Signal-dependent hydrolysis of phosphatidylinositol 4,5-bisphosphate without activation of phospholipase C: implications on gating of Drosophila TRPL (transient receptor potential-like) channel.

By elscape_admin
Created 5/28/2012
By elscape_admin May 28, 2012


Abstract:

In Drosophila, a phospholipase C (PLC)-mediated signaling cascade, couples photo-excitation of rhodopsin to the opening of the transient receptor potential (TRP) and TRP-like (TRPL) channels. A lipid product of PLC, diacylglycerol (DAG), and its metabolites, polyunsaturated fatty acids (PUFAs) may function as second messengers of channel activation. However, how can one separate between the increase in putative second messengers, change in pH, and phosphatidylinositol 4,5-bisphosphate (PI(4,5)P(2)) depletion when exploring the TRPL gating mechanism? To answer this question we co-expressed the TRPL channels together with the muscarinic (M1) receptor, enabling the openings of TRPL channels via G-protein activation of PLC. To dissect PLC activation of TRPL into its molecular components, we used a powerful method that reduced plasma membrane-associated PI(4,5)P(2) in HEK cells within seconds without activating PLC. Upon the addition of a dimerizing drug, PI(4,5)P(2) was selectively hydrolyzed in the cell membrane without producing DAG, inositol trisphosphate, or calcium signals. We show that PI(4,5)P(2) is not an inhibitor of TRPL channel activation. PI(4,5)P(2) hydrolysis combined with either acidification or application of DAG analogs failed to activate the channels, whereas PUFA did activate the channels. Moreover, a reduction in PI(4,5)P(2) levels or inhibition of DAG lipase during PLC activity suppressed the PLC-activated TRPL current. This suggests that PI(4,5)P(2) is a crucial substrate for PLC-mediated activation of the channels, whereas PUFA may function as the channel activator. Together, this study defines a narrow range of possible mechanisms for TRPL gating.

Journal:
The Journal of biological chemistry

Volume:
287

Issue:
2
UPCOMING EVENTS

Learn more about our exciting upcoming events!

read more

Studying at ELSC

Our Int'l Ph.D. program provides outstanding students with top-notch courses in computational neuroscience.

read more

The Building

The Jerusalem Brain Sciences Building will provide a state-of-the-art research and teaching facility for the Edmond and Lily Safra Center for Brain Sciences.

read more

ELSC Media Channel

Get into our media channel and investigate ELSC’s latest videos: seminars, public lectures, courses and video articles.

read more

Source URL: https://elsc.huji.ac.il/minke/publications/signal-dependent-hydrolysis-phosphatidylinositol-45-bisphosphate-without-activati