This Week in The Journal

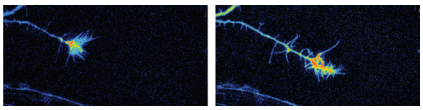
● Cellular/Molecular

BDNF Enables β-Actin Translation by Phosphorylating ZBP1

Yukio Sasaki, Kristy Welshhans, Zhexing Wen, Jiaqi Yao, Mei Xu, et al.

(see pages 9349–9358)

Localized guidance cues and synaptic activity direct axonal growth and strengthen specific synapses, respectively, by inducing localized protein synthesis. For this to occur, mRNAs must be transported to sites of synthesis in growth cones and dendritic spines, and their translation must be repressed until the appropriate signal arises. Both of these tasks are accomplished by mRNA binding proteins, which bind to specific mRNAs. For example, zipcode binding protein ZBP1 binds to β-actin mRNA, represses its translation, and targets it to the leading edge of axonal growth cones. Brain-derived neurotrophic factor (BDNF) stimulates translation of β-actin mRNA, resulting in growth cone turning toward the source of BDNF. Sasaki et al. show that BDNF induces phosphorylation of ZBP1, which decreases its affinity for β-actin mRNA, thus allowing translation. Preventing phosphorylation did not affect localization of β-actin mRNA in growth cones of cultured neurons, but it blocked BDNF-mediated increases in β-actin synthesis and abolished growth cone turning.



BDNF stimulates translation of a fluorescent reporter molecule linked to the 3′ untranslated region of β-actin mRNA. Left, Before BDNF; right, after BDNF. See the article by Sasaki et al. for details.

▲ Development/Plasticity/Repair

Transcription Factor teashirt3 *Helps Shape Respiratory Network*

Xavier Caubit, Muriel Thoby-Brisson, Nicolas Voituron, Pierre Filippi, Michelle Bévengut, et al.

(see pages 9465–9476)

Breathing is controlled by a pattern generator in the brainstem that drives motor neurons to produce inspiratory and expiratory movements. During development, the first rhythmic activity occurs in the embryonic parafacial oscillator (e-pF), and this is thought to entrain the rhythm of the preBötzinger complex (preBötC). Initially synchronous bursting in these areas drifts out of phase, so that the preBötC drives inspiration, and the parafacial respiratory group/retrotrapezoid nucleus, which arises from the e-pF, drives expiration. Serially active transcription factors shape embryonic development of the respiratory network, ensuring that it is functional at birth. Caubit et al. found that one important transcription factor is *teashirt3* (*Tshz3*). Although e-pF neurons develop in *Tshz3*-null mice, they do not produce normal bursts. Likely as a result, the preBötC produces only a slow rhythm. Furthermore, motor neurons of the nucleus ambiguus, which expand the airways during inhalation, degenerate in *Tshz3*-null mice. Therefore, newborn mice fail to inflate the lungs and soon die.

■ Behavioral/Systems/Cognitive

Zebrafish touché *Mutants Have Impaired Mechanotransduction*

Sean E. Low, Joel Ryan, Shawn M. Sprague, Hiromi Hirata, Wilson W. Cui, et al.

(see pages 9359–9367)

Animals discriminate a wide variety of tactile stimuli and have a correspondingly large array of somatosensory neurons. Little is known about the molecular underpinnings of this variety, including the mechanotransduction molecules involved. To identify candidates, Low et al. screened mutant zebrafish embryos and found one family—named *touché* mutants—that were unresponsive to light touch, but responded normally to nociceptive stimuli and stimuli that activate previously identified candidate mechanotransducers. Touch insensitivity could result from loss or mistargeting of sensory neurons, impaired mechanotransduction, dysfunctional propagation of action potentials, failure to release transmitter, or downstream dysfunction. But touch-sensitive neurons were present in normal numbers and with similar innervation patterns, and when channel-rhodopsin was expressed in these neurons, illumination triggered similar motor behaviors in wild-type and mutant embryos. In contrast, mechanical stimulation of neurites evoked graded receptor potentials only in wild-type neurons, suggesting *touché* mutants have deficient mechanotransduction. Identification of the gene responsible might therefore reveal a novel mechanotransduction molecule.

♦ Neurobiology of Disease

Decreased VGF May Contribute to Bipolar Disorder

Smita Thakker-Varia, Ying Y. Jean, Payal Parikh, Caroline F. Sizer, Jennifer Jernstedt Ayer, et al.

(see pages 9368–9380)

Because attributing human moods to animal behavior is problematic, researchers studying the physiological bases of mood disorders resort to studying animal behaviors that mimic symptoms of the disorder and that respond to treatments of the disorder. For example, the discovery that brain-derived neurotrophic factor (BDNF) is upregulated by several treatments for depression, including electroconvulsive shock, exercise, and antidepressant drugs, implicated BDNF dysfunction in depression. Similar studies found that BDNF and exercise induce upregulation of VGF—a neuropeptide that regulates energy balance—in rodents, suggesting VGF is a downstream mediator of BDNF's effects. Thakker-Varia et al. now report that VGF levels are reduced in postmortem hippocampus and prefrontal cortex of people with bipolar disorder. In rodents, VGF mimicked the effects of lithium, an effective treatment for bipolar disorder, in both a model of depression and a model of manic behavior. Moreover, VGF and lithium activated some of the same signaling molecules, and VGF-deficient mice did not respond to lithium treatment.