When LDH says “open,” channels listen

A channel that protects cardiac cells from ischemia uses a rapid metabolite detection system to perceive dangerous conditions, according to new results from Russell Crawford, Aleksander Jovanovic, and colleagues (University of Dundee, Dundee, UK).

A heart attack damages cells when anaerobic conditions disrupt active ion transport, leading to a toxic increase in intracellular Ca$^{2+}$. A decrease in ATP levels initially impairs ion transport, causing depolarization and Ca$^{2+}$ import. However, low ATP may also trigger opening of ATP-sensitive K$^+$ (K$^+$ATP) channels, which would counteract the depolarization, ultimately reducing the time for Ca$^{2+}$ influx.

But ATP regulation is not the whole story, as K$^+$ATP channels open before intracellular ATP levels drop enough to open the channel. This prompted the group to search for additional components. They have now found that lactate dehydrogenase (LDH) interacts directly with the channel subunits. LDH catalyzes the reversible conversion of pyruvate to lactate, and thus may supply a local concentration of lactate to the channel. Indeed, the group demonstrated that lactate opened the channel despite high levels of ATP. Further, this regulated opening was crucial for the channel’s ability to protect from ischemia.

Reference: Crawford, R.M., et al. 2002. EMBO J. 21:3936–3948.

Seeing in motion

A class of neurons known as starburst amacrine cells compute the direction of a visual stimulus, according to new results from Thomas Euler, Peter Detwiler (University of Washington, Seattle, WA), and Winfried Denk (Max Planck Institute for Medical Research, Heidelberg, Germany). The experiments show that starburst dendrites signal independently of the electrical activity of the soma, an ability that dendrites of other neurons may share.

Starburst cells are radially symmetric interneurons with synaptic outputs and inputs coexisting on neuronal processes, called dendrites. Based on their position in the retina, starburst amacrine cells have been hypothesized to activate directionally selective ganglion cells. Genetic experiments have supported this theory, but how the cells calculate direction was unknown.

Now, the power of these cells to use Ca$^{2+}$ to report direction is shown. Euler et al. found that, unlike membrane voltage in the soma, dendritic Ca$^{2+}$ signals are directionally selective. Larger Ca$^{2+}$ increases were evoked by light moving outward from the cell soma to the end of the dendrites, where synaptic outputs are clustered, than were evoked by the same stimulus moving toward the soma. Thus, a starburst dendrite acts as an independent module to compute stimulus direction. How different Ca$^{2+}$ responses are generated based on direction is unclear. Possibly, the specific dendrite morphology promotes temporal summation of the signal when the stimulus moves toward the periphery, but not in the reverse direction.

Reference: Euler, T., et al. 2002. Nature. 10.1038/nature01006.

Traveling backward

A new study of antigen-presenting cells has revealed a previously unseen pathway for recovering proteins from lysosomes, normally a dead-end for proteins. Amy Chow, Ira Mellman, and colleagues (Yale University, New Haven, CT) have visualized a selective retrograde transport pathway to the plasma membrane.

The pathway, which has also been seen by Marianne Boes, Hidde Ploegh (Harvard Medical School, Boston, MA), and colleagues, starts at lysosomes, which in most cells are highly degradative. But in immature dendritic cells (DCs), lysosomes house internalized antigens and MHC class II molecules until the cells mature. After maturation, MHC II molecules reside on the plasma membrane, where they activate T cells. Previous microscopy of maturing DCs has given glimpses of tubulating lysosomes and nonlysosomal vesicles that contain MHC II molecules, hinting at the presence of an unusual transport pathway.

Chow et al. have now put the pathway together by combining conventional microscopy with total internal reflectance fluorescence microscopy, which can be used to visualize fusion events. Examining live DCs expressing GFP-labeled MHC II molecules, says Mellman, "we see that transporters can leave lysosomes and travel all the way to the cell surface carrying the cargo we expected." Thus, MHC II molecules and their bound antigens end up on the plasma membrane instead of being degraded. Other cells may also be capable of retrograde transport from lysosomes, although it is most easily seen in maturing DCs because the process is synchronized.

References: Chow, A., et al. 2002. Nature. 10.1038/nature01006. Boes, M., et al. 2002. Nature. 10.1038/nature01004.