This Week in The Journal

● Cellular/Molecular

Protein Phosphatase 2A Plays Role in Active Zone Maturation

Natasha M. Viquez, Petra Füger, Vera Valakh, Richard W. Daniels, Tobias M. Rasse, et al.

(see pages 11484–11494)

At *Drosophila* neuromuscular junctions (NMJs), motor neurons terminate in a branched chain of many synaptic boutons, each of which has many individual release sites apposed to postsynaptic receptor clusters. The coordinated development and maintenance of these closely apposed pre- and postsynaptic structures is essential for maximizing synaptic efficiency. Viquez et al. previously showed that inhibition of protein phosphatase 2A (PP2A) alters the morphology of NMJ presynaptic boutons. They now report that PP2A is also required for proper maturation of active zones. Expression of dominant-negative PP2A in motor neurons after the NMJ had formed reduced the amplitude of excitatory junctional potentials (EJPs), caused accumulation of synaptic proteins in the axon, and decreased the density of active zones in boutons, leaving many postsynaptic receptor clusters unapposed. Inhibiting glycogen synthase kinase-3β suppressed the appearance of unapposed receptor clusters, but did not restore EJP amplitude or prevent axonal protein accumulation, suggesting these phenotypes are regulated independently.

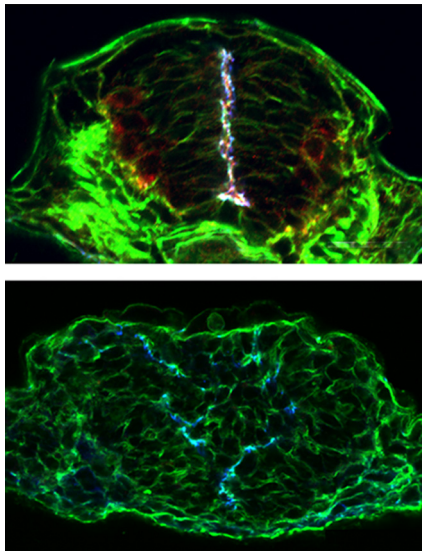
▲ Development/Plasticity/Repair

Premature Lin7c Expression Produces Multiaxial Mirror Symmetry

Xiaojun Yang, Jian Zou, David R. Hyde, Lance A. Davidson, and Xiangyun Wei

(see pages 11426–11440)

In the earliest stages of nervous system development, the cells that form the disc-shaped neural plate migrate medially, converge, and intercalate. Continued cell movements create the neural tube, which eventually forms the spinal cord and brain. These morphological changes require cells to balance the ability to move relative to each other with the need to maintain the integrity of the neuroepithelial sheet via cell–cell adhesions. Many mutations that impair neurulation disrupt proteins associated with tight junctions between cells that maintain cells' apicobasal polarity. Yang et al. have examined the role of one such protein, Lin7c, in zebrafish neurulation. Knockdown of Lin7c did not affect early steps in neurulation, but disrupted polarity at later stages, and prevented proper alignment of cells at the midline. Premature expression of Lin7c caused more drastic changes, including the development of two neural tubes, as a result of abnormal cell alignment and cell divisions.



Tight junction markers (blue) localize to the apical region of neural rod cells, which align at the midline in wild-type zebrafish (top). Knockdown of Lin7c disrupts this arrangement (bottom). See the article by Yang et al. for details.

■ Behavioral/Systems/Cognitive

Urgency to Respond Explains Response Time in Decision Task

Paul Cisek, Geneviève Aude Puskas, and Stephany El-Murr

(see pages 11560–11571)

Prominent models of decision making propose that sensory information is accumulated and integrated until a threshold level of evidence is obtained, at which point a decision is made. Such models explain why reaction times increase in difficult choice tasks: when evidence is weak, it takes longer to accumulate to threshold. These models also receive support from recordings of cortical neurons in monkeys: during decision-making tasks, firing rate increases; when a threshold firing rate is reached, the choice is made. Cisek et al. suggest an alternative model to explain these data. They hypothesize that over time, the urgency to respond increases. An urgency-related signal combines with evidence-related signals, and when the product of these signals reaches a threshold, a decision is made. To distinguish between these models, they designed a task in which the evidence in favor of each choice changes over time. Their results using human subjects supports their "urgency gating" model, but not integrator models.

♦ Neurobiology of Disease

Calmodulin Fragment Improves HD-Related Phenotype

Ying Dai, Nichole L. Dudek, Qian Li, Stephen C. Fowler, and Nancy A. Muma

(see pages 11550–11559)

Huntington's disease (HD) is caused by expansion of a polyglutamine sequence in huntingtin protein (htt), which might lead to abnormal associations with other proteins. Transglutaminase, which catalyzes formation of a covalent bond between htt glutamines and other residues, is elevated in HD and may contribute to HD pathophysiology. Calmodulin, which increases transglutaminase activity, colocalizes with htt and transglutaminase in the intranuclear inclusions that characterize HD. In cell cultures, expression of a calmodulin fragment reduced calmodulin binding to htt, decreased transglutaminase modification of htt, and reduced cytotoxicity. Dai et al. now report the effects of virus-mediated expression of the calmodulin fragment *in vivo*, in a mouse model of HD. Treatment reduced weight loss and improved locomotion in mutant mice, and reduced transglutaminase modification of htt, as well as the number and size of intranuclear htt aggregates. Nonetheless, treated mice showed more aggregates than wild-type, and treatment did not increase survival or prevent striatal atrophy.