This Week in The Journal

● Cellular/Molecular

The Ligand-Binding Site and Glutamate Receptor Trafficking

Stephanie J. Mah, Elizabeth Cornell, Nicholas A. Mitchell, and Mark W. Fleck
(see pages 2215–2225)

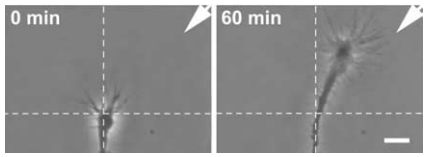
The extracellular domains of glutamate receptors share homology with bacterial periplasmic binding proteins, an observation that jump-started studies of the ligand-binding domains of AMPA receptor subunits. Mah et al. set out to extend these observations to the kainate receptor subunit, glutamate receptor 6 (GluR6), by mutating conserved residues (R523, T690, or E738) in the ligand-binding pocket. As expected, agonist binding and functional responses were eliminated, but something more happened. Homomeric mutant receptors were retained in the endoplasmic reticulum (ER). The mutants formed oligomers in the ER and were brought to the surface when expressed with wild-type GluR6 subunits. Thus the retention did not seem to be attributable to misfolding. The authors suggest that the ER can monitor the functional state of fully assembled GluR channels and retain those that cannot bind agonist, perhaps because high intracellular glutamate causes nascent receptor to be exported in their bound conformation. Many car manufacturers could learn from such a rigorous quality-control process.

▲ Development/Plasticity/Repair

A Growth Cone Turn Signal

Ming Jin, Chen-bing Guan, Yun-ai Jiang, Gang Chen, Chun-tao Zhao, Kai Cui, Yuan-quan Song, Chien-ping Wu, Mu-ming Poo, and Xiao-bing Yuan
(see pages 2338–2347)

Axons not only extend but also retract, and even make sharp turns as they find their targets. The roster of signaling mechanisms that guide axon growth includes Rho GTPases as well as cytoplasmic calcium transients. In response to extracellular factors, the Rho GTPases act as switches that trigger the cytoskeletal rearrangement required for an axonal direction change. This week, Jin et al. suggest a mechanism that links calcium and Rho GTPases in the turning of growth cones. The authors presented cultured *Xenopus* spinal neurons with an extracellular ryanodine gradient, triggering release of calcium in an asymmetrical pattern across the growth cone. The growth cone turned toward the source. Turning was dependent on calcium-dependent upregulation of the Rho GTPase, Cdc42, likely via protein kinase C- and Ca^{2+}/calmodulin-dependent protein kinase II-dependent phosphorylation. It seems that calcium is the green light in this turn signal.



A growth cone of a cultured *Xenopus* spinal neuron is shown at the beginning (0 min) and end (60 min) of exposure to pulsed application of ryanodine from the pipette at top right. Scale bar, 10 μm. See the article by Jin et al. for details.

■ Behavioral/Systems/Cognitive

Horizontal Cells Define Their Turf

Benjamin E. Reese, Mary A. Raven, and Stephanie B. Stagg
(see pages 2167–2175)

Horizontal cell dendrites on the retina distribute themselves like people on an elevator: evenly distributed across the space. And this week, Reese et al. show that the same factor is responsible in both cases (i.e., not a genetic program but rather proximity to others). The authors took advantage of several strains of mice in which, despite a large disparity in horizontal cell number, dendrites remained uniformly spread. Accordingly, the size of the dendritic fields, a sort of neuronal "personal space," varied inversely with cell number. To test the influence of afferent input, they ablated cone photoreceptors using cone-specific diphtheria toxin expression. The organization of horizontal cells in the outer plexiform layer was normal in the absence of cone synapses, as was the trademark size of the dendritic field. However, afferent input was important: dendrites in the coneless retina branched excessively and did not show the clusters of terminals normally seen at cone pedicles.

♦ Neurobiology of Disease

Neonatal Coxsackievirus Infection of Neuronal Progenitors

Ralph Feuer, Robb R. Pagarigan, Stephanie Harkins, Fei Liu, Isabelle P. Hunziker, and J. Lindsay Whitton
(see pages 2434–2444)

Coxsackievirus B (CVB) infections can cause serious consequences such as meningoencephalitis, particularly in newborns and young children. This week, Feuer et al. track the insidious path of CVB3 infection in neonatal mice. The virus seemed to preferentially attack dividing neuronal progenitor cells in the subventricular zone (SVZ). Infected cells in the SVZ no longer proliferated, based on their lack of immunoreactivity to the nuclear antigen Ki67. However, they retained their migratory capacity. Infected cells followed the rostral migratory stream or radial glial cells to reach the olfactory bulb or cerebral cortex, respectively. Infected cells also appeared to differentiate normally, although they were still capable of producing viral proteins. The virus thus hopped a ride onto proliferating neuronal precursors only to cause virus-induced lysis of mature cells at the end of the line. The authors suggest that depletion of infected mature cells may cause the neurodevelopmental deficits associated with CNS infection with CVB.