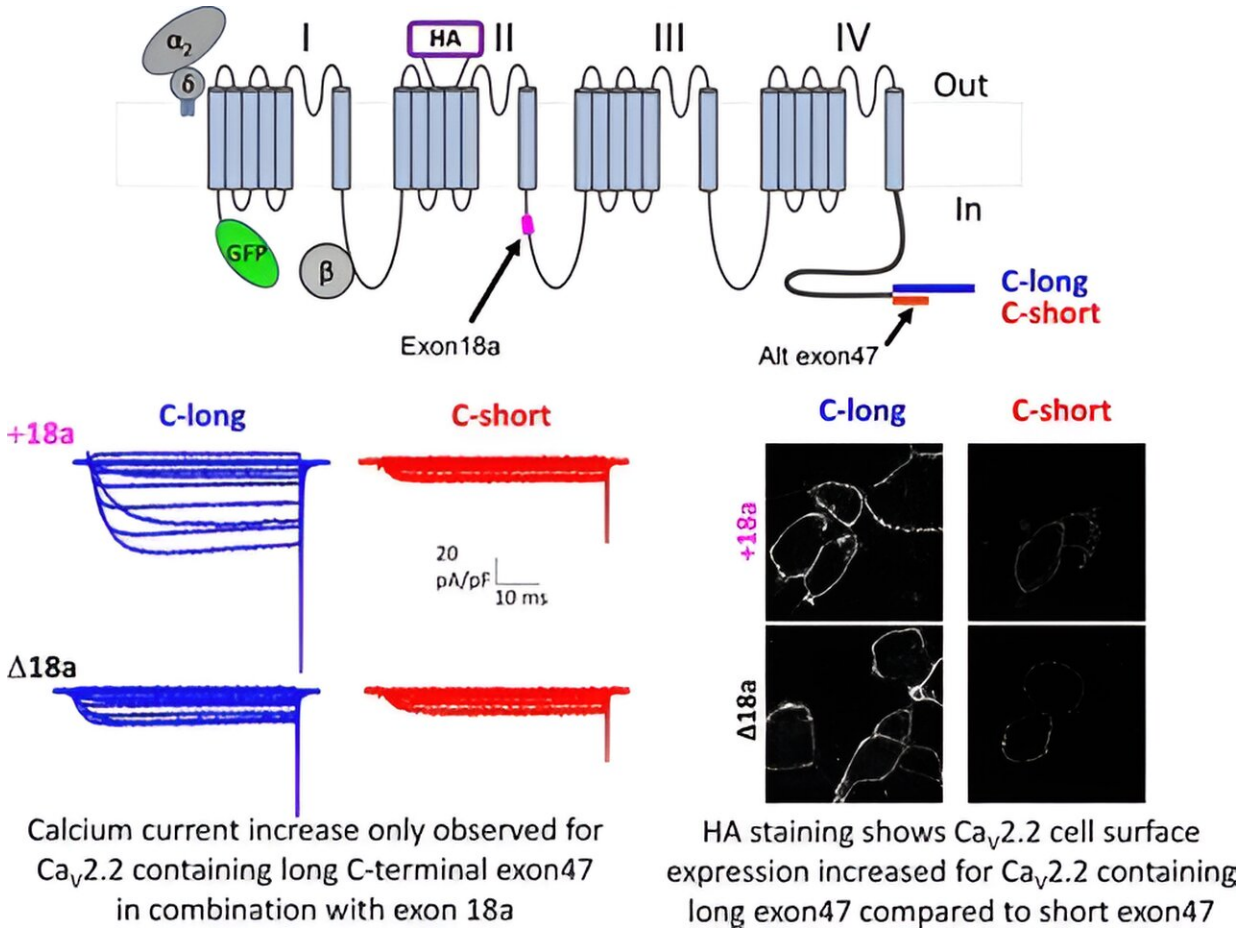
Study highlights importance of not investigating exon splicing in isolation

November 20 2023



Calcium current increase only observed for $Ca_V2.2$ containing long C-terminal exon47 in combination with exon 18a

HA staining shows $Ca_V2.2$ cell surface expression increased for $Ca_V2.2$ containing long exon47 compared to short exon47

Credit: *Function* (2023). DOI: 10.1093/function/zqad060

A study published in the journal *Function* highlights the importance of

not investigating exon splicing in isolation. Exon splicing is the process by which introns are removed from pre-mRNA and exons are spliced back together.

Researchers were initially investigating the functional importance of the short compared to the long version of exon 47 present in a specific calcium channel called the N-type channel that is important for neurotransmitter release. The N-type channel's release at the first synapse in the pain pathway of the spinal cord makes it a target for drug discovery.

In the available sequence databases, short exon 47 was only present in channel sequences that did not contain another exon, according to researchers from University College London. In addition, researchers discovered that long exon 47, resulted in much larger N-type calcium channel currents than the other three combinations only if exon 18a is present.

By comparison, cell surface expression of the channel was increased by long exon 47 as opposed to short exon 47, regardless of whether exon 18a is present. Thus, the additional presence of exon 18a must affect channel function at the level of increasing its ability to open, rather than by enhancing the amount of channel on the cell surface.

"Our study highlights the importance of investigating the combinatorial effects of exon inclusion, rather than each in isolation, to increase our understanding of calcium channel function, and for future drug discovery," said Annette Dolphin, Ph.D., one of the authors of the study.

More information: Shehrazade Dahimene et al, The Interplay Between Splicing of Two Exon Combinations Differentially Affects Membrane Targeting And Function of Human CaV2.2, *Function* (2023). DOI: 10.1093/function/zqad060

Provided by American Physiological Society