This Week in The Journal

Cellular/Molecular

Arrestin–GRK1 Competition Affects Rhodopsin Active Time

Thuy Doan, Anthony W. Azevedo, James B. Hurley, and Fred Rieke
(see pages 11867–11879)

Phototransduction begins when a photon activates a rhodopsin molecule. Activated rhodopsin activates the G-protein transducin, which activates phosphodiesterase, leading to decreased cGMP concentration and closure of cyclic-nucleotide-gated channels. Termination of this process requires inactivation of rhodopsin and transducin. The former is mediated by arrestin, which separates the bleached chromophore from the opsin. The affinity of arrestin for rhodopsin is increased by triple phosphorylation of the rhodopsin by the G-protein-coupled-receptor kinase GRK1. But arrestin can also bind to unphosphorylated and semiphosphorylated rhodopsin, leading Doan et al. to hypothesize that competition for rhodopsin binding between GRK1 and arrestin influences the rate of rhodopsin inactivation. Analysis of single-photon responses in mice that expressed reduced levels of either GRK1 or arrestin provided support for this hypothesis. In addition, the results suggested that, contrary to previous reports, the active time of rhodopsin was longer than that of transducin. The authors show this depends on recording conditions.

Behavioral/Systems/Cognitive

Concurrent Excitation and Inhibition Control Aplysia Feeding

Kosei Sasaki, Vladimir Brezina, Klaudiusz R. Weiss, and Jian Jing
(see pages 11732–11744)

Aplysia eat by extending and opening the radula, which grasps food and pulls it back into the buccal cavity. If food is unpalatable, the radula grasps it and pushes it out. These movements are controlled by a multifunctional central pattern generator that causes motor neurons to fire at different times relative to each other. Specifically, during ingestion, motor neuron B8, which allows the radula to grasp food, fires mainly during radula retraction, whereas during egestion, B8 fires mainly during protraction. Sasaki et al. show that the timing of B8 activity is determined by concurrent excitation and inhibition. The level of inhibition during retraction depends on the ongoing motor pattern: it is greater during egestive patterns. Concurrent excitation and inhibition is common in cortical networks, where it is thought to increase spike timing variability. It might be especially useful for shaping the activity of neurons that have different firing patterns in different tasks.

Development/Plasticity/Repair

γ-Protocadherins Mediate Astrocyte–Neuron Contacts

Andrew M. Garrett and Joshua A. Weiner
(see pages 11723–11731)

Astrocytes extend numerous fine processes that surround neuronal somata, dendrites, and synapses, and they help ensure proper synaptic function by limiting neurotransmitter diffusion and regulating ionic balance. During nervous system development, astrocytes promote synaptogenesis, in part by secreting molecules required for development of the presynaptic terminal. Astrocytes also stimulate postsynaptic development, and these effects require direct contacts between astrocytes and neurons. This week, Garrett and Weiner provide evidence that γ-protocadherins mediate these contacts between neurons and astrocytes. γ-Protocadherins colocalized with perisynaptic markers in mouse cortical and spinal cord astrocytes in cultures and in situ. In young cocultures of wild-type spinal cord neurons with astrocytes that lacked γ-protocadherin, the number of synapses was greatly reduced compared to controls. The number of synapses recovered to control levels within a few days, however. Similarly, astrocyte-specific knockout of γ-protocadherin in spinal cord in vivo delayed, but did not prevent synapse formation.

Neurobiology of Disease

Transplantation Improves Motor Function in Mutant Mice

Stefania Corti, Monica Nizzardo, Martina Nardini, Chiara Donadoni, Sabrina Salani, et al.
(see pages 11761–11771)

Spinal muscular atrophy with respiratory distress type 1 (SMARD1) is a rare infantile motor neuron disease that causes paralysis of the diaphragm and progressive muscle weakness in distal limbs. Corti et al. have obtained promising results by transplanting healthy motor neurons into spinal cords of mice harboring a defective form of the gene mutated in SMARD1. Neural stem cells obtained from healthy embryonic mice were induced to differentiate into motor neurons in culture. Purified motor neurons were then transplanted into the spinal cords of 10-day-old mutant mice, where they extended axons and improved motor performance and survival. Supplementing transplantation with pharmacological treatments to promote axon growth and overcome inhibition by myelin allowed axons to enter muscles and led to further improvements in motor function and survival, although these remained well below wild-type levels. In addition, transplantation reduced chemokine and proinflammatory cytokine levels in mutant spinal cords and improved survival of endogenous motor neurons.