MedicalXpress

Unexpected role for calcium ion channel protein revealed

March 28 2017, by Sarah Plumridge

A new study published in *Nature Communications* and co-authored by Northwestern Medicine scientists shows how two proteins of the Ca2+ release-activated Ca2+ (CRAC) channel family interact with each other to control the flow of calcium ions into cells and modulate downstream immune responses.

Using mouse models, the scientists explored how the CRAC channel proteins, ORAI1 and ORAI2, control CRAC channel activity and immune responses.

"Most of the research has historically been focused on ORAI1," said Murali Prakriya, PhD, associate professor of Pharmacology. "We have a reasonable understanding of how ORAI1 channels open, where they are expressed especially in the immune system, and we know that mutations in ORAI1 that kill its activity give rise to severe immunodeficiencies. Then there is this other related protein, ORAI2, which also yields CRAC currents if it is over-expressed, but until now, exactly what this protein is doing in native tissues wasn't at all clear."

The scientists showed that ORAI2 slows down or puts a "brake" on ORAI1's ability to conduct calcium ions. By deleting the ORAI2 protein from the CRAC channel, the scientists showed that the flow of calcium ions into cells was markedly increased.

Furthermore, they found the deletion of both proteins caused the CRAC channel to lose function, resulting in impaired T-cell function.

While mice deficient in both proteins had impaired immune responses, they were protected from two autoimmune diseases, colitis and graft-versus-host disease, both of which are T-cell-mediated.

The authors suggest that their results show how ORAI2 adjusts the amount of calcium ions flowing through ORAI1 channels with both proteins synergizing to control immune responses.

More information: Martin Vaeth et al. ORAI2 modulates store-operated calcium entry and T cell-mediated immunity, *Nature Communications* (2017). DOI: 10.1038/ncomms14714

Provided by Northwestern University