Sensing voltage for function

The first protein to sense changes in membrane potential but not function as an ion transporter is now identified by Yoshimichi Murata, Hirohide Iwasaki, Mari Sasaki, Yasushi Okamura, and colleagues (National Institutes of Natural Sciences, Aichi, Japan). Activation of this sensor probably induces phosphorylation-based signaling events.

The group discovered this sea squirt protein, Ci-VSP, based on its sequence homology with ion channels. But the homology was confined to four transmembrane segments that comprise a voltage sensor. This domain functions just like the voltage sensor domains of channel proteins. Ci-VSP also contains a cytoplasmic phosphatase domain, but lacks a pore domain to transport ions across the plasma membrane.

Using an in vivo bioassay, Okamura’s group showed that Ci-VSP changes cellular phosphoinositide concentrations in response to membrane potential changes. “These data provide the first evidence since the Hodgkin-Huxley age that a molecular function other than that of ion channels is regulated by membrane voltage,” he says.

Ci-VSP is expressed in sperm and might function in sperm motility or morphology. The authors’ next goal is to identify the natural substrate of Ci-VSP, which they suspect is PIP3, so that they can determine whether membrane hyperpolarization or depolarization activates the enzyme. JCB

Reference: Murata, Y., et al. 2005. Nature. 435:1239–1243.

Voltage-gated channel

Ci-VSP

Ci-VSP’s voltage sensor (blue) regulates a phosphatase domain (green), not a pore domain (pink), as in voltage-gated channels.

Fiber flex

Fibrin fibers bend much more than they stretch, according to Jean-Philippe Collet, John Weisel (University of Pennsylvania, Philadelphia, PA), and colleagues. This flexibility lends the necessary elasticity to blood clots.

Blood clots, which are composed of fibrin fibers, are both elastic and plastic—they mostly return to their original form after stretching but can also be irreversibly deformed. This viscoelasticity makes clots stiff enough to stem blood flow but pliable enough not to become obstructive.

Weisel’s group investigated the mechanical properties of individual fibers that confer viscoelasticity to clots. They used laser tweezers to pull on beads attached to fibrin fibers within clots that were prepared from blood plasma. By measuring the force required to displace the bead a given distance, they calculated the fiber stiffness and found that individual fibrin fibers are 300 times more pliant for bending than they are for stretching. “From these measurements and from the clot structure,” says Weisel, “we can say that fibrin is not rubber-like,” which some scientists had previously hypothesized to account for clot elasticity.

Fibers could be stiffened nearly tenfold by the addition of factor XIIIa, an enzyme that stabilizes clots by creating covalent linkages between fibrin molecules. Weisel’s group now plans to model how the mechanical properties of individual fibers relate to the viscoelasticity of whole clots. Weisel notes, “I hope this research gets the attention of clinicians as well as researchers, because the mechanical properties of clots are important for understanding their function and pathology.” JCB

Reference: Collet, J.P., et al. 2005. Proc. Natl. Acad. Sci. USA. 102:9133–9137.

Smell’s different

Odorant amplification occurs automatically in an activated rod cell, but not so simply in olfactory cells, according to Vikas Bhandawat, Johannes Reisert, and King-Wai Yau (Johns Hopkins University, Baltimore, MD).

Photon activation of a single rhodopsin molecule activates many G proteins, thereby amplifying the signal until rhodopsin is inactivated by phosphorylation. “Based on this one well-studied system, it has generally been assumed that other G protein pathways behave similarly,” says Yau. Now, his group’s analyses of single olfactory receptor neurons reveal a low amplification system.

An individual odorant-bound receptor exhibited a very low probability of activating even one downstream G protein molecule, as odorant receptor binding was transient—lasting 1 ms or less. “We expect many other ligand-triggered G protein pathways to behave similarly,” says Yau.

Olfaction amplification therefore requires increasing the probability of G protein activation. This could be achieved either via many odorant molecules that continuously bind to receptors, or via a large number of receptors, so that odorants at low concentrations will still be able to find a receptor. “When these events are summated across all receptor molecules on the cell, and all cells express the same receptor protein,” says Bhandawat, “this produces substantial signal amplification and therefore high sensitivity in the brain.” JCB

Reference: Bhandawat, V., et al. 2005. Science. 308:1931–1934.