# *This Week in The Journal*

## ● Cellular/Molecular

### *ProBDNF as a Death Signal*

Henry K. Teng, Kenneth K. Teng, Ramee Lee, Saundrene Wright, Seema Tevar, Ramiro D. Almeida, Pouneh Kermani, Risa Torkin, Zhe-Yu Chen, Francis S. Lee, Rosemary T. Kraemer, Anders Nykjaer, and Barbara L. Hempstead
(see pages 5455–5463)

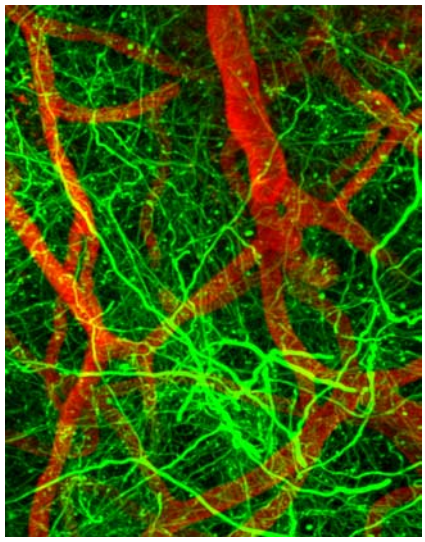
Neurotrophins are synthesized as precursors that undergo intracellular cleavage before they are secreted. Many of the actions of the mature forms result from activation of Trk receptor tyrosine kinases. However, precursors such as proNGF can also be secreted. In the case of proNGF, recent studies indicate that it can bind to the $p75^{NTR}$ receptor and a coreceptor, sortilin, and thus mediate apoptosis. This week, Teng et al. report that proBDNF also is secreted from neurons but did not bind to TrkB receptor tyrosine kinase. Rather, proBDNF acted as a proapoptotic signal as examined in sympathetic neurons. ProBDNF-induced cell death required expression of both $p75^{NTR}$ and sortilin. Preformed complexes of proBDNF and the soluble extracellular segment of sortilin were not apoptotic, indicating that both $p75^{NTR}$ and sortilin must be activated at the cell surface. These results provide additional support for a previously unappreciated role of neurotrophin precursors.

## ▲ Development/Plasticity/Repair

### *Dendritic Spine "Survival" during Ischemia*

Shengxiang Zhang, Jamie Boyd, Kerry Delaney, and Timothy H. Murphy
(see pages 5333–5338)

At a macroscopic level, we know well what happens in a stroke. Block of an artery for any extended period leads to loss of tissue in the center of the perfusion territory and partial damage in the surrounding "penumbra." The immediate therapeutic goal is to restore perfusion before damage to key structures such as synapses becomes permanent. This week, Zhang et al. dynamically monitored dendritic spines in the mouse somatosensory cortex during ischemia. Two-photon imaging of yellow fluorescent protein (YFP)-expressing neurons allowed continuous visualization of spines. To simulate the penumbra, they reduced local blood supply to ~50% with the vasoconstrictor endothelin; for the core, they used photoactivation of the clot-forming dye Rose Bengal that reduced blood supply to <10%. With moderate ischemia, spines remained stable even after 5 h. During severe ischemia, however, spines were not so resilient. After only 10–40 min, spines were rapidly lost. Reperfusion within 20–60 min restored spines, albeit in altered locations.



Projection image showing Texas Red-labeled vasculature and YFP-labeled dendrites (green) from a transgenic mouse before induction of ischemia *in vivo*. Note the cerebral vessels coursing through the dendritic arbors. See the article by Zhang et al. for details.

## ■ Behavioral/Systems/Cognitive

### *Chattering Cells Listen to Synaptic Input*

Jessica A. Cardin, Larry A. Palmer, and Diego Contreras
(see pages 5339–5350)

One class of cortical neurons called fast rhythmic bursting (FRB) cells, or chattering cells, is so named because these cells fire bursts of action potentials in the 30–50 Hz range. These γ-frequency oscillations are thought to arise primarily from intrinsic membrane conductances. This week, Cardin et al. show that FRB cells are distributed throughout layers 2–6 of the cat primary visual cortex *in vivo* and that they have both simple and complex receptive field properties. FRB cells responded to depolarizing current injections with γ-frequency bursts. Although simple and complex cells displayed identical burst characteristics in response to current injection, they responded quite differently to visual input. The γ-frequency band of simple, but not complex, cell bursts was altered by orientation- and contrast-dependent stimuli, indicating that network activation generated the rhythmic bursting. In addition, membrane hyperpolarization did not prevent burst firing, suggesting that γ bursts are generated by network activity impinging on FRB cells.

## ♦ Neurobiology of Disease

### *Human Tau and Neuronal Death in the Mouse*

Cathy Andorfer, Christopher M. Acker, Yvonne Kress, Patrick R. Hof, Karen Duff, and Peter Davies
(see pages 5446–5454)

Among the unexplained elements of Alzheimer's disease is the connection between the microtubule-associated protein tau, its hyperphosphorylated aggregates, called neurofibrillary tangles (NFTs), and cell death. Although the three are inextricably linked in tauopathies, the relationship between tau pathology and neuronal degeneration remains poorly defined. This week, Andorfer et al. address the problem using htau mice. These mice do not express mouse tau; rather, they express nonmutant human tau at approximately four times the normal level. By 15 months of age, the mice developed NFTs, DNA fragmentation, and neuronal death. Interestingly, neuronal death did not seem to correlate in individual cells with the presence of NFTs. However, cells in htau mice showed aberrant expression of cell-cycle proteins, similar to what has been observed in human Alzheimer's disease in areas of extensive cell loss. The authors suggest that neuronal death may be linked to abnormal or incomplete reentry into the cell cycle.