# This Week in The Journal

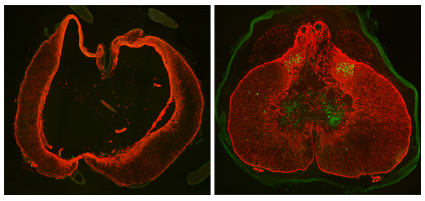
## Development/Plasticity/Repair

### *Chondroitinase ABC Alters Macrophage Phenotype*

Katalin Bartus, Nicholas D. James, Athanasios Didangelos, Karen D. Bosch, Joost Verhaagen, et al.

(see pages 4822–4836)

Most spinal cord injuries result from blunt force, which compresses the spinal cord without severing it. Much of the functional loss associated with such injuries arises after the initial trauma, as a result of ischemia, inflammation, and reactive astrocytosis. Recovery is limited by neuron death and molecules like chondroitin sulphate proteoglycans (CSPGs) that inhibit axon regeneration. Several studies have shown that degrading CSPGs with chondroitinase ABC (ChABC) can increase recovery of function, but most such studies were conducted in animals after spinal transection—which causes much less damage than contusion injury—and/or required repeated administration of ChABC. Now Bartus et al. report that virally expressing ChABC in rat spinal cord produced long-lasting reduction of CSPGs and reduced secondary injury after contusion injury: more neurons survived and functional recovery was greater in virus-treated animals than in controls. Unexpectedly, ChABC altered the predominant phenotype of spinal cord macrophages, increasing the proportion of neuroprotective, repair-promoting M2-type macrophages while decreasing the proportion of the neurotoxic M1 type.



Injection of lentivirus expressing ChABC greatly reduced damage from spinal cord contusion injury. The glial scar (red) was more diffuse, more neurons (green) survived, and much less cavitation occurred in treated animals (right) than in controls (left). See the article by Bartus et al. for details.

## Systems/Circuits

### *Orientation Selectivity Does Not Shape Connections within V1*

Xiaoying Huang, Yishai M. Elyada, William H. Bosking, Theo Walker, and David Fitzpatrick

(see pages 4976–4990)

Neurons in primary visual cortex (V1) of most carnivores and primates can be distinguished by their responses to stimuli of different orientations; neurons with similar orientation selectivity cluster in orientation domains. Orientation selectivity arises from selective integration of inputs from thalamic neurons, which show no orientation preference, and horizontal inputs from within V1. Although anatomical evidence has suggested that horizontal connections in V1 predominantly link cells with similar orientation selectivity, a growing body of electrophysiological data argues against this hypothesis. Huang et al. add to this electrophysiological evidence with experiments combining *in vivo* optical stimulation of pyramidal neurons in single orientation domains with multiunit electrophysiological recordings from nearby areas in layer 2/3 of tree shrew V1. In general, optical stimulation of a single orientation domain appeared to increase firing of recorded neurons throughout the neighboring region, regardless of the recorded neurons' orientation preference: recorded neurons responded similarly regardless of whether the stimulated domain had the same or the orthogonal orientation selectivity.

## Behavioral/Cognitive

### *14-3-3 Proteins Affect Expression of NMDA Receptor Subunits*

Haifa Qiao, Molly Foote, Kourtney Graham, Yuying Wu, and Yi Zhou

(see pages 4801–4808)

The 14-3-3 family of proteins has seven members that are expressed in all eukaryotic cells, but they are most prominent in the brain. These proteins affect the functions of numerous other proteins, usually by binding to phosphorylated residues, and they regulate many cellular processes, including signal transduction, metabolism, cell cycle progression, trafficking, secretion, and apoptosis. Some 14-3-3 proteins are enriched at synapses, where they are important in synaptic plasticity and learning. To further investigate the function of these proteins in neurons *in vivo*, Qiao et al. generated transgenic mice that expressed difopein, an inhibitor of all 14-3-3 proteins, in hippocampal pyramidal neurons beginning at perinatal ages. These mice were impaired in contextual fear conditioning and passive avoidance learning tests. Furthermore, long-term potentiation was diminished in difopein-expressing neurons in hippocampal slices from the mice. The expression of NMDA receptor GluN1 and GluN2A was also lower in difopein-expressing neurons than controls, resulting in smaller NMDA receptor currents that likely contributed to learning deficits.

## Neurobiology of Disease

### *$Cl^-$ Transporter Expression May Contribute to Schizophrenia*

Yukitaka Morita, Joseph H. Callicott, Lauren R. Testa, Michelle I. Mighdoll, Dwight Dickinson, et al.

(see pages 4929–4940)

Weakened inhibition of cortical pyramidal neurons, particularly in the dorsolateral prefrontal cortex (DLPFC), is thought to underlie some symptoms of schizophrenia. The deficit likely arises partly from reduced synthesis of GABA in interneurons, but reduced IPSPs might also play a role. The postsynaptic effect of GABA depends on the $Cl^-$ equilibrium potential, which is determined by the relative expression of two $Cl^-$ transporters, NKCC1, which imports $Cl^-$, and KCC2, which exports $Cl^-$. The NKCC1:KCC2 ratio decreases during development, causing GABA's effect to change from depolarizing to hyperpolarizing. Morita et al. asked whether abnormal expression of NKCC1 isoforms in adults might contribute to decreased cortical inhibition in schizophrenia. Studies in healthy humans identified four alternatively spliced NKCC1 transcripts that are commonly expressed in the brain. Expression of two of these transcripts was significantly reduced in DFPLC of schizophrenics. Furthermore, a single-nucleotide polymorphism in NKCC1 was associated with decreased expression of transcript NKCC1b in adult DFPLC and a slight increase in schizophrenia risk.