A lipid required for vision identified in fruit flies

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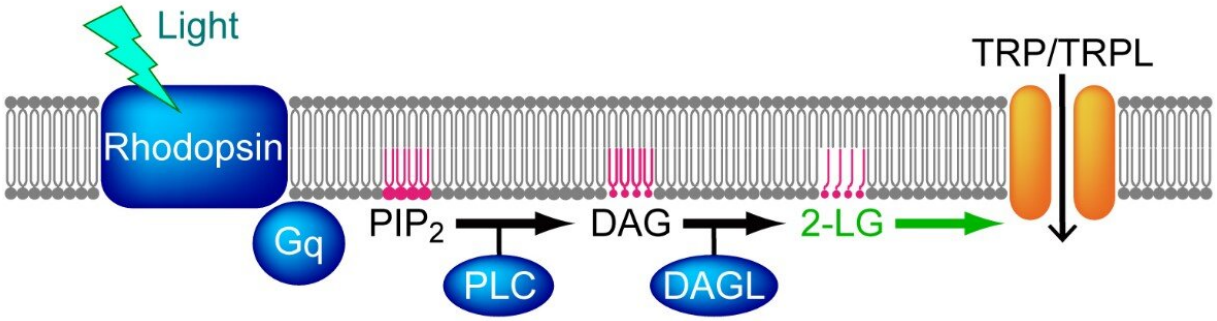

The Drosophila phototransduction cascade is shown. The signaling cascade downstream of DAG was unclear. This study identified an endocannabinoid 2-LG as a TRP channel activator. Credit: Takaaki Sokabe

Decades of studies on Drosophila vision have revealed multiple components required for the signaling events upon light stimulation. Light first turns on the photosensitive rhodopsin and, following several intermediate steps, leads to activation of Transient Receptor Potential (TRP) channels. Lipids are thought to lead to opening of TRP channels and stimulation of photoreceptor cells. However, the essential lipid molecules that directly activate TRP channels were unclear. In this study, researchers identified an endocannabinoid that plays important roles in the channel activation in photoreceptor cells.

Drosophila visual transduction is a classical model of signaling cascades

that culminate with the activation of TRP cation channels. In humans, these channels have many roles, including pain sensation, taste and light detection. In Drosophila, light stimulates rhodopsin in photoreceptor cells, thereby facilitating activation of a protein called Gq. The Gq then turns on an enzyme, phospholipase C (PLC), to produce a lipid—diacylglycerol (DAG). The TRP channels need DAG or a subsequently produced lipid, although the precise lipid was not known.

Takaaki Sokabe at the National Institute for Physiological Sciences and Craig Montell at the University of California, Santa Barbara found a lipid—an endocannabinoid—which increased upon light stimulation and activated the TRP and TRPL channels. The particular endocannabinoid that activates these channels, 2-linoleoyl glycerol (2-LG), is related to the active ingredient in marijuana, tetrahydrocannabinol (THC). They recently published their findings in *Science Signaling*.

"We expected that we could find the essential lipids for activating the TRP channels by identifying lipids that increased in fly heads upon light stimulation," Sokabe says. "However, it was not quite as easy as that. We first spent five years just to establish conditions to stably observe changes in lipids using hundreds of flies in every sample."

This effort led to the demonstration that 2-LG increased upon illumination. This change in 2-LG levels depended on the PLC and on another enzyme, called DAG lipase, which had been reported to be involved in visual transduction. Furthermore, they showed that 2-LG stimulated the TRP channels in isolated photoreceptor cells.

"Identification of the endocannabinoid in the cascade at least partially connects the gap between DAG production and the TRP channel activation," says Takaaki Sokabe. "The same signaling cascade is conserved in one type of mammalian photoreceptor cells, and the mechanism may be applicable to other TRP channel-dependent cascades

in various type of cells."

This work could promote our understanding of visual systems and other sensory systems.

More information: Takaaki Sokabe et al, Endocannabinoids produced in photoreceptor cells in response to light activate Drosophila TRP channels, *Science Signaling* (2022). DOI: 10.1126/scisignal.abl6179

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