Researchers illuminate link between sodium, calcium and heartbeat

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That flutter in your heart may have more to do with the movement of sodium ions than the glance of a certain someone across a crowded room.

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The contraction and relaxation of heart muscle cells depend on minute but finely regulated electrical impulses that are created when charged atoms – or ions – of metals such as sodium, potassium and calcium pass through complex molecular channels inside and between cells. Irregular heartbeats, referred to medically as arrhythmias, can happen when these

channels leak or otherwise malfunction. Professors Filip van Petegem and Christopher Ahern, members of UBC's Cardiovascular Research Group, used the CLS to determine the molecular structure of a part of the channel that controls the flow of sodium to cells in the heart, as well as in other electrically-excitable cells such as in the nervous system.

"The heart is an electrical organ that depends on precise electrical signals to contract [and pump blood]" explains van Petegem. "It is crucial for heart rate that the signalling, controlled by the movement of sodium, be exact. So the entry of sodium into the cell is tightly regulated."

The sodium channel that passes through the outer membrane of heart cells is actually a huge, intertwined four-part molecule. The teams of Van Petegem and Ahern chose a section of the molecule that appeared to regulate the closing of the channel by forming a plug, thus stopping sodium from getting through.

The researchers were surprised to discover that a protein called calmodulin binds to the sodium channel, keeping it open by preventing the plug from forming. Calcium ions, in turn, regulate the connection between the protein and the channel: calcium ions cause the protein to hook up to the channel, keeping it open and letting sodium through.

Problems occur with the system when genetic mutations change the shape of the channel at the site where the protein binds, affecting how well the channel can open and close. The result – the flow of sodium into the muscle cells is disrupted and the heart does not beat regularly.

The scientists have been able to identify mutations in the site that lead to two different kinds of heart arrhythmia: Brugada Syndrome and Long Q-T type 3, so-called from the tell-tale trace doctors see on the ECG of patients suffering from the problem. Brugada syndrome is considered to be caused by not enough sodium getting into cells, while long Q-T is the

result of too much sodium.

The results of the study could pave the way for the development of new drugs that can shore up how the calmodulin protein binds to the sodium channel, effectively treating both conditions as well as other arrhythmias.

"It's really a very elegant mechanism," notes van Petegem. "Many channels are regulated by calmodulin but not in such a simple way."

Provided by Canadian Light Source