This Week in The Journal

Cellular/Molecular

**Adenylyl Cyclase Is Required for Long-Term Fear**
Qiang Shan, Guy C.-K. Chan, and Daniel R. Storm
(see pages 12864–12867)

The hippocampus is required for memory formation, but once formed, long-term memory retention requires the cortex. In mice, contextual fear memory no longer requires hippocampal activity after a few weeks, and instead relies on anterior cingulate cortex. Shan et al. examined the role of a calcium–calmodulin-dependent type 1 adenylyl cyclase (AC1) in long-term (remote) fear memory by examining mice lacking or overexpressing this protein. Contextual fear was induced by delivering a foot shock to mice in a specific chamber. When returned to the chamber, all mice spent a significant amount of time freezing, suggesting that contextual fear learning was not impaired. No difference in freezing between wild-type and mutant mice was measured during the first 5 weeks, but at 11 weeks, mice lacking AC1 froze significantly less often than controls. At 22 weeks, freezing was reduced in wild-type mice, but was significantly more frequent in mice overexpressing AC1, suggesting that AC1 activity enhances remote fear retention.

Development/Plasticity/Repair

**Neogenin Helps Form Neural Tube**
Nigel Kee, Nicole Wilson, Melissa De Vries, DanaKai Bradford, Brian Key, and Helen M. Cooper
(see pages 12643–12653)

Development of the nervous system begins when cells on the dorsal surface of the embryo form the neural tube. Next, deep layer cells in the lateral regions of the plate elongate toward the dorsal surface and intercalate with superficial cells, forming neural folds. The neural folds elevate, eventually bending toward the midline and fusing to form the neural tube. Defects in neural tube closure occur in 1:1000 human pregnancies, causing anencephaly or spina bifida. Kee et al. now report that the receptor protein neogenin is essential in neural fold elevation. In Xenopus, knockdown of neogenin, which was expressed laterally in the neural plate, prevented elongation and intercalation of deep cells with superficial cells, likely by disrupting microtubule organization. Although the neural tube eventually formed, loss of neogenin disrupted intracellular interactions. Neuroepithelia cells did not adhere to each other or to the apical or basal surfaces, and therefore were highly disordered.

Behavioral/Systems/Cognitive

**Neuropeptide Y Enhances Fear Extinction**
Alisa R. Gutman, Yong Yang, Kerry J. Ressler, and Michael Davis
(see pages 12682–12690)

Neuropeptide Y (NPY) is widely expressed in the brain and is thought to moderate animals’ response to stress. Reduced levels of NPY have been tied to alcoholism, anxiety, and post-traumatic stress disorder. Experiments reported this week by Gutman et al. suggest that NPY may promote resilience to stress in part by enhancing retention of fear extinction. Sudden acoustic stimuli produce startle responses in rats, and responses are increased when the sound is presented with a conditioned stimulus tied to foot shock. If the conditioned stimulus is repeatedly presented without foot shock, the fear is extinguished, and the conditioned stimulus no longer potentiates acoustic startle responses. Gutman et al. found that infusion of NPY into the basolateral amygdala reduced fear potentiation of startle and accelerated fear extinction. Moreover, NPY enhanced retention of extinction memory across sessions, whereas an NPY receptor antagonist reduced extinction retention, suggesting that NPY is involved in fear extinction learning.