

# This Week in The Journal

## ● Cellular/Molecular

### *Extranuclear Control of Neuronal Survival by cAMP*

An Extranuclear Locus of cAMP-Dependent Protein Kinase Action Is Necessary and Sufficient for Promotion of Spiral Ganglion Neuronal Survival by cAMP

Jinwoong Bok, Xiang-Ming Zha, Yang-Sun Cho, and Steven H. Green

(see pages 777-787)

Multiple signaling pathways are involved in the life and death of neurons during neuronal development and in response to stress. The second messenger, cAMP, is one of the best-known mediators of neuronal survival, ultimately eliciting PKA-mediated phosphorylation of substrates in the nucleus and cytoplasm, including the nuclear transcription factor cAMP-responsive element binding protein (CREB). However, cAMP also affects neuronal survival by post-translational modification of proapoptotic or prosurvival cytoplasmic proteins. In this issue, Bok et al. tracked the role of PKA in nuclear versus cytoplasmic events by tagging PKA with green fluorescent protein and either a nuclear localization signal (nls) or a nuclear export signal (nes). The tagged molecules were introduced into cultured spiral ganglion neurons (sensory neurons of the cochlea), whose survival is promoted by PKA as well as depolarization. The nes-tagged PKA, but not the nls-tagged PKA, promoted neuronal survival, indicating an extranuclear action of PKA. CREB was phosphorylated by cAMP in these experiments but was not required for cAMP-mediated neuronal survival. Overexpression of Bad, a known proapoptotic protein whose action is inhibited by PKA phosphorylation, led to increased neuronal death. Thus the authors suggest that inhibition of Bad is involved in spiral ganglion cell survival by this extranuclear mechanism.

## ▲ Development/Plasticity/Repair

### *Neuronal–Glial Signaling in the Hypothalamus*

Neuron-to-Glia Signaling Mediated by Excitatory Amino Acid Receptors Regulates

ErbB Receptor Function in Astroglial Cells of the Neuroendocrine Brain

Barbara Dzedzic, Vincent Prevot, Alejandro Lomniczi, Heike Jung, Anda Cornea, and Sergio R. Ojeda

(see pages 915-926)

The initiation of mammalian puberty is regulated by increased secretion of luteinizing hormone-releasing hormone (LHRH) from hypothalamic neurons. In this system, Ojeda and coworkers previously demonstrated the activation of two parallel signaling pathways in interconnected neuronal–glial networks. ErbB receptors on glial cells are stimulated by neuregulins and transforming growth factor- $\alpha$  providing the central drive to stimulate LHRH secretion at puberty. This is accompanied by increased glutamate-mediated activation of neuroendocrine neurons containing LHRH. In the current issue, Dzedzic et al. link these two signaling pathways. They report that two glutamate receptors (GluRs), metabotropic GluR type 5 (mGluR5) and an ionotropic AMPA receptor containing GluR2 and GluR3 subunits, are expressed by hypothalamic astrocytes. These receptors were associated with the same clustering proteins, Homer and PICK1 (protein interacting with C-kinase), as found at synapses. Activation of the astrocytic glutamate receptors triggered a molecular cascade involving membrane recruitment of erbB receptors, their concomitant transactivation by matrix metalloproteinase processing of erbB ligands, and enhanced erbB gene expression. Thus, coordinated activation of LHRH neurons and hypothalamic astrocytes by glutamate leads to increased LHRH secretion. This signaling network provides the hypothalamus with a means for coordinating trans-synaptic and astroglial input to LHRH neurons. This mechanism may serve as a strategy for coregulating neuron–neuron and neuron–glial signaling networks in other central neural networks

## ■ Behavioral/Systems/Cognitive

### *Getting in Tune for the Summer*

Seasonal Plasticity of Peripheral Auditory Frequency Sensitivity

Joseph A. Sisneros and Andrew H. Bass

(see pages 1049-1058)

Species have developed elaborate mechanisms to enhance their procreation. For species with

reproductive cycles, the basis of seasonal plasticity can involve specific vocalizations to attract their mates. In this issue, Sisneros and Bass explore seasonal plasticity in the reception of sound in female midshipman fish collected in the Monterey Bay off the coast of California. These nocturnally active fish migrate from the deep ocean to intertidal zones in late spring and summer to spawn. Females lay eggs and then leave, while the males care for the fertilized eggs. Males “hum” to attract females. These hums have a fundamental frequency of  $\sim 100$  Hz but include prominent harmonics up to 400 Hz. Females respond to the hums only during the period just before egg-laying. To measure the auditory response, the authors recorded the auditory afferent activity of immobilized fish in an underwater chamber. Summer (reproductive) females showed robust responses to pure tones in the range of the higher harmonics of the hum, whereas nonreproductive females responded only up to 100 Hz. The authors suggest that the increased responsiveness in the higher-frequency harmonics may increase detection in the shallow water in which nesting occurs. Thus the female auditory sensitivity shows seasonal plasticity that optimizes their response to the male vocalization. Their studies do not elucidate the underlying mechanisms, although direct or genomic effects of gonadal steroids, which peak before spawning and then drop rapidly, are a likely factor. In any case, selective listening seems to be keeping midshipman fish alive and “swimming.”



A female (left) and male (right) midshipman fish in their nest in the intertidal zone; their rocky shelter has been lifted away to reveal their cave-like dwelling at low tide.