



# Indicators of genetic markers of sudden cardiac death in patients with ventricular arrhythmias and in patients with atrial fibrillation

**Study Period:  
2011 – 2015**

## Personalized medicine a step closer?

Whole-genome sequencing can provide useful and clinically relevant information for individual patients, suggests a study of a patient with a family history of vascular disease and early **sudden death**.

Of note, **sequence analysis revealed rare variants in three genes associated with sudden cardiac death, namely *TMEM43*, *DSP*, and *MYBPC3***.

Euan Ashley (Stanford University, California, USA)  
*Lancet* 2010; Advance online publication 30 April 2010

## Genetics of sudden cardiac death

Looking at the genetics of sudden cardiac death, Dr. Gordon F. Tomaselli (Johns Hopkins University, Baltimore, MD, USA) pointed out that “this is on the one hand a mature field for some of the rare [genetic] variants... but very much an evolving field with [regards to] more common variants”.

He noted that, as a result, “genetic testing is available and should be used in patients with rare variants, but we’re not yet ready to do genetic testing for more common variants associated with sudden death”.

*58<sup>th</sup> Scientific Sessions of ACC (2009)*

## Gene Variant May Predict Sudden Cardiac Death Risk for Blacks

Researchers at Duke University Medical Center have pinpointed a common gene variant in blacks that may be associated with the development of life-threatening heart arrhythmias.

*Jason I. Koontz, Svati H. Shah, Jonathan P. Piccini, Kent R. Nilsson, Jr., Damian Craig, Carol Haynes, Simon G. Gregory, and Patrick M. Hranitzky.*

*By Duke Medicine News and Communications*

*May 10, 2011*

## ***PITX2* Insufficiency Leads to Atrial Electrical and Structural Remodeling Linked to Arrhythmogenesis**

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### **Variants on 4q25 affect risk for AF recurrence after catheter ablation**

Writing in the *Journal of the American College of Cardiology*, Daniela Husser (Leipzig University, Germany) and team explain that recent genome-wide studies identified a haplotype block containing two nucleotide polymorphisms (SNPs), near the gene *PITX2* on chromosome 4q25, that predisposes to AF.

## White men have high AF risk

To investigate, Ann Borzecki (Boston University School of Public Health, Massachusetts) and colleagues examined AF prevalence in 664,754 male veterans registered in the Veterans Health Administration databases.

Overall, 5.3% of the participants were diagnosed with AF. In particular, the age-adjusted prevalence of AF was 5.7% in Whites, 3.4% in Blacks, 3.0% in Hispanics, 5.4% in native Americans/Alaskans, 3.6% in Asians, and 5.2% in Pacific Islanders.

Whites were more likely to have valvular heart disease, coronary artery disease, and congestive heart failure than other ethnic groups; Blacks were more likely to have hypertension; Hispanics had the highest diabetes prevalence; and Native Americans had the highest prevalence of chronic lung disease.

"The highest risk was seen in Whites, followed by Pacific Islanders and Native Americans; Blacks and Hispanics had the lowest risk."

They speculate that variations in genetic or environmental factors might underlie these ethnic differences, but stress that further research is necessary to verify and establish the reasons for this ethnic predisposition to AF.

**18 February 2008.**

**The major goal of the research:**

**We plan to study epidemiology of Sudden Cardiac Disease and Atrial Fibrillation in Kazakhstan and evaluate possible predispositions (genetic markers) in patients of Kazakh origin and other ethnicities living in Kazakhstan**

## Registry for SCD and AF has been completed



Collectoin of Database for SCD and AF in Kazakhstan

## **High risk Sudden Heart Disease**

### **Normal structure heart**

- Long QT syndrom
- Brugada Syndrom
- Short QT syndrom
- Early Repolarization Disease
- Catecholaminergic Polymorphic Ventricular Tachycardia

### **Cardiomyopathy**

### **Coronary Heart Disease**

## **PATIENTS**

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graph TD; PATIENTS --> Box1["-Normal structure heart with VA<br/>-Cardiomyopathy with and without VA<br/>-Coronary Heart Disease with and without VA"]; PATIENTS --> Box2["Atrial Fibrillation<br/>-idiopathic<br/>- Coronary Heart Disease with and without AF"]; Box1 -.-> HSDD["High risk Sudden Heart Disease<br/>Normal structure heart<br/>-- Long QT syndrom<br/>--Brugada Syndrom<br/>--Short QT syndrom<br/>--Early Repolarization Disease<br/>--Catecholaminergic Polymorphic Ventricular Tachycardia<br/>Cardiomyopathy<br/>Coronary Heart Disease"];
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**-Normal structure heart with VA**

**-Cardiomyopathy with and without VA**

**-Coronary Heart Disease with and without VA**

### **Atrial Fibrillation**

- idiopathic
- Coronary Heart Disease with and without AF

# Three stages of study

## Stage 1. Preparatory work (2011)

- Epidemiologic database collection of patients with ventricular arrhythmias and atrial fibrillation in Kazakhstan
- Collection of general information about patients
- Patient selection
- Confirmation of diagnosis
- Creating Patient database

## Stage 2. Fundamental (2012-2014)

- Further development of the database
- Carrying out genetic studies

## Stage 3. Analysis (2015)

Database analysis and development of standards of effective and modern evaluation of patients at high risk of sudden cardiac death.

## Suggested Partners

- Center for Genomic Medicine Duke  
Institute for Genome Sciences & Policy,  
Duke University (Durham, NC, USA)
- University hospital in Grats, Austria.
- BGI Beijing Genomic Institute (Shenzhen,  
China)

## **Anticipated results**

**Evaluation of possible predispositions (genetic markers) in patients at high risk for Sudden Cardiac Disease and Atrial Fibrillation in Kazakhs and other representatives of ethnicities living in Kazakhstan.**

**The major goal of the research is to prevent sudden heart death and atrial fibrillation.**

*We often don't get a second  
bite of the apple*

Dr. Gordon Tomaselli