**This Week in The Journal**

- **Cellular/Molecular**
  
  **Mitochondrial Channels and Synaptic Transmission**
  
  Modulation of Synaptic Transmission by the BCL-2 Family Protein BCL-xL
  
  
  (see pages 8423–8431)
  
  The BCL-2 protein family is known primarily for its role in cell death. Both pro-apoptotic and anti-apoptotic family members regulate the permeability of the outer mitochondrial membrane to pro-apoptotic molecules such as cytochrome c. Mitochondria also affect cell excitability by influencing intracellular ATP and calcium handling. In this issue, Jonas et al. provide a potential link between these apparently discrete mitochondrial functions. Using a clever double-barreled recording patch electrode pipette, they measured ion channel activity in mitochondrial membranes in presynaptic terminals of squid giant stellate ganglia. When the anti-apoptotic protein BCL-xL was included in the patch pipette, mitochondrial membrane channel activity increased, synaptic responses were enhanced, and recovery from synaptic depression was more rapid. Conversely, injection of a pro-apoptotic cleavage product of the protein reduced synaptic responses. Although the actions seemed to be independent of mitochondrial handling of presynaptic calcium, ATP injection to the presynaptic terminal mimicked the action of BCL-xL. The authors suggest that BCL-xL, by influencing the release of mitochondrial ATP, may regulate the readily releasable pool of synaptic vesicles.

- **Development/Plasticity/Repair**

  **Neuronal–Glial Interactions in the Fly**
  
  Reciprocal Interactions between Neurons and Glia Are Required for Drosophila Peripheral Nervous System Development
  
  Katharine J. Sepp and Vanessa J. Auld
  
  (see pages 8221–8230)
  
  During development of the peripheral nervous system (PNS), sensory neurons depend on glia for maturation and guidance of axonal projections. A report by Sepp and Auld examines whether this relationship is reciprocal. The authors overexpressed the apoptotic gene grim to ablate selectively either neurons or glia in Drosophila. Grim blocks the activity of Drosophila inhibitor of apoptosis protein (DIAP1), and thus overexpression of grim results in caspase activation and subsequent apoptosis. The ablations produced embryonic defects consistent with neuronal–glial interdependence. The authors next explored the possible role of receptor tyrosine kinase signaling pathways in neuronal–glial interactions. Disruption of glial migration and ensheathment by overexpression of Rho GTPase did not alter sensory axon guidance. However, disruption of glial differentiation using expression of dominant-negative Ras GTPase markedly altered the pathfinding ability of sensory axons. The results suggest an important role for the epidermal growth factor receptor (EGFR)/Ras signaling cascade in PNS neuronal–glial interactions.

- **Behavioral/Systems/Cognitive**

  **Tracing the Corticocerebellar Loop-De-Loop**
  
  Cerebellar Loops with Motor Cortex and Prefrontal Cortex of a Nonhuman Primate
  
  Roberta M. Kelly and Peter L. Strick
  
  (see pages 8432–8444)
  
  Corticocerebellar circuits have been considered as an open-loop system, with inputs from diffuse cortical areas converging on the cerebellum and the cerebellar output converging on the primary motor cortex (M1). New anatomical methods are challenging that concept. For example, transneuronal tracing using herpes simplex virus type 1 (HSV1) has revealed that the cerebellum sends nonoverlapping outputs to cortical areas in addition to M1. In this issue, Kelly and Strick combined HSV1 and retrograde transneuronal tracing using rabies virus to map cerebellar connections with the arm area of M1 and area 46 in the prefrontal cortex of Cebus apella monkeys. They found multiple, discrete closed loops. M1 neurons projected primarily to lobules IV–VI of the cerebellar cortex and received input from that same area. Likewise, area 46 formed a closed loop with Purkinje cells of Crus II. Because the tracers were not used in the same animal, it remains to be seen whether the topographic specificity extends to the single neuron level. However, the data suggest that the input–output relationships of the cerebellum and cortex consist of a series of parallel closed loops. The authors suggest that one manifestation of this organization is distinct circuit loops for cognitive and motor functions.

A wild-type stage 16 Drosophila embryo shows glial nuclei stained with anti-Repo (blue, arrows) associated with two major sensory tracts stained with anti-Futsch (brown, anterior fascicles (af) and posterior fascicles (pf)). See the article by Sepp and Auld for details.