MedicalXpress

DNA sequence variations linked to electrical signal conduction in the heart

November 14 2010

(PhysOrg.com) -- Scientists studying genetic data from nearly 50,000 people have uncovered several DNA sequence variations associated with the electrical impulses that make the heart beat. The findings, reported in *Nature Genetics*, may pave the way for a greater understanding of the mechanisms for abnormal heart rhythms and sudden cardiac death.

"Regulation of the heart's rhythm is exceedingly complex," says co-author Glenn I. Fishman, MD, the William Goldring Professor of Medicine and the director of the Leon H. Charney Division of Cardiology at NYU Langone Medical Center. "This study provides new clues about the biologic pathways that influence cardiac conduction. Our hope is that this information will translate into novel approaches to prevent or treat serious rhythm disorders, including sudden cardiac death."

Normally, signals start from specialized muscle cells called pacemaker cells, travel through the heart and cause rhythmical muscle contractions – a system called cardiac conduction. The signals register on heart monitors as the electrocardiogram, or ECG. Abnormalities in cardiac conduction, particularly in the ventricles of the heart, can be extremely dangerous, leading to sudden cardiac death which affects approximately 250,000 people each year in the United States. Treatment with a pacemaker or a specialized device known as an implantable defibrillator may be needed to regulate the heart's rhythm.

Researchers have known for some time that genetic factors contribute to

electrical activity in the heart, including conduction of the electrical signal throughout the heart chambers. The new study reports on several previously unsuspected regions in the genome associated with cardiac electrical activity.

An international collaboration of scientists identified genetic associations with cardiac ventricular conduction in 22 regions of the genome in the largest study of its kind in conduction. The data was generated by an analysis of 15 European and American centers, representing nearly 50,000 individuals of European descent. Genome-wide association studies examine hundreds of thousands of genetic variants in thousands of people to try to find sequence variants and genes associated with particular diseases or conditions.

Some of these genetic variations were found in two sodium channel genes that sit side-by-side on the human genome. Sodium channels are molecular gated pores in living cells that control the flow of sodium ions – electrically charged particles – critical for the heart beat. The first gene, SCN5A, is well known to be involved in cardiac conduction. The second, SCN10A, has only recently been found in the heart.

As part of the study, Dr. Fishman and his team at NYU Langone identified where in the heart the SCN10A channels reside and discovered they were particularly abundant in specialized conduction fibers of the mouse heart key to the orderly contraction of the heart. The researchers then treated mice with a drug that selectively blocked this sodium channel and found that cardiac conduction was delayed, affecting the ECG. In addition to cardiac sodium channel genes, the study found that a number of other genes and genetic pathways involved in cardiac conduction, including calcium handling processes and transcription factors which influence cardiac development and formation. Dysfunctions in these processes before birth can lead to heart malformations in newborns.