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Protein provides link between calcium signaling in excitable and non-excitable cells

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A calcium-sensing protein, STIM1, known to activate store-operated calcium channels has been found to also inhibit voltage-operated calcium channels, according to researchers at Temple University.

The researchers published their findings, The Calcium Store Sensor, STIM1, Reciprocally Controls Orai and Cav1.2 Channels, in the Oct. 1 issue of *Science* magazine.

Calcium, not just important for bones and teeth, is a universal signaling agent that is pivotal in controlling a wide range of cell functions including fast muscle and nerve responses and slower response such as cell division, cell growth, apoptosis or programmed cell death and even fertilization of eggs.

Calcium is stored in cells and rapidly released out and pumped back to control things like contraction of muscle or the triggering of immune cells said Donald Gill, Professor and Chair of Biochemistry in Temple's School of Medicine and the study's lead researcher.

He said that the STIM1 protein, which he helped discover about 5 years ago, was found to play a major role in sensing the low levels of calcium in cell stores and activating the highly selective Orai calcium channel to allow calcium to flow back into the cell.

"We thought it seemed crazy that the STIM1 protein goes through this incredible dance but the only thing it does is activate the Orai channel,"

he said. "It seemed difficult to believe it only had this one specific function."

About two years ago, Gill and his colleagues noticed that in addition to activating the Orai channel to allow calcium to trickle back into the cell stores, STIM1 was also inhibiting the function of the crucial and widespread voltage-operated calcium channel, known as the L-type—channel.

"At the time, we thought only electrically excitable cells, like cardiac, neural and skeletal cells, had L-type (or long-lasting) calcium channels," he said. "So it was surprising that the STIM1 protein known to function mostly in non-excitable cells was having a pretty profound effect on the L-type calcium channels".

"This is particularly true in tissue like smooth muscle where it is sort of like a hybrid between an excitable and a non-excitable cell, because it has the voltage-operated calcium channel and the Orai calcium channel, as well as the very powerful STIM sensing system," he said.

Gill said that the researchers' finding gives a common mechanism for calcium signaling in both excitable and non-excitable cells, a link that was never before known.

"It's a very basic finding, but it's another whole area of control that people didn't know about before," he said. "They knew there were L-type calcium channels in many non-excitable cells, but they didn't seem to have any function. Now it seems very possible that the reason they didn't function is that the STIM1 protein was suppressing their function."

More information: www.sciencemag.org

Provided by Temple University