

Differences between skeletal and heart muscle ion channel lends insight into inherited heart disease

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Skeletal muscle sodium channel structure shown in yellow connecting to calmodulin, shown in purple. Credit: Sandra Gabelli

Johns Hopkins Medicine researchers recently found a key structural differences in channels that regulate how and when heart and skeletal muscles contract. Identifying the differences between the two, say researchers, provides scientists with new potential drug targets to treat inherited heart disease.

Muscle function depends on a voltage gradient between the inside of the cell and the outside—positive charges build up outside of the cell and negative charges remain inside. When signaled to contract, the cells open channels through their cell membranes, allowing positively charged molecules to flow in.

The researchers found that skeletal muscles can be regulated by a calcium-carrying protein called calmodulin. In the presence of calcium, this protein connects to the [sodium ion channel](#) and dampens

its response, slowing the rate at which it transports [sodium ions](#) into the cell. The researchers say this may allow the cells to finely tune the strength of their contractions. On the other hand, the sodium ion channels in heart muscle cells do not change their sodium conductance in response to calmodulin.

The researchers suspect that genetic mutations could cause the sodium ion channel in heart muscle cells to behave more like the [skeletal muscle](#) channel, causing the cells to respond to calmodulin when they should not. This, say the researchers, could contribute to inherited arrhythmias, such as cold-aggravated myotonia and potassium-aggravated myotonia. There are currently no treatments addressing the cause of these diseases, and identifying the differences between the sodium ion channels in these two muscle types provides an opening for targeted [drug development](#).

Authors of this study include Jesse Yoder, Federica Farinelli, Lakshmi Srinivasan, Sophie Shoemaker, Sandra Gabelli and Mario Amzel of the Johns Hopkins University School of Medicine; Manu Ben-Johny of Columbia University; and Gordon Tomaselli of the Albert Einstein College of Medicine.

The study is published on April 3 in *Nature Communications*.

More information: Jesse B. Yoder et al. Ca²⁺-dependent regulation of sodium channels NaV1.4 and NaV1.5 is controlled by the post-IQ motif, *Nature Communications* (2019). [DOI: 10.1038/s41467-019-09570-7](https://doi.org/10.1038/s41467-019-09570-7)

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