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Rhythm is it: Ion channels ensure the heart keeps time

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The heartbeat is the result of rhythmic contractions of the heart muscle, which are in turn regulated by electrical signals called action potentials. Action potentials result from the controlled flow of ions into heart muscle cells (depolarization) through channels in their membranes, and are followed by a compensating reverse ion current (repolarization), which restores the original state. If the duration of the repolarization phase is not just right, the risk of ventricular arrhythmia and sudden cardiac death increases significantly.

Research groups led by Professors Martin Biel and Christian Wahl-Schott at the Department of Pharmacy at LMU Munich have now described a new function of the so-called HCN channels in the heart. Four subtypes of HCN channels are known, which are essential for the repolarization phase. The ion current that passes through these channels is often referred to as the pacemaker current, because it is instrumental for the control of heartbeat.

"It has been known for a long time that members of this family of ion channels are present in the pacemaker cells in the sinoatrial node of the heart. These cells display spontaneous electrical activity, and it was known that their HCN channels contribute to an increase in the heart rate under certain conditions," says Wahl-Schott. "However, the role of the HCN channels in the normal contractile function of the heart muscle has been unclear."

Using a new animal model, in which one of the subtypes of HCN

channel proteins (HCN3) is missing, the researchers observed a significant reduction in the duration of the repolarization phase that follows the action potential in the portion of the myocardium that undergoes active contractions.

"Our results demonstrate that HCN channels are important for normal repolarization," says Biel. "And that is a completely new physiological concept, which underlines the biomedical relevance of these channels – and can perhaps be exploited therapeutically."

The project was carried out under the auspices, and with the support, of the Center for Integrated Protein Science Munich (CIPSM), a Cluster of Excellence at LMU.

More information: HCN3 contributes to the ventricular action potential waveform in the murine heart, Stefanie Fenske et al. Circulation Research online, 8 September 2011. Doi: 10.1161/CIRCRESAHA.111.246173

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