New view of the heartbeat

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The human cardiac voltage-gated sodium channel (Nav1.5) plays a critical role in maintaining regular heartbeats. Mutations in Nav1.5 cause life-threatening heart rhythm disorders (arrhythmias).

Nav1.5 is sensitive to the calcium-ion sensor protein calmodulin (CaM); however, the exact mechanism of how CaM exerts its effect on Nav1.5 is not well understood.

In a study published in the journal *Structure*, Christopher Johnson, Ph.D., Walter Chazin, Ph.D., and their colleagues integrated structural biology data from multiple techniques to show that CaM engages a portion of Nav1.5 known as the "inactivation gate" in a unique manner.

Then they determined that this calcium-dependent binding of CaM promotes the resetting of the channel after it opens, to help prepare for the next heartbeat.

Their work suggests a mechanism for how calcium and calmodulin fine tune cardiac sodium channels and may help in the development of novel therapeutics and improvements to existing treatments for cardiac arrhythmias.

More information: Christopher N. Johnson et al. A Mechanism of Calmodulin Modulation of the Human Cardiac Sodium Channel, *Structure* (2018). DOI: 10.1016/j.str.2018.03.005