This Week in The Journal

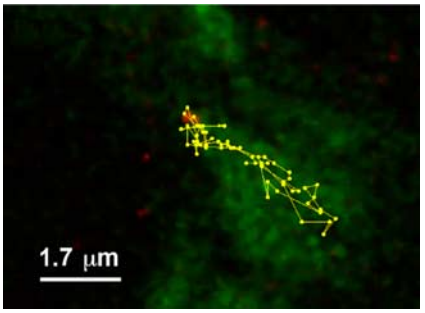
● Cellular/Molecular

Herding Potassium Channels

Kristen M. S. O'Connell, Annah S. Rolig, Jennifer D. Whitesell, and Michael M. Tamkun

(see pages 9609–9618)

Voltage-gated ion channels have to be in just the right spots for proper neuronal function. This week, O'Connell et al. examined the mechanisms governing localization of the delayed-rectifier channel Kv2.1. Previous work showed that these channels are clustered in the membrane of hippocampal neurons and transfected HEK (human embryonic kidney) cells. Using live imaging of cells expressing GFP (green fluorescent protein)-tagged Kv2.1, the authors found that individual channels within clusters were highly mobile. To watch the channels, they used FRAP (fluorescence recovery after photobleaching). To be sure that they were watching channels in the membrane, they also biotinylated channels and then tracked them using streptavidin-coated quantum dots. The high surface mobility appears inconsistent with tethering to scaffolding proteins. Instead, the clustering may involve the sequestration of mobile channels within what the authors call a "perimeter fence." New Kv2.1 channels were delivered to clusters by fusion of adjacent surface clusters and fusion of intracellular transport vesicles that contained channels.



The track of a quantum dot (QD) is shown for a hippocampal neuron transfected with green fluorescent protein–Kv2.1. Channels were biotinylated and tracked with streptavidin-coated QDs. The dot began at the top left (red dot) and was tracked at 0.56 s intervals.

▲ Development/Plasticity/Repair

NT-3 and Axon Bridging After Injury

Laura Taylor, Leonard Jones, Mark H. Tuszynski, and Armin Blesch

(see pages 9713–9721)

Neurotrophic factors can stimulate the growth of axons after spinal cord injury. For example, when genetically modified cells expressing the neurotrophin NT-3 are grafted into the site of injury, axons grow into the lesion. However, these axons rarely exit the graft to innervate the adjoining spinal cord. This week, Taylor et al. tried to overcome this stumbling block to regeneration. They transplanted grafts of syngeneic marrow stromal cells overexpressing NT-3 into dorsal column lesions in the adult rat spinal cord; this fiber tract carries ascending sensory axons. The authors then injected lentiviral vectors expressing NT-3 at sites rostral to the graft, thus establishing an extended gradient of neurotrophic factor to guide axon growth. In injected animals, axons indeed bridged the gap and extended beyond the graft boundary but did not proceed further than 500 μm, although NT-3 gradients extended further. Thus, the growth pattern was not strictly "chemotropic."

■ Behavioral/Systems/Cognitive

The Value of Singing to Yourself

Jon T. Sakata and Michael S. Brainard

(see pages 9619–9628)

We have something in common with birds when it comes to how we communicate. Both species rely on hearing the sounds they produce to learn and maintain accurate vocalization, a built-in quality-control mechanism. Likewise, loss of hearing leads to deterioration of speech and song. In humans, auditory feedback contributes to speech in real time, and so it is for birdsong, as Sakata and Brainard show this week. They recorded target "syllables" from the songs of the Bengalese finch and played them back at a short and fixed latency, so that the singing bird heard the computerized feedback superimposed onto its own song. When the feedback was altered, birds changed their normal tempo and sequencing of specific syllables. This behavioral response to momentary targeted disruptions was ~80 ms or about the duration of an individual syllable, suggesting rapid feedback of auditory information to the song premotor circuitry.

♦ Neurobiology of Disease

FGF-20 and Survival of Dopamine Neurons

Sachiko Murase and Ronald D. McKay

(see pages 9750–9760)

Neurotrophins are being explored as potential neuroprotective agents in Parkinson's disease (PD). This week, Murase and McKay explore a possible role for fibroblast growth factor 20 (FGF-20) in the survival of dopaminergic neurons. They were interested because polymorphisms in FGF-20 are associated with an increased risk of PD, and FGF-20 is specifically expressed in the substantia nigra. Using cultures from rat midbrain, they found that FGF-20 protected calbindin-negative dopaminergic neurons, the subset of cells preferentially lost in PD patients, from damage induced by the toxin 6-OHDA. FGF-20 rapidly activated anti-apoptotic events in these cells, such as phosphorylation of Bad and downregulation of Bax, which may explain the neuroprotective effect. In addition to promoting survival, FGF-20 increased tyrosine hydroxylase expression, resulting in increased levels of dopamine synthesis and release. The specificity to calbindin-negative neurons appears to be explained by selective expression of the receptor FGFR1c in these cells.