

# Gene associated with sudden cardiac death identified by ICD monitoring

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A gene associated with sudden cardiac death in the general population has been identified using implantable cardioverter defibrillator (ICD) monitoring in research presented for the first time at ESC Congress today. The research included patients from the DISCOVERY trial and Oregon-SUDS and discovered that a polymorphism in the GNAS gene predicted ventricular tachyarrhythmias and sudden cardiac death.

"This is the first time a gene has been identified using ICD monitoring and then confirmed to be associated with [sudden cardiac death](#) in the [general population](#)," said principal investigator Professor Heiner Wieneke, chief physician in the Department of Cardiology, Contilia Heart and Vessel Centre, St. Marien-Hospital Mülheim, Germany. "Epidemiological studies have suggested that genetic factors contribute to sudden [cardiac death](#) but only a few genes have been identified."

Sudden cardiac death is one of the leading causes of death in Western countries and cardiac arrhythmias have been reported as the cause in many cases. Prior clinical studies have suggested that an individual's genes may contribute to the risk of cardiac arrhythmias and sudden cardiac death.

ICDs are indicated for [patients](#) who either have survived a life threatening cardiac arrhythmia or have a high risk for sudden cardiac death due to cardiac arrhythmias. ICDs continuously monitor a patient's cardiac rhythm. They also can diagnose and treat cardiac arrhythmias, potentially preventing sudden cardiac death.

Part one of the study was the DISCOVERY trial, a prospective, international, multicentre study in 1 145 patients who received an ICD for primary prevention of sudden cardiac death. ICDs were used to monitor and store [cardiac arrhythmia](#) data to study whether specific genes were associated with an increased risk of potentially life-threatening

ventricular tachyarrhythmias. The researchers genotyped seven single nucleotide polymorphisms (SNPs) in three genes (GNB3, GNAQ and GNAS) coding G-protein subunits.<sup>2</sup> G-proteins interact with stimulated adrenoreceptors, angiotensin II receptors and ion channels in myocardial cells. Abnormal G-protein signal transduction has been suggested as a mechanism contributing to sudden cardiac death.

In the second part of the study, the genes found to be associated with cardiac arrhythmias in the DISCOVERY trial were evaluated in 1 335 patients from Oregon-SUDS (Sudden Unexpected Death Study), a community-based study analysing causes of sudden cardiac death in the Portland, Oregon metropolitan area.<sup>3</sup>

In the DISCOVERY trial, 297 patients had a ventricular tachyarrhythmia. In univariate analysis, genotypes of two SNPs in the GNAS gene were significantly predictive of ventricular tachyarrhythmias. The increased risk remained significant after adjustment for non-genetic covariates. One of these SNPs, GNAS c.393C>T, was significantly associated with sudden cardiac death in the Oregon-SUDS under the additive (odds ratio [OR]=1.2 [1.0-1.4], p=0.039) and recessive (OR=1.5 [1.1-2.1], p=0.01) genetic models.

"Using ICD monitoring and a sample of sudden cardiac death patients from the community we found that a polymorphism in the GNAS gene predicts ventricular tachyarrhythmias and sudden cardiac death," said Professor Wieneke. "Our results suggest that GNAS mediated signal transduction may have an important role in ventricular arrhythmogenesis."

He concluded: "We believe this is the first time that a gene variant has been identified by monitoring ventricular tachyarrhythmias in patients with ICDs and then confirmed in a wider population. The

findings may help to identify patients at increased risk of sudden cardiac death."

**More information:** Professor Wieneke will present the abstract 'Polymorphism in the GNAS gene predicts ventricular tachyarrhythmias and sudden cardiac death: results from the DISCOVERY trial and Oregon Sudden Death Study'

Provided by European Society of Cardiology

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