This Week in The Journal

● Cellular/Molecular

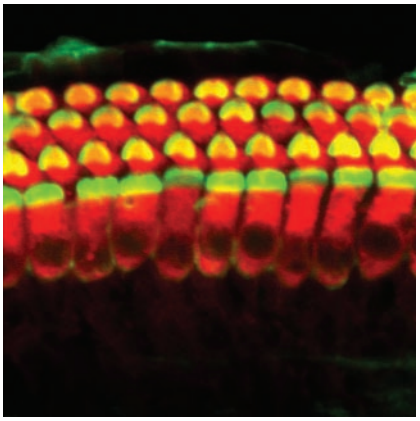
Sensory Cells Light Up

Lighting up the Senses: FM1-43 Loading of Sensory Cells through Nonselective Ion Channels

Jason R. Meyers, Richard B. MacDonald, Anne Duggan, David Lenzi, David G. Standaert, Jeffrey T. Corwin, and David P. Corey

(see pages 4054 – 4065)

This week, Meyers et al. report a novel method to specifically label sensory neurons with FM1-43, the styryl dye best known for its ability to partition into cell membranes and label endocytosed synaptic vesicles. Because the dye labels cytoplasm of hair cells of the inner ear, it has been suggested that this divalent cationic dye might also permeate the nonselective cation channels in the tips of hair cell stereocilia. Meyers et al. show that this is indeed the case. Dye uptake was prevented by pharmacological block or mechanical inactivation of the channels. After subcutaneous injection of FM1-43, a surprising number of other sensory cells of all sizes and nearly all sensory ganglia were labeled, presumably via ion channels expressed at sensory endings. Cultured human embryonic kidney cells also took up the dye through both vanilloid and ATP-gated ion channels. This newly described action of FM1-43 should be useful for identification of sensory neurons as well as in probing the properties of the diverse family of sensory channels.



Mouse cochlear hair cells were labeled with AM1-43 (red), a fixable analog of FM1-43, and counterstained with phalloidin (green). AM1-43 fills the cytoplasm by permeating through transduction channels in the hair bundles. See Meyers et al. for details.

▲ Development/Plasticity/Repair

Nogo-66 and the Road to Recovery from Spinal Injury

Delayed Systemic Nogo-66 Receptor Antagonist Promotes Recovery from Spinal Cord Injury

Shuxin Li and Stephen M. Strittmatter

(see pages 4219 – 4227)

Spinal cord injury is not only functionally devastating, but therapeutic options have been meager because of the limited regenerative capacity of the adult CNS. Recent studies of the postinjury signaling pathways (both growth-promoting and inhibiting) provide a better view of ways to enhance the regeneration and targeting of axons. In this issue, Li and Strittmatter focus on Nogo-66 receptor (NgR), the axonal receptor for three inhibitory myelin-derived signal molecules. A peptide antagonist of NgR has been shown previously to increase axonal regrowth when applied intrathecally at the time of trauma. Immediate and targeted treatment, however, have limited utility in the typical clinical setting, as is the case for "neuroprotective" strategies in stroke and global ischemia. However, the present experiments suggest that the therapeutic window in spinal cord injury may be measured in days in some cases. Subcutaneous treatment with the NgR antagonist NEP1–40 (Nogo extracellular peptide, residues 1–40) had the same beneficial action even when given 7 d after dorsal hemisection. Treated mice had enhanced axonal regrowth and synapse formation, an upregulated growth protein, and better locomotor function during recovery. The breach in the blood–brain barrier that accompanies spinal trauma provided the avenue necessary for subcutaneous delivery. Perhaps time is on the side of those working to improve recovery after spinal cord injury.

■ Behavioral/Systems/Cognitive

Regulating the Sleep–Wake Cycle

A_1 Receptor and Adenosinergic Homeostatic Regulation of Sleep-Wakefulness: Effects of Antisense to the A_1 Receptor in the Cholinergic Basal Forebrain

Mahesh M. Thakkar, Stuart Winston, and Robert W. McCarley

(see pages 4278 – 4287)

Nitric Oxide-Mediated Cortical Activation: A Diffuse Wake-Up System

Jorge Mariño and Javier Cudeiro

(see pages 4299 – 4307)

Two reports this week examine the actions of neuromodulators on the sleep–wake cycle. Both groups focused on cholinergic neurons of the basal forebrain (BF) that are involved in cortical arousal. However, the groups used different approaches and found opposing actions of two well known neuromodulators, adenosine and nitric oxide (NO). Thakkar et al. locally delivered antisense oligonucleotides directed against the mRNA of adenosine A_1 receptors to block the action of adenosine in the BF of freely behaving rats. Disabling A_1 receptors relieved the tonic inhibition of BF neurons by adenosine and thereby increased wakefulness and decreased non-rapid eye movement sleep time. The authors suggest that build up of adenosine during wakefulness arises from increased ATP hydrolysis, and that the action of adenosine at the A_1 receptors contributes to the transition to sleep. Mariño and Cudeiro, in contrast, studied the EEG patterns of anesthetized cats to observe the effects of NO. When they blocked NO synthase activity locally in the cortex, BF stimulation was less effective in eliciting a cortical activation typical of the awake state. The level of cortical NO evoked by BF stimulation was also reduced. The two studies emphasize the role of the BF in the homeostatic control of sleep and arousal.