UC SANTA BARBARA

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Subtle Flavors

Evolution is a tinkerer, not an engineer. “Evolution does not produce novelties from scratch. It works with what already exists,” wrote Nobel laureate François Jacob in 1977, and biologists continue to find this to be true.

Case in point: A team of scientists led by researchers at UC Santa Barbara has discovered that multiple opsin proteins, known for decades to be required for vision, also function as taste receptors. The finding, which appears in Current Biology, represents a light-independent function for opsins, and raises questions about the purpose these proteins served in ancient organisms.

“This is the first example of a role of opsins in taste, or in any form of chemical sensation,” said coauthor Craig Montell, a distinguished professor of molecular, cellular, and developmental biology.

Scientists in the late 1800s discovered the light-sensing role of rhodopsin — which consists of an opsin bound to retinal, a form of vitamin A — and it has since become the most studied sensory receptor. Until recently, researchers believed that the family of rhodopsin proteins was involved only in light reception. However, in 2011, Montell and his colleagues found that an opsin enables the fruit fly *Drosophila melanogaster* to detect small temperature changes within its comfortable range.

Animals have many types of sensory proteins that respond to stimuli from the environment. Some require a strong stimulus, such as scalding heat, to activate. Rhodopsins are able to respond to very subtle changes or very low levels of stimuli—

like those in very dim light conditions — and then initiate a molecular cascade that amplifies the signal, ultimately activating a sensory response.

Researchers in Montell's lab used aristolochic acid — a toxic, bitter compound found in some plants — to study taste receptors in fruit flies. High concentrations of this bitter chemical activate the flies' taste neurons by directly opening a channel protein called TRPA1, which lets calcium and sodium into the cells. This leads to a bitter taste the animals avoid. However, the flies also avoid even highly diluted aristolochic acid, which isn't a strong enough signal to open the channels directly.

Montell and lead author Nicole Leung, who recently completed her predoctoral studies at UC Santa Barbara, suspected opsin molecules might be at work in detecting subtle chemical signals as well, via a signal amplification process.

They presented flies with a choice between sugar alone or sugar spiked with dilute aristolochic acid. Unsurprisingly, the flies rejected the sugar laced with the bitter chemical and ate the pure sugar.

The scientists then raised fruit flies with mutations that prevented them from synthesizing different opsin proteins. They found that flies with defects in any one of three types of opsins couldn't detect the small concentrations of acid, and ate nearly equal amounts of the sugar laced with the bitter compound as the pure sugar. However, the mutant animals were still sensitive to large amounts of the bitter compound, which they continued to avoid. According to Montell, the large amounts of the bitter chemical directly activated the TRPA1 channel, which was still present in the flies missing the opsins.

The team showed that aristolochic acid activated these opsins by binding to the same site that retinal normally does in rhodopsin. Much like rhodopsins turned on by very dim light, the chemically-activated opsins then initiated a molecular cascade that amplified the small signals. This enabled the flies to detect concentrations of the compound that would otherwise be insufficient to trigger a response in their sensory neurons.

"Rhodopsins were discovered back in the 1870s," Montell said, "so to discover that opsins have roles in taste after 150 years or so is pretty exciting."

Montell speculates that chemoreception may have been the original role of opsin proteins. Chemical reception, he said, is a more basic requirement for life than is

light reception. Knowing what to eat and what dangerous chemicals to avoid serves a more ancient survival function than does the ability to detect light. Perhaps by chance, he ventured, a retinal became bound to an opsin and conferred light sensitivity to the opsin.

Following Montell's 2011 discovery that opsins function in temperature sensation, another group found that opsins play a role in hearing in flies. Now, with the demonstration that opsins are taste receptors as well, Montell suspects they may be involved in still additional senses.

"In every case, they provide a mechanism for sensing low levels of stimuli by initiating an amplification cascade," he said.

The new finding likely extends beyond the fruit flies the scientists studied. "The ramifications are that maybe opsins represent a new class of taste receptor in mammals, including humans," said Montell, a hypothesis the team is currently investigating.

About UC Santa Barbara

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