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RESEARCH NEWS

Mechanotransduction by Membrane Proteins

Worms find PEZO-1's function easy to swallow

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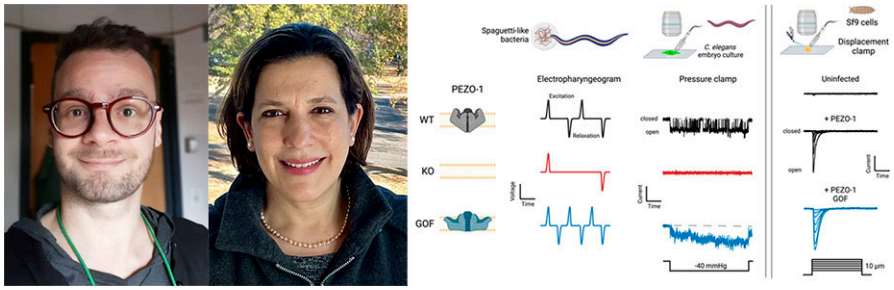
JGP study finds that the _C. elegans_ orthologue of the PIEZO family is a mechanosensitive ion channel that regulates pharyngeal pumping and food sensation.

The PIEZO family of mechanosensitive cation channels has been implicated in a wide variety of physiological processes in mammals and is also associated with human disease. Mammalian genomes encode two family members, known as *Piezo1* and *Piezo2*, but invertebrates such as the nematode *Caenorhabditis elegans* only possess a single *Piezo*-related gene (1). The function of the *C. elegans* orthologue, known as *pezo-1*, has largely remained obscure, but, in this issue of *JGP*, Millet et al. reveal that it encodes a bona fide mechanosensitive ion channel that regulates pharyngeal activity (2).



Jonathan Millet (left), Valeria Vásquez (center), and colleagues reveal that *pezo-1*, the sole PIEZO family member in *C. elegans*, is a mechanosensitive ion channel that regulates pharyngeal pumping and food sensation, particularly when worms are fed with large and stiff bacterial filaments that are difficult to swallow (graphic created with BioRender.com).

In 2020, an elegant study demonstrated that *pezo-1* controls *C. elegans* ovulation and fertilization (3). However, explains Valeria Vásquez from the University of Tennessee Health Science Center, whether *pezo-1* encodes for a mechanosensitive ion channel was unknown. "PEZO-1 is expressed in many tissues, including the pharynx, which is the organ we decided to concentrate on in our study," Vásquez says.

Muscle cells in the *C. elegans* pharynx rhythmically contract and relax to pump food into the worm's intestine. Vásquez and colleagues, including first author Jonathan Millet, found that PEZO-1 is expressed in several different pharyngeal cell types (2), including the gland cells whose secretions lubricate the pharynx, and the proprioceptive NSM neurons that are thought to sense the presence of food within the pharynx lumen and release serotonin to increase the rate of pharyngeal pumping.

Millet et al. analyzed pharyngeal pumping in worms lacking *pezo-1*, as well as in animals expressing a *pezo-1* point mutant that, in human *Piezo1*, increases channel function by slowing channel deactivation and inactivation. Loss or gain of *pezo-1* function had surprisingly little effect on pharyngeal activity, causing only mild alterations in the duration and frequency of pumping induced by serotonin, and more obvious effects when challenged with high osmolarity solutions.

Worms cultured in the laboratory are usually fed a diet of small, easily ingested *Escherichia coli* cells and, both loss and gain of *pezo-1* function increased the pharynx's response to this type of food. In their natural habitat, however, *C. elegans* encounter bacteria of various shapes and sizes, some of which might be harder to swallow. "It occurred to me that it might make a difference if we fed the worms with bacteria that were stiffer and longer," Vásquez says.

The researchers therefore provided their *pezo-1* mutants with *E. coli* treated with cephalexin, an antibiotic that inhibits cell separation and causes the bacteria to form long, spaghetti-like filaments. Compared with wild-type worms fed with this diet, pharyngeal activity was markedly enhanced by the gain-of-function *pezo-1* mutant, but substantially reduced in the absence of *pezo-1*, almost as if the worms were "choking" on the bacterial filaments.

Crucially, by performing patch-clamp experiments on both cultured *C. elegans* cells and insect cells expressing recombinant *pezo-1*, Millet et al. confirmed that

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This work is part of a special issue on mechanotransduction by membrane proteins.

PEZO-1 is, indeed, a mechanosensitive ion channel. However, it remains to be seen exactly how PEZO-1 helps the pharynx sense the physical parameters of food and adjust its pumping activity accordingly. One possibility is that the channel acts within the proprioceptive neurons to regulate the release of serotonin.

Intriguingly, the *Drosophila* PIEZO orthologue controls feeding behavior in flies (4). "However, it's not known which mechanosensitive channels are important in the pharyngeal system of mammals," Vásquez says. "Our studies in *C. elegans* could therefore open an opportunity to understand food sensation in humans."

References

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