Heart rhythm gene revealed in new research

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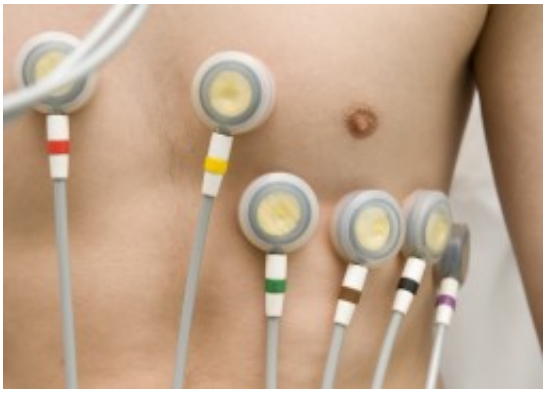

The researchers identified the new gene by analysing people's electrocardiogram readings

(PhysOrg.com) -- A gene that regulates the rhythm of the heart is revealed in new research published today in Nature Genetics. The authors of the study, from Imperial College London, say their discovery helps them to understand how the body's heartbeat is controlled and could ultimately help scientists design more targeted drugs to prevent and treat certain heart problems.

Heart disease is the leading cause of death in the world, accounting for almost seven million deaths per year. Over half of these deaths are sudden and caused by serious heart rhythm disturbances such as ventricular fibrillation. The gene identified in today's study is linked to these heart rhythm disturbances and reveals a new mechanism that controls the heartbeat.

A person's heartbeat is controlled by electrical signals, which start in one central place - the heart's pacemaker - and travel around the heart muscle. This electrical signal is transmitted by specialised proteins in heart muscle cells called ion channels. Today's study reports the discovery of a new ion channel in the heart called SCN10A, which directly influences heart rhythm disturbances and a person's risk of cardiac arrest caused by ventricular fibrillation.

The mutation identified in the SCN10A gene is common and, at an individual level, has a modest effect on a person's risk of having heart rhythm problems. Further research is needed to determine what other mutations exist in this gene, and whether these might variants might have a stronger effect.

The authors of the study, funded by the Wellcome Trust, BBSRC and the British Heart Foundation, hope their findings will enable scientists to develop new ways to prevent and treat heart rhythm disturbances.

Dr John Chambers, lead author of the study from the School of Public Health at Imperial College London, said: "Genetic variation is like the two sides of a coin. One side is associated with increased risk, the other with decreased risk. We have identified a gene that influences heart rhythm, and people with different variants of the gene will have increased or decreased risks of developing heart rhythm problems.

"Though the gene variant itself may only have a small effect on a person's risk of having heart rhythm problems, our study gives us important new insight into the mechanisms affecting disordered heart rhythm," added Dr Chambers.

Professor Jaspal S Kooner, corresponding author of the study from the Division of Epidemiology, Public Health and Primary Care at Imperial College London, said: "These results may enable us to predict and

diagnose serious heart rhythm disturbances better, and in the future develop improved treatments for preventing ventricular fibrillation, which is a leading cause of death worldwide."

In today's study, the researchers analysed the genetic make-up of almost 20,000 people to look for genetic factors influencing the heartbeat. They studied the electrocardiogram (ECG, a recording of the heartbeat) of each person, and measured the time taken for electrical signals to travel to different parts of the heart. The researchers discovered that variation in the gene that encodes the ion channel SCN10A was associated with slow and irregular heart rhythms, including risk of ventricular fibrillation.

The researchers then identified the protein in human and mouse heart muscle cells. Although scientists had previously discovered the protein in nerve cells, this is the first time it has been identified in heart muscle cells.

The scientists then tested their findings by comparing the heart rhythm of mice with and without the SCN10A gene. The results showed that mice without a functioning SCN10A gene had shortened heartbeats, providing confirmation that the gene regulates heart rhythm.

Professor Peter Weissberg, Medical Director at the British Heart Foundation, said: "These findings are important and exciting. By looking at how differences in our genes are linked to differences in our heartbeat, this research has discovered that a single letter change in a gene can make some people more prone to heart rhythm disturbances. Before this, we didn't even realise that the protein produced by this gene was present in heart cells - now it looks like it could be a target for drug development to prevent life-threatening heart rhythm problems. Importantly, because this study was performed in a predominantly UK Indian Asian community and verified in white Europeans, we can be

sure that the finding is relevant to most of the UK population. We're proud to have funded much of the research that led to this breakthrough."

Professor Douglas Kell, BBSRC Chief Executive, said: "Having an understanding of the genetics behind a healthy heart gives us access to appreciating what has gone wrong when a person's cardiovascular health suffers. This research gives us part of a very complicated picture of how the heart works on a molecular level."

More information: "Genetic variation in SCN10A influences cardiac conduction and risk of ventricular fibrillation" *Nature Genetics*, Sunday 10 January 2010.

Provided by Imperial College London