This Week in The Journal

● Cellular/Molecular

BDNF, mTOR, and Dendritic Protein Synthesis

Nobuyuki Takei, Naoko Inamura, Mihoko Kawamura, Hisaaki Namba, Kenta Hara, Kazuyoshi Yonezawa, and Hiroyuki Nawa
(see pages 9760–9769)

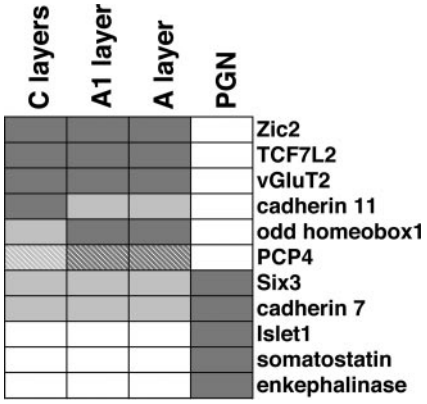
The presence of ribosomes and mRNAs in dendrites has fueled a 25 year search for local protein synthesis as a mechanism of activity-dependent synaptic plasticity. Takei et al. this week examine the molecular cascades involved in perisynaptic and dendritic protein translation. They focused on brain-derived neurotrophic factor (BDNF) because it can regulate synaptic plasticity and induces protein synthesis of prominent dendritic mRNAs such as calcium/calmodulin-dependent kinase II and Arc. They also examined the dependence of translation on mammalian target of rapamycin (mTOR). The immunosuppressant rapamycin suppresses plasticity in some cases by inhibiting mTOR, a kinase that activates downstream translation regulatory molecules. The authors incubated cultured neurons in tritium-labeled amino acids, treated them with BDNF and/or rapamycin, and then assessed protein synthesis with autoradiography. BDNF initiated neuritic protein synthesis that was completely or partially blocked by rapamycin. The results are consistent with local activation of translation in dendrites by both mTOR-dependent and -independent cascades.

▲ Development/Plasticity/Repair

Molecular Subdivisions of the Ferret LGN

Hiroshi Kawasaki, Justin C. Crowley, Frederick J. Livesey, and Lawrence C. Katz
(see pages 9962–9970)

This week, Kawasaki et al. examine gene expression patterns among segregated processing streams of the ferret visual system. Like primates, ferrets process object- and color-related information in the parvocellular or "X" stream and motion-related information in the magnocellular or "Y" stream. Using tissue from neonatal ferret lateral geniculate nucleus (LGN), they created a customized ferret cDNA microarray; they also examined monkey thalamic tissue using a commercial microarray. A handful of transcription factors in the ferret differed between neurons of the LGN and the adjacent perigeniculate nucleus (PGN). Furthermore, Y-stream but not X-stream cells expressed the neuron-specific protein Purkinje cell protein 4 (PCP4). Although the X and Y pathways are physiologically distinct, the neurons intermingle in the LGN. The primate homolog of PCP4 also distinguished monkey magnocellular neurons. This early marker was detected at postnatal day 7, providing a clue about when Y cells are specified.



Differential expression patterns define functional structures in the visual thalamus, including the LGN and PGN. Dark shading indicates strong expression, whereas white represents no expression. Hatched fill indicates that subpopulations of the cells are positive. See the article by Kawasaki et al. for details.

■ Behavioral/Systems/Cognitive

The S6 Kinase II and Drosophila *Learning*

Gabriele Putz, Franco Bertolucci, Thomas Raabe, Troy Zars, and Martin Heisenberg
(see pages 9745–9751)

Many different approaches and animal models have been used to study the mechanisms underlying memories. In this week's *Journal*, Putz et al. examine the role of a serine–threonine kinase in *Drosophila* memory. Ribosomal S6 kinase II (S6KII) has been implicated in the MAPK (mitogen-activated protein kinase) signaling cascade. Furthermore, its homolog in humans has been linked to an X-linked syndrome including mental retardation. Thus the authors assessed the role of S6KII in operant and classical conditioning in *Drosophila* but found quite different results. Flies were trained to avoid a compartment of a heat box in an operant conditioning paradigm in which specific consequences follow actions. For classical conditioning, they paired certain odors with a shock. In flies lacking the *S6KII* gene, only classical conditioning was impaired and was rescued with expression of an *S6KII* transgene. However, a P-element insertion mutant that had reduced amounts of S6KII only had deficits in operant conditioning. In contrast, overexpression of S6KII had a dominant-negative effect on operant conditioning.

◆ Neurobiology of Disease

Impaired Channel Subunit Interaction in a Family with Epilepsy

J. Spampanato, J. A. Kearney, G. de Haan, D. P. McEwen, A. Escayg, I. Aradi, B. T. MacDonald, S. I. Levin, I. Soltesz, P. Benna, E. Montalenti, L. L. Isom, A. L. Goldin, and M. H. Meisler
(see pages 10022–10034)

Most cases of generalized epilepsy with febrile seizures plus (GEFS+) are caused by mutations in the SCN family of voltage-dependent sodium channel subunits. In this issue, Spampanato et al. chronicle the effects on channel function caused by a newly discovered mutation in one family with GEFS+. The mutation in the SCN1A subunit, a C-terminal substitution of a negatively charged aspartate residue, weakened direct interactions between the α and β1 subunits. The authors expressed the D1866Y mutant channels of the SCN1 α subunit with wild-type β subunits in oocytes. Although the voltage dependence of activation was unchanged, channel inactivation shifted to more depolarized voltages. The shift in inactivation increased the sustained current or so-called window current within a particular voltage range. The net result will be an increase in cell excitability near threshold voltages, thus tipping the balance toward seizure generation.