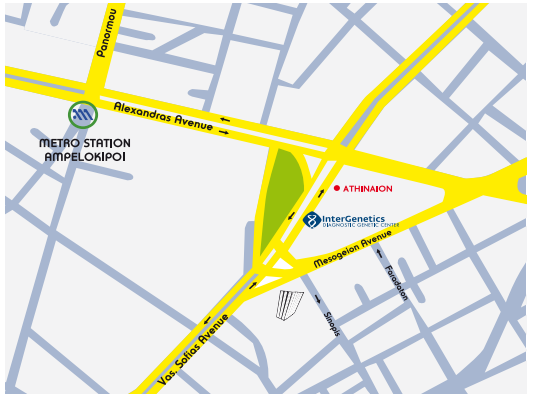
How genomic testing is performed and how long does it take to be completed

The test involves the parallel analysis of the DNA sequence of all the exons of ~90 genes associated with various types of cardiogenetic disorders, analyzing genes associated both with syndromic and non-syndromic forms of the disease.

The test is based on the method of next generation sequencing (NGS) and utilizes a special Genome Analyzer instrument together with complex and highly specialized software tools. The test is generally completed within 3-4 months.

Genetic counseling

Proper clinical genetic assessment of each case and genetic counseling, both before and following the test, is essential in order to determine the appropriate strategy for laboratory testing and to interpret correctly the concepts of pathological and normal.



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GENOMIC TESTING OF CARDIOGENETIC DISEASES

- ✓ *relatively common disorders, with increased morbidity and mortality*
- ✓ *genetic testing was selective and incomplete, often without a conclusive diagnosis*
- ✓ *comprehensive genomic testing of all genes currently known to be associated with cardiogenetic disorders, leads in a single step to successful diagnosis and disease management*

Categories of cardiogenetic diseases and their genetic basis

Cardiac arrhythmias are globally one of the main causes of morbidity and mortality. Congenital cardiac arrhythmias are a distinct group of cardiac disorders resulting from lesions in the electro-physiological properties of the heart. Specifically, proper cardiac activity includes, among others, synchronized and sequential opening and closing of ion channels in response to the electric potential and transmits the potential action to each compartment of the heart.

Although environmental factors clearly contribute to arrhythmogenesis, familial and population studies have clearly established the existence of a genetic etiology. For example, mutations in >20 genes, encoding and regulating ion channels, are associated with different forms of arrhythmogenic disorders, occurring in an otherwise structurally normal heart.

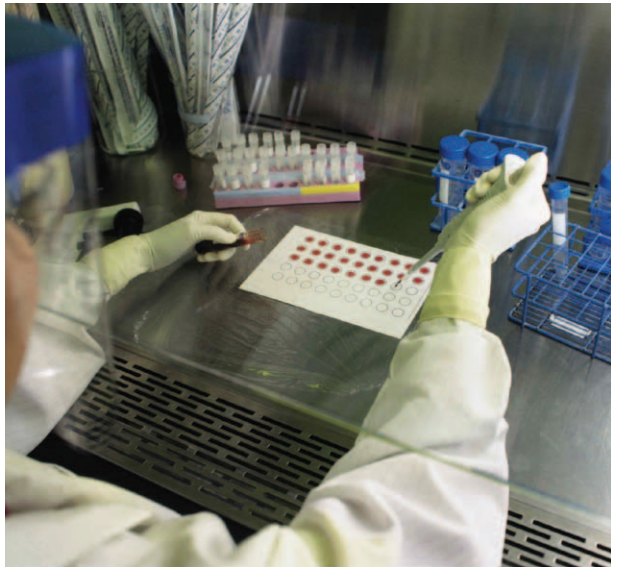
An example of such a disorder is Brugada syndrome (BRS), which is associated with mutations in at least seven different genes and is characterized by an increased risk of fatal ventricular arrhythmias.

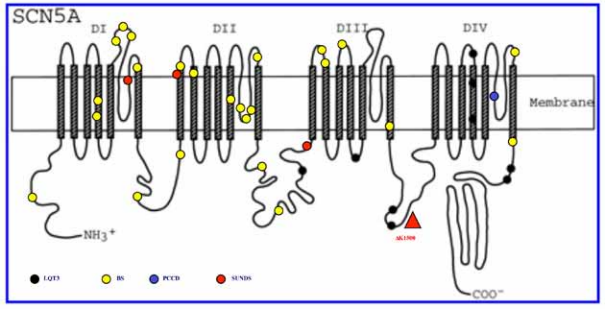
Sudden cardiac death (Sudden Cardiac Death - SCD) (or sudden unexplained death) is a common cause of mortality, affecting all ages. The basic cause of sudden cardiac death in people older than 45 years is due mainly to atherosclerotic coronary artery disease. However, in individuals <45 years, heritable genetic lesions in specific genes are associated with the disorder in up to 80% of cases.

The most common category of cardiogenetic disorders among young people are the cardiomyopathies. Both dilated as well as hypertrophic cardiomyopathies to a large extent are due to mutations in dozens of different genes.

Mode of inheritance of cardiogenetic disorders

Generally, the majority of cardiogenetic disorders express themselves or are inherited in an autosomal dominant manner, meaning that individuals with a mutation in only one copy of a particular gene have an increased risk of being affected with a cardiogenetic disorder, and all first-degree relatives of young patients have a 50% risk to inherit the disease. It is also important to note that different mutations in the same gene may lead to a different type of a cardiogenetic disorder.





Why is genomic testing for cardiogenetic disorders useful?

The currently available options of genetic testing for cardiogenetic disorders were extremely slow (months or years) and deficient (testing only for a few genes), leading to an inability to uncover the genetic causes - mutations in patients with hereditary and congenital heart disease.

Therefore, to the extent that genetic testing until now was selective, incomplete and often expensive, screening of all known genes through genomic testing, today leads in only one step to a successful and definitive diagnosis. The identification of the pathological mutation is important for genetic counseling of patients and families, thus facilitating the detection of individuals at risk.

Furthermore, in many cases the exact knowledge of the genetic cause, leads to a more effective management of symptoms and permits the application of the appropriate individualized medication or treatment.