This Week in The Journal

● Cellular/Molecular

Calibrating Endogenous Calcium Buffers

Andreas Müller, Maria Kukley, Pia Stausberg, Heinz Beck, Wolfgang Müller, and Dirk Dietrich
(see pages 558–565)

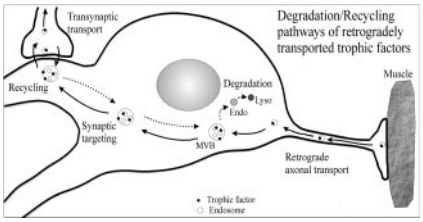
The importance of diffusible intracellular calcium-binding proteins is undisputed in that they create a mechanism for fine-tuning the spatiotemporal profile of cytoplasmic calcium. Müller et al. use a clever combination of patch-clamp recording and immunohistochemistry to measure the concentration of calbindin-D28k in rat hippocampal cells. They first confirmed that calbindin-D28k is mobile, because single-cell calbindin-D28k immunoreactivity decreased with whole-cell recording ($\tau = 10$ min). Next, they filled pipettes with purified calbindin to calibrate the immunofluorescent intensity of hippocampal cells. They concluded that mature granule cells, CA1 pyramidal cells, and CA3 stratum radiatum interneurons all contained ~40 μM, whereas newborn granule cells contained only about half as much. With four calcium-binding sites per molecule, the buffering capacity in mature cells is 160 μM. So what, it's just a number? Well, armed with these figures, the authors conclude, for example, that the mobile buffering substantially reduces free calcium at distances of 100–200 nm from a point source of calcium influx.

▲ Development/Plasticity/Repair

Take a Trophic Factor and Pass it Along

Howard B. Rind, Rafal Butowt, and Christopher S. von Bartheld
(see pages 539–549)

Tetanus toxin, when presented to peripheral nerve terminals, is rapidly transported back to the cell soma, shuttled out to postsynaptic sites on dendrites, and then retrogradely passed to presynaptic terminals by "transsynaptic transcytosis." This week, Rind et al. ask whether endogenous trophic factor molecules can be passed along in the same way or whether they are simply degraded. The authors delivered glial cell-derived neurotrophic factor (GDNF), brain-derived neurotrophic factor (BDNF), and cardiotrophin-1 (CT-1) to nerve terminals of hypoglossal motoneurons in neonatal rats. Using quantitative autoradiographic electron microscopy to assess transport, the authors found that GDNF and BDNF could be transferred transsynaptically, albeit a bit more slowly than tetanus toxin. CT-1, on the other hand, was degraded in the motoneurons. Their work illustrates the economy of neuronal transport of target-derived trophic factors and may provide avenues for CNS delivery of therapeutic agents.



Summary of the trafficking of retrogradely transported trophic factors destined for degradation in the cell body (CT-1) or for additional dendritic and synaptic targeting (GDNF/BDNF). See the article by Rind et al. for details.

■ Behavioral/Systems/Cognitive

Locating One's Self at the Temporoparietal Junction

Olaf Blanke, Christine Mohr, Christoph M. Michel, Alvaro Pascual-Leone, Peter Brugger, Margitta Seeck, Theodor Landis, and Gregor Thut
(see pages 550–557)

In this week's *Journal*, Blanke et al. attempt to link the phenomenon known as an out-of-body experience (OBE) with specific brain activity. During an OBE, one senses that the "self" departs the body so that the body and the world can be viewed from "outside." Being intrepid scientists rather than philosophers, the authors sought to find the "self." To examine this phenomenon, the authors instructed healthy volunteers to imagine an OBE, mentally shifting their visual perspective and body position. During this exercise, evoked potential mapping revealed selective activation at the temporoparietal junction (TPJ). In addition, transcranial magnetic stimulation over the TPJ interfered with this own-body transformation. The authors also describe a patient with epilepsy whose OBE experiences were triggered by seizures originating at the TPJ. It seems that out of the body is not necessarily out of the brain.

♦ Neurobiology of Disease

Pre-mRNA Splicing and Retinal Degeneration

Liya Yuan, Mariko Kawada, Necat Havlioglu, Hao Tang, and Jane Y. Wu
(see pages 748–757)

Retinitis pigmentosa (RP) is a heterogeneous disorder in which retinal degeneration, characterized by night blindness and loss of photoreceptors, can result from mutations in any of a number of different genes. Mutations in PRPF31, a pre-mRNA splicing gene, can cause autosomal dominant RP. Unlike some retina-specific genes that cause RP, PRPF31 is widely expressed in other tissues. This week, Yuan et al. examine how defects in the PRPRF1 gene product can lead to RP. Immunoprecipitation with a PRPF31 antibody produced >100 mRNAs associated with RPR31-containing splicing complexes. The authors focused on two retinal-specific targets of RP11: rhodopsin (RHO) and rod cell outer membrane protein 1 (ROM1). When human RP mutations of PRPF31 were expressed in primary cultured mouse retinal cells, splicing of RHO at intron 3 failed, and expression was reduced. Caspase-dependent apoptotic cell death was increased, perhaps explaining the retina-specific phenotype.