Fitting Kv potassium channels in the PIP2 puzzle

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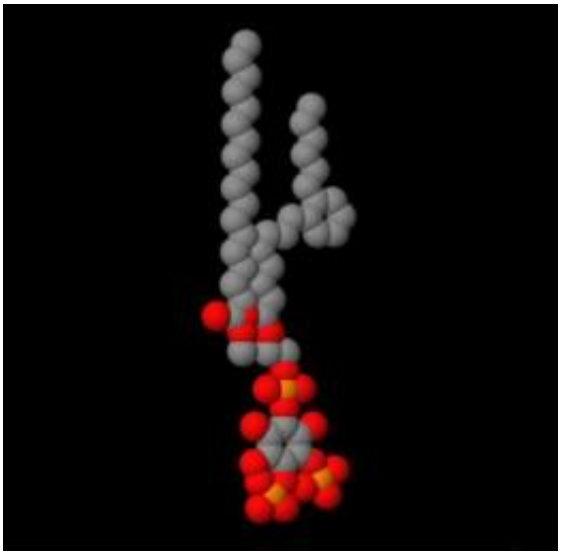

A recent JGP study brings new insights to an area of ion channel regulation: whether voltage-gated potassium (Kv) channels can be regulated by physiological changes to PIP2 (shown here), a minor phospholipid component of cell membranes that binds to various membrane proteins and modulates their activity. Credit: Adler, E.M. 2012. J. Gen. Physiol. doi:10.1085/jgp.201210877 (image created with Jmol)

A recent study in the *Journal of General Physiology* brings new insights to an area of ion channel regulation: whether voltage-gated potassium (Kv) channels can be regulated by physiological changes to PIP_2.

Potassium channels, microscopic pores that allow potassium ions to cross

cell membranes, are crucial to such diverse processes as conduction of the nerve impulse, regulation of the heartbeat, and the secretion of hormones such as insulin. PIP_2, a minor phospholipid component of cell membranes, regulates the activity of various proteins in the cell membrane, and previous studies have indicated that it might be a very important regulator of such channels. To probe the cell signaling roles of PIP_2 under physiological conditions, Bertil Hille (University of Washington) and colleagues used a set of sophisticated molecular tools to rapidly deplete PIP_2 in the membranes of intact cells and simultaneously monitor the PIP_2 changes that occurred. Using this approach, they confirmed previous studies showing that the activity of "inward rectifier" potassium channels was strongly dependent on PIP_2. Surprisingly, however, they found that various members of the Kv channel family thought to be PIP_2 sensitive on the basis of studies that analyzed their activity in isolated patches of cell membrane were, in fact, unaffected by PIP_2 depletion. Thus, the group demonstrated that large PIP_2 changes at the membranes of intact cells did not modulate the function of these Kv channels, contrary to expectations.

According to Donald Hilgemann (UT Southwestern Medical Center at Dallas) in commentary appearing in the September 2012 issue of *JGP*, the findings are an important step forward in our understanding of PIP_2 effects on Kv channels. Furthermore, the tools employed by the Hille group can now be used to address questions about PIP_2 functions in other cellular processes. In addition to its complex roles in cytoskeleton regulation and endocytosis, PIP_2 appears to influence many cell membrane processes, including the formation of membrane domains, membrane budding, and membrane turnover.

More information: Hilgemann, D.W., et al. 2012. J. Gen. Physiol. doi:10.1085/jgp.201210874.
Kruse, M., G.R.V. Hammond, and B. Hille. 2012. J. Gen. Physiol. doi:10.1085/jgp.201210806