This Week in The Journal

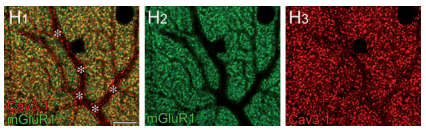
● Cellular/Molecular

A Functional Link Between T-type Channels and mGluR1

Michael E. Hildebrand, Philippe Isope, Taisuke Miyazaki, Toshitaka Nakaya, Esperanza Garcia, et al.

(see pages 9668 –9682)

The activation of T-type voltage-dependent calcium channels permits calcium influx in cells, which, in the case of neurons, leads to excitation and neurotransmitter release. T-type channels are present in the dendritic spines of many types of neurons, including the Purkinje cells (PCs) of the cerebellum, which also express the metabotropic glutamate receptor-subtype 1 (mGluR1). This receptor plays a central role in inducing long-term potentiation at the synapses between parallel fibers and PC dendrites. Hildebrand et al. have therefore looked for a possible interaction between mGluR1 receptors and T-type channels. They found that the Cav3.1 T-type channel boosts calcium currents within rodent PC dendritic spines in response to trains of parallel fiber stimulations and that this activity is selectively modulated by mGluR1. The association between the two channels, the authors suggest, could confine the activation of T-type calcium channels to synaptically activated dendritic spines.



Double immunofluorescence with mGluR1 (green) showed an extensive overlap with Cav3.1 staining (red) in Purkinje cell dendritic spines but not in dendritic shafts (marked by asterisk). See article by Hildebrand et al. for details.

▲ Development/Plasticity/Repair

Serotonin Receptors Play a Role in Enteric Neurogenesis

Min-Tsai Liu, Yung-Hui Kuan, Jingwen Wang, René Hen, and Michael D. Gershon

(see pages 9683–9699)

Aging can have some unpleasant "side effects," such as less frequent bowel movements. Neurons in the gut (enteric neurons), which are responsible for gastrointestinal motility and secretion, express many types of serotonin (5-hydroxytryptamine, 5-HT) receptor. Defects in these receptors have been linked to chronic constipation, a condition also associated with a decline in the number of enteric neurons. Enteric neuron stem cells are present in the postnatal murine bowel and could provide a source of new neurons later in life. To test this possibility, Liu et al. genetically engineered mice in which the 5-HT receptor isoform 5-HT4 was inactivated, or knocked out. Whereas in wild-type mice the number of enteric neurons increases through 4 months of age and declines thereafter, in the 5-HT4 knock-out mice the early increase does not occur and the later decline is more severe; moreover, drugs that activate 5-HT4 receptors stimulate the generation of new enteric neurons.

■ Behavioral/Systems/Cognitive

The Lateral Amygdala and the Memory of Fear

Jeong-Tae Kwon and June-Seek Choi

(see pages 9700 –9703)

Simply hearing the repeating two-note musical theme from the 1970s thriller "Jaws" sends shivers up the spine. That's because fearful experiences are not easily forgotten. To study how the memory of fear is established, researchers typically use a Pavlovian conditioning scheme. A neutral conditioned stimulus, such as a tone, is associated with an aversive unconditioned stimulus, such as a foot shock, until an animal learns to respond to the previously neutral stimulus with a defensive response, such as freezing. Evidence from many studies suggests that the lateral amygdala (LA) is involved in the acquisition and storage of fear memory, but until now its role had not been directly demonstrated. Here, Kwon and Choi show that the conditioned stimulus can be replaced with electrical stimulation of the medial division of the medial geniculate nucleus of the thalamus, which projects directly to the LA. Pairing this stimulation in rats with foot shocks resulted in long-term potentiation in the LA and freezing responses.

♦ Neurobiology of Disease

Increased Synaptic Activity May Protect from Alzheimer's Disease

Davide Tampellini, Nawreen Rahman, Eduardo F. Gallo, Zhenyong Huang, Magali Dumont, et al.

(see pages 9704 –9713)

Does increasing synaptic activity have positive or negative outcomes for people with Alzheimer's disease (AD)? Tampellini et al. set out to address this question by looking at the effects of amyloid beta (Aβ)—the rogue peptide that accumulates in the neurons of AD patients—on synapses. Several studies have indicated that increased synaptic activity promotes the secretion of Aβ to the extracellular space. Although both intracellular and extracellular Aβ have been shown to have toxic effects, Tampellini et al. reveal that synaptic activity increases extracellular Aβ and at the same time reduces intraneuronal Aβ, and that the overall effect is beneficial to the functioning of synapses. The increase in extracellular Aβ occurs because synaptic activity promotes the anterograde transport of the amyloid precursor protein in dendrites to synapses, where it is cleaved to produce Aβ. On the other hand, the decrease in intraneuronal Aβ is due to the action of the protease neprilysin.