This Week in The Journal

● Cellular/Molecular

Camphor's TRP

Haoxing Xu, Nathaniel T. Blair, and David E. Clapham

(see pages 8924 – 8937)

Camphor, an age-old component of home remedies, is a plant derivative that acts as a topical anesthetic. This week, Xu et al. explored the mechanism of action of camphor by examining its effects on members of the large and complex transient receptor potential (TRP) channel family. In heterologous cells, camphor activated the capsaicin-sensitive channel TRP vanilloid subtype 1 (TRPV1). Camphor-activated TRPV1-like currents were also found in dorsal root ganglion neurons. Although camphor was less potent than capsaicin in TRPV1 activation, desensitization was more complete, suggesting that the desensitizing action could contribute to analgesia. However, camphor inhibited other TRP channels such as TRPA1 (also expressed in nociceptors) that may also contribute to its effects. Although camphor can also activate TRPV3, this response sensitized with repeated exposure, suggesting that TRPV3 does not contribute to analgesia, but it may underlie the warm sensation produced by camphor.

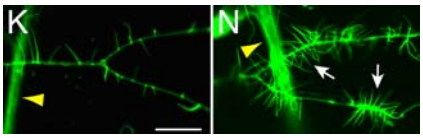
▲ Development/Plasticity/Repair

CaMKII and Dendritic Filopodia in Drosophila

Ryan Andersen, Yimei Li, Mary Resseguie, and Jay E. Brenman

(see pages 8878 – 8888)

Filopodia are the small protrusions that make time-lapse movies of dendrites worth watching. They serve as precursors to dendritic spines and pioneer the development of dendritic arbors. This week, Andersen et al. examined the effects of cytoskeletal regulatory molecules on filopodial plasticity in *Drosophila* larvae. They focused on dendritic arborization (da) peripheral neurons. Expression of a constitutively active mutant form of calcium/calmodulin-dependent kinase II (CaMKII), T287D, increased the number of filopodia on da dendrites and increased actin turnover. In contrast, the T287A mutant, which is only active in the continuous presence of calcium, increased the length but not the number of filopodia. Rac1, which also modifies the actin cytoskeleton, increased filopodial formation as well. CaMKII affected only neurons that normally contained filopodia, whereas Rac1 caused *de novo* synthesis of filopodia in all da neurons. These results suggest different pathways for the actions of CaMKII and Rac1 on dendritic filopodia.



Equivalent dendritic branches from the class III ddaA neuron had marked increases in filopodia when expressing CaMKII T287D (right) compared with wild type (left). See the article by Andersen et al. for details.

■ Behavioral/Systems/Cognitive

Trading Spaces: Neural Activity and Tissue Oxygen

Jeffrey K. Thompson, Matthew R. Peterson, and Ralph D. Freeman

(see pages 9046 –9058)

Although brain imaging is an invaluable tool, the signals are indirect and complex measures of the underlying neural activity or metabolism. For example, the blood oxygen level-dependent response, the basis of functional magnetic resonance imaging, depends on cerebral blood flow, blood volume, and the metabolic rate of oxygen. To assess the spatiotemporal characteristics of these changes, Thompson et al. used a microelectrode sensor to simultaneously measure local tissue oxygen and multiunit neural activity. The sensor provides a weighted average tissue pressure of oxygen in a tissue volume of ~60 μm in diameter. The authors recorded from the lateral geniculate nucleus, which is organized into small receptive fields allowing for fine spatial control of activity, and from the visual cortex in the cat. Near the sensor, oxygen levels dipped, whereas neural activity that extended over the range of several millimeters caused an increase in oxygen levels. These spatiotemporal constraints shape the resolution of functional neuroimaging methods.

♦ Neurobiology of Disease

Cdk5 and Neuronal Death

Michael J. O'Hare, Neena Kushwaha, Yi Zhang, Hossein Aleyasin, Steven M. Callaghan, Ruth S. Slack, Paul R. Albert, Inez Vincent, and David S. Park

(see pages 8954 – 8966)

Neuronal activation of cyclin-dependent kinase 5 (cdk5) depends on the neuron-specific expression of its partners, p35 and p39. When p35 is cleaved to p25 by calpain, cdk5 acts as a pro-death molecule, but cdk5 can also promote survival. Thus, O'Hare et al. set out to determine what factors influence cdk5 action. They compared *in vitro* cell death caused by the DNA-damaging agent camptothecin (CA) with excitotoxic cell death. After CA, levels of p35 in cultured cortical neurons fell as p25 rose, and cdk5 activity declined. Complexes of p25/cdk5 were elevated in the nucleus, but apparently too late to affect cell death. The decline of p35/cdk5 complexes in the cytoplasm, however, sensitized cells to apoptosis. In cerebellar granule neurons treated with an excitotoxic dose of glutamate, p35 was rapidly cleaved to p25. Inhibition of nuclear cdk5 prevented excitotoxic cell death. Thus, pro-survival p35/cdk5 signaling was cytoplasmic, whereas pro-death p25/cdk5 signaling was nuclear.