

A new concept in the field of voltage-gated ion channels

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(Phys.org) -- Virginia Commonwealth University School of Medicine researchers have uncovered a novel way by which the activity of voltage-gated potassium channels are regulated, according to a study published online last week in the Early Edition of the *Proceedings of the National Academy of Sciences*.

The findings may allow researchers to better understand and control how external signals – for example, hormones and neurotransmitters – can modulate excitability of cells. This understanding provides critical information on how to adjust cellular excitability when it needs to be stimulated.

By conducting basic science research, the team, led by Diomedes Logothetis, Ph.D., an internationally recognized leader in the study of ion channels and chair of the VCU School of Medicine's Department of Physiology and Biophysics, is hoping to understand the fundamental mechanisms by which membrane lipid-protein interactions regulate the activity of proteins, such as potassium (Kv) channels.

In this new study, Logothetis and his team have clarified the role of phospholipid phosphatidylinositol-bisphosphate, PIP₂, a minor component of the inner leaflet of the plasma membrane that controls the activity of most ion channels and transporters.

They found PIP₂ to be responsible for controlling the activation mechanism of Kv channels that reside in cells that generate electrical



impulses to control heart rate and brain signaling.

Since the 1980s, investigators have known that the part of voltage-gated channels that senses membrane voltage changes is coupled to the pore via a linker called the S4-S5 linker. But it was not known until now that PIP₂ regulates the activity of Kv channels by interacting with this helical linker.

"Our study showed that this helical structure interacts with PIP₂ in the membrane to regulate how much the voltage sensor can pull on the pore to open it," said Logothetis.

More information: www.pnas.org/content/early/201 ... 8/10/1207901109.long

Provided by Virginia Commonwealth University

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