Waste removal in worms reveals new mechanism to regulate calcium signaling

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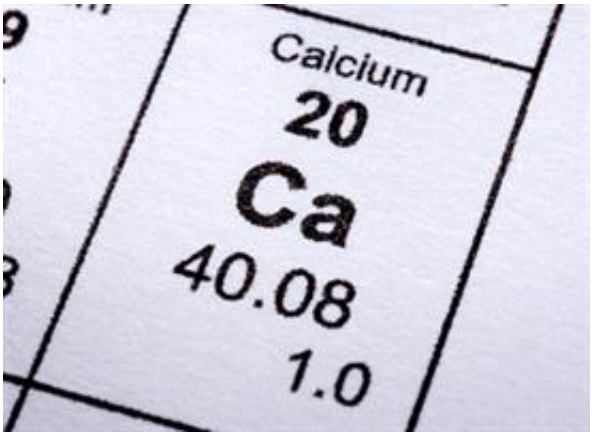

Calcium is so much more than the mineral that makes our bones and teeth strong: It is a ubiquitous signaling molecule that provides crucial information inside of and between cells. Calcium is used to help our hearts beat regularly, our guts to function appropriately and even for fertilization to occur. It is also needed to help muscles and blood vessels contract, to secrete hormones and enzymes and to send messages throughout the nervous system.

In a study published in Current Biology, scientists from the University of Rochester Medical Center, Marquette University and Oberlin College discovered a new way in which calcium signaling may be controlled. Study authors say their findings define a mechanism for regulating

calcium signaling that has never been recognized before and should be of great help to the thousands of scientists who study the extremely important role of calcium signaling in health and disease.

"It is hard to find a biological process that is not influenced by calcium signaling," said Keith Nehrke, Ph.D., study author and associate professor of Nephrology and Pharmacology & Physiology at the Medical Center. "In many cases, calcium signaling is absolutely central. The rise and fall of calcium is the molecular clock that times the execution of important processes like the regular and coordinated beating of our hearts."

Nehrke, along with lead study authors Allison L. Abbott, Ph.D., and Benedict J. Kemp, Ph.D., of Marquette University, made the finding while studying an unglamorous, yet scientifically ideal subject matter – worm poop.

Worms produce their own body weight in embryos every day, which requires immense caloric intake. However, as in all other animals, food is transformed into waste, which must be expelled from the body. As a result of their rapid nutrient intake, worms defecate a lot and fast – every 50 seconds. The fidelity of this biological rhythm is critical for good health and relies on a specific sequence of events: One can imagine what might happen if the bowels were to contract without a valve opening to let out the waste.

The rhythmic process is jumpstarted by a spike of calcium in cells in the end of the intestine. The initial spike triggers a wave of calcium through the remainder of the intestine, stimulating muscle contractions and forcing waste out of the worm's body. The team wondered what ensures that the wave always starts in the right place – the end of the intestine – as opposed to the middle or front?

"It's like dominos lined up in a row," said Erik Allman, Ph.D., a study author and graduate student in Nehrke's lab at the Medical Center. "We wanted to find out what provides the 'push' that topples that first domino and starts the sequence."

The team's analysis revealed that a molecule called a microRNA is required for the entire waste removal process to run smoothly. microRNA-786 is present in the two most posterior intestinal cells of worms and tags these cells as the pacemakers or leaders. These pacemakers dictate when and where the primary calcium spike occurs, activating the movement of waste through the worm's body. When the team removed microRNA-786 from worms the process went awry; the calcium wave started in the wrong place and the waste cycle was irregular and longer than normal.

"As a developmental biologist, I am interested in how cells become different from one another," said Abbott. "This microRNA acts to make the posterior cells different from their neighbors by changing the calcium signaling activity. This difference allows these cells to function as the pacemaker."

"What is really exciting here is that this particular microRNA appears to exert a subtle effect," added Nehrke. "Since calcium signaling is so ubiquitous, it is important to realize that fine tuning its output may be what helps to discriminate between its many biological functions. The next step is to find out if this specific microRNA has a similar effect on calcium signaling processes in people as it does in worms."

Provided by University of Rochester Medical Center

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