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News Release

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Genetic Risk Factors Identified for Sudden Cardiac Death

An international science consortium with Dr. Arne Pfeufer of the Institute of human Genetics (Technische Universitaet Muenchen and Helmholtz Zentrum Muenchen) at its head has identified common gene variants in the human genome which influence the electrical activity of the heart muscle in humans and thus can be linked to cardiac arrhythmias and sudden cardiac death (SCD). Building on these findings, the scientists want to obtain further insights into the pathogenesic mechanisms of the disease and gain perspectives for early diagnosis and therapy. The results of the genome-wide study have been published online in the journal Nature Genetics.

Together with scientists of the international research consortium QTSCD (QT Interval and Sudden Cardiac Death), Dr. Arne Pfeufer of the Institute of human Genetics at Technische Universitaet Muenchen and Helmholtz Zentrum Muenchen has identified 10 gene variants which predispose to an elevated risk for arrhythmias and SCD. In interaction with other, still undiscovered factors, these gene variants influence heart repolarization and raise or lower the risk of cardiac arrhythmias. In their study, the scientists examined the electrocardiograms of more than 15,000 persons from Germany, Italy and the U.S.

"The results of a second science consortium, QTGEN, were nearly identical to our findings," said Pfeufer. This provides assurance for the scientists involved in the study - the Munich research team led by Professor Thomas Meitinger, institute director at Helmholtz Zentrum München and holder of the chair in human genetics at the Technische Universitaet Muenchen (TUM) and Assistant Professor Stefan Kääb, MD, senior physician at the University Hospital of Munich, Campus Grosshadern, along with their German, Italian and American colleagues - that their approach was correct and that the findings are absolutely reliable.

"For clinicians, an important indicator for increased arrhythmia risk is the QT interval in the ECG," Stefan Kääb explained. The QT interval describes the time span needed to send the electrical impulse into the heart ventricles and then to recharge. A prolonged QT interval can - depending on the underlying disease - increase the risk of arrhythmias and SCD up to five-fold.

The scientists were not looking for rare variants carried by only a few people. Rather, they were particularly interested in common gene variants, which in each person can influence the length of the QT interval. They do not increase the personal disease risk as single genes, but

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rather in combination of genetic factors and in context with other risk factors such as medications or ischemia.

"We view this form of genome-wide search for common gene variants associated with widespread diseases as a very promising approach for making discoveries in totally uncharted territory," said Thomas Meitinger, describing the method. "In contrast to the study of single genes, this genome-wide approach offers entirely new starting points for the investigation of common diseases such as sudden cardiac death."

The provision of highly valid population-based data of test persons from the KORA study platform headed by Professor H.-Erich Wichmann, director of the Institute of Epidemiology at Helmholtz Zentrum München, formed an essential basis for the successful realization of the research project.

The QTSCD study arose from long-standing close collaboration between human geneticists, cardiologists, epidemiologists and informaticians of Helmholtz Zentrum Muenchen, the university hospital Klinikum rechts der Isar of the Technische Universität Muenchen and the university hospital of Ludwig Maximilian University (LMU), Campus Grosshadern. Other partners of Helmholtz Zentrum München in the QTSCD consortium were the scientists of the Heinz Nixdorf RECALL Study in Essen and the research center Life & Brain of the University of Bonn. Professor Aravinda Chakravarti of John Hopkins University in Baltimore was director of the project.

In a next step, follow-up studies shall confirm the connection between the new gene variants and sudden cardiac death. "We want to collect and evaluate further data on the respective individual genetic risk for arrhythmias in a large number of patients," Dr. Kääb said. The common objective of the Helmholtz scientists and their clinical partners through these studies is to gain further insights into pathogenetic mechanisms and thus gain perspectives for improved risk prediction and more successful therapy.

In Germany the research project was funded by Germany's Federal Ministry for Education and Research (BMBF) within the framework of the National Genome Research Network (NGFN). Funds were also provided by the Excellence Initiative of Ludwig Maximilian University Munich and the French Fondation Leducq to combat cardiovascular disease.

The Institute of Human Genetics of Technische Universitaet Muenchen, Klinikum rechts der Isar, and Helmholtz Zentrum Muenchen (Director: Professor Thomas Meitinger, PhD) is concerned with the identification of disease genes and the characterization of their functions. The focus of the research projects is on genome-wide DNA and RNA studies to elucidate the genetic causes of complex diseases, particularly in the fields of neurology and cardiology. Another focus is the systemic analysis of the interaction of genetic variance and

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environmental factors, using proteomic methods.
Further information: http://ihg2.helmholtz-muenchen.de

Original Publications:

QTCSD
Pfeufer, A. et al: Common variants at ten loci modulate the QT interval duration in the QTSCD Study. Nature Genetics online - Publication March 22, 2009 (DOI 10.1038/ng.362)

QTGEN
Newton-Cheh, C. et al. Common variants at ten loci influence QT interval duration in the QTGEN Study. Nat. Genet. Advance online publication March 22, 2009 (DOI: 10.1038/ng.361

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