Keeping a beating heart in rhythm

March 31 2011

Screening for a group of genetic mutations in people with a special heart condition could help doctors determine who is at risk for cardiac arrest or sudden death, reports a new study in *Science Translational Medicine* today.

The condition is called long QT syndrome, an inherited heart rhythm disorder that can cause fast, chaotic heartbeats. These rapid heartbeats may trigger fainting or seizure, and in severe cases, sudden death. The term "long QT" refers to an abnormal pattern seen on an electrocardiogram, which measures and records the heart's electrical activity. It is the electrocardiogram that displays frantic signals slowing to a dramatic stop after a character's death in many movies and television shows.

In people with long QT syndrome, the heart takes a longer amount of time than normal to relax after each contraction. This can upset the careful timing of the heartbeat and trigger a dangerous, abnormal rhythm. Under normal circumstances, the 24/7 beating of the heart is sustained by a symphony of tiny pores on the surface of muscle cells rhythmically opening and closing on cue. These pores or ion channels open and close to let electrically charged sodium, calcium, and potassium ions flow in and out of the cell, which helps the heart pump blood.

Here, Coeli Lopes and colleagues show that the speed at which potassium channels in heart muscles open can serve as an indicator of risk for developing severe heart problems associated with long QT

syndrome. In the study, seventeen different mutations in potassium channels were identified in a group of almost 400 individuals with long QT syndrome. The authors expressed the mutated channels in cells in the lab. Analysis showed that the mutated channels carried less electrical current and tended to open more slowly than normal channels.

When the team analyzed the clinical history of patients carrying these mutations, they found that slow channel opening correlated with episodes of cardiac arrest and sudden death. But how does slowing down the opening of potassium channels disturb the beating heart enough to cause cardiac problems" The authors used a computer model to find out. Their analysis revealed that beating heart cells that carry the slow-opening mutant channels are in a relaxed state for longer periods of time, and have lost the ability to recover from any early beats experienced by the heart, prompting a sustained irregular heart rate.

More information: "Use of Mutant-Specific Ion Channel Characteristics for Risk Stratification of Long QT Syndrome Patients," by C. Jons et al., *Science Translational Medicine*. (2011)

Provided by AAAS