynaptic CB1 receptors. The end result is reduced GABA release and heightened network excitability. In hippocampal slices from seizure-naive rats, tetanic stimulation potentiated DSI in a CB1 receptor-dependent manner. However, tetanization did not potentiate DSI in slices from animals that had experienced *in vivo* hypothermia-induced febrile seizures, in which DSI was already elevated. *In vivo*, a CB1 antagonist blocked the seizure-induced DSI potentiation, the associated upregulation of CB1 receptors, and diminished long-term hippocampal excitability.