New clues to the structural dynamics of BK channels

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BK channels (large-conductance, Ca2+-dependent K+ channels) are essential for the regulation of important biological processes such as smooth muscle tone and neuronal excitability. New research shows that BK channel activation involves structural rearrangements formerly not understood. The study appears in the August 2011 issue of the *Journal of General Physiology*.

Previous research pointed to a possible unified theory of activation gating in K+ channels, with the "activation gate" formed by the bundle crossing of four S6 transmembrane helices from the four subunits. Recent studies, however, have suggested a different structure for BK channels, but the exact location of the activation gate remained a mystery.

A new study by Xixi Chen and Richard Aldrich (The University of Texas at Austin) provides important clues to this question. The research identifies a single residue M314, halfway down S6, that appears to change conformation during the opening of the BK channel, rotating its side chain from a position in the closed state not exposed to the hydrophilic pore to one that is so exposed in the open state. The results further show that M314 might not actually form the part of the activation gate that blocks ion passage, but that motions in the deep pore may be required for blocking ion passage elsewhere in the channel.

The findings point to new directions for research regarding the molecular mechanisms of BK channel activation, according to

Commentary by Daniel Cox (Tufts University School of Medicine) and Toshinori Hoshi (University of Pennsylvania). Importantly, they say, the study demonstrates that BK channel activation is not an open-and-shut case as previously suspected.

More information: Cox, D.H., and T. Hoshi. 2011. J. Gen. Physiol. doi:10.1085/jgp.201110681.
Chen, X., and R.W. Aldrich. 2011. J. Gen. Physiol. doi:10.1085/jgp.201110632.