# *This Week in The Journal*

## ● Cellular/Molecular

### *Sensory Signals Barreling into Cortical Layer 1*

Yinghua Zhu and J. Julius Zhu
(see pages 1272-1279)

Specific sensory input to neocortex arrives in layer 4, whereas nonspecific input, such as information about salience or novelty, is thought to arrive in layer 1. This scheme might imply a slower arrival of inputs to layer 1. In this issue, Zhu and Zhu examine this question using paired whole-cell recording *in vivo* from layer 1 nonpyramidal cells and the dendrites of the output pyramidal neurons in layer 5. They measured the latency of EPSCs evoked by natural stimulation of whiskers. Surprisingly, the latency in layer 1 was 5–7 msec, the same as in layer 4. As expected, layer 1 cells had larger receptive fields responding to 6–15 whiskers. Because concurrent signals in layers 1 and 4 lower the threshold for dendritic calcium action potentials and thus enhance burst firing in the output cells in layer 5, the authors postulate that the concurrent inputs may serve as a coincidence detector.

## ▲ Development/Plasticity/Repair

### *Glycosaminoglycan Chains and Axon Regeneration*

Barbara Grimpe and Jerry Silver
(see pages 1393-1397)

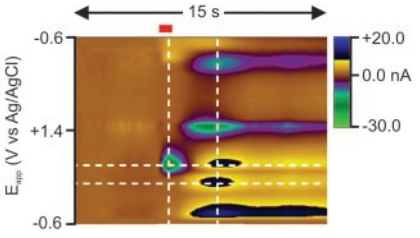
Extracellular matrix molecules are produced in and around lesions in the CNS. The inhibition of axon regeneration by molecules such as the chondroitin sulfate proteoglycans (CSPGs) constitutes a major impediment to CNS repair. The bacterial enzyme chondroitinase ABC degrades carbohydrate side chains on CSPGs and can improve axon regeneration. However, the action of this enzyme is incomplete, leaving a "carbohydrate stub" that can still inhibit axon growth. To overcome this limitation, Grimpe and Silver designed a DNA enzyme that specifically targets the mRNA for xylosyltransferase-1 (XT-1). Because XT-1 initiates glycosylation of the protein backbone, the DNA enzyme should inhibit formation of carbohydrate side chains. Consistent with this hypothesis, the new reagent reduced fully glycosylated proteoglycans and allowed regeneration of adult sensory neurons past a spinal cord stab lesion.

## ■ Behavioral/Systems/Cognitive

### *Dopamine and Food-Seeking in Real Time*

Mitchell F. Roitman, Garret D. Stuber, Paul E. M. Phillips, R. Mark Wightman, and Regina M. Carelli
(see pages 1265-1271)

The nucleus accumbens, a component of the reward system, is required for food-motivated learning. Dopamine is released in the nucleus accumbens by axon terminals arriving from the ventral tegmental area. This week, Roitman et al. provide new information on the temporal relationship between dopamine release and behavior by implanting a carbon fiber electrode and using fast-scan cyclic voltammetry to electrochemically detect dopamine every 100 msec. Rats were trained to press a lever in response to a cue light for which they received a sweet treat, intraoral sucrose. Dopamine was released in the nucleus accumbens with presentation of the cue, and in most cases the animal responded immediately by pressing the lever to receive the food reward. Because dopamine was not released in response to the cue in rats trained without reward, or in response to lever pressing, the authors conclude that dopamine release is tied to a cue that promises imminent food reward.




The electrochemical signal in the nucleus accumbens evoked by electrical stimulation.

## ♦ Neurobiology of Disease

### *Adenosine as an Immunomodulator*

Shigeki Tsutsui, Jurgen Schnermann, Farshid Noorbakhsh, Scot Henry, V. Wee Yong, Brent W. Winston, Kenneth Warren, and Christopher Power
(see pages 1521-1529)

As neuroscientists, we generally think of modulators in terms of their effect on neurons or glia. However in the case of adenosine, this purine nucleoside also regulates the expression and release of pro-inflammatory molecules from activated immune cells. In this issue, Tsutsui et al. use an A1 adenosine receptor (A1AR)-deficient mouse to examine adenosine modulation of experimental allergic encephalomyelitis (EAE), a standard experimental model for multiple sclerosis (MS). Their results suggest that the A1AR plays a far-reaching role in this autoimmune disease. In A1AR-deficient mice, pro-inflammatory molecules were upregulated and anti-inflammatory molecules were downregulated, with disastrous consequences. The mice displayed increased myelin degeneration, axon loss, and macrophage activation. In keeping with evidence from MS patients, A1AR was downregulated in wild-type mice with EAE. Remarkably, caffeine or an A1AR agonist alleviated the loss of receptors, and the ensuing neuroinflammation, in wild-type mice. These results offer an alternative strategy for immunomodulation.