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New studies reveal downstream processes of ion channel inactivation

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Two studies by researchers at The Johns Hopkins University School of Medicine reveal new details of the mechanisms of ion channel inactivation. The papers appear in the March issue of *The Journal of General Physiology*.

After opening, many ion channels spontaneously close by inactivation, a process distinct from that involved in opening. The inactivation of channels is important for a variety of biological processes, including the timing of action potentials and the control of calcium permeability, which affects many aspects of intracellular signaling. Although the events of Ca^{2+}-dependent inactivation (CDI) and voltage-dependent inactivation (VDI) have been unveiled in the past decade, the downstream mechanisms remained unclear.

Tadross et al. studied both CDI and VDI in Cav1.3 channels and showed them to differ not only in their initiation mechanisms but also in their distinct molecular endpoints. For CDI, a clear pattern emerges: activation-enhancing mutations proportionately weaken inactivation, supporting the idea that CDI reduces channel permeability by allosteric hindrance of the activation gate. For VDI, the data implicate a "hinged lid-shield" mechanism, similar to a hinged-lid process, with a previously unrecognized feature, a "shield" in Cav1.3 channels that is specialized to repel lid closure.

In a Commentary accompanying the papers, Jianmin Cui (Washington University, St. Louis) examines the mechanisms of inactivation and

provides context for the importance of the new findings by Tadross et al.

More information: References:

Cui, J. 2010. J. Gen. Physiol. doi:10.1085/jgp.201010421.
Tadross, M.R., et al. 2010. J. Gen. Physiol. doi:10.1085/jgp.200910308.
Tadross, M.R., and D.T. Yue. 2010. J. Gen. Physiol. doi:10.1085/jgp.200910309.

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