HEARTGENETICS
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# GENETIC TEST BOOKLET

A guide for patients

2013

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# OUR MISSION

TO PLAY A LEADING ROLE IN CHANGING THE STATUS QUO OF GENETICS, BY BRINGING UP INNOVATIVE KNOWLEDGE THAT WILL HELP PHYSICIANS IMPROVE HEART MEDICINE.

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# OUR SOLUTION

A DISRUPTIVE METHODOLOGY BASED ON THE INTEGRATION OF ADVANCED GENOMIC TECHNOLOGIES AND SOPHISTICATED COMPUTATIONAL METHODS.

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# GENETIC TEST KEY POINTS

## WHAT IS A GENETIC TEST?

A genetic test analyzes the presence or absence of a known genetic alteration, known as mutation, by examining the sequence of bases of a gene, which corresponds to the genetic sequence that contains the information needed to construct a protein.

Cardiovascular and associated cardiac diseases are the leading causes of morbidity and mortality in industrialized countries, being the diagnosis and early treatment an emergent issue nowadays. In the last few years, significant advances have been made in the understanding of the genetic basis of inherited heart diseases. As so, genetic based diagnostic tests emerged as a useful tool in patient's clinical management of cardiovascular genetic diseases. Genetic diagnosis is being considered a valuable contribution to heart medicine enabling the prediction of risk of developing a specific cardiovascular disease , allowing physicians and medical geneticists to indicate preventative measures as lifestyle counselling and adequate therapeutics.

HeartGenetics is a company that has developed a set of cardiac genetic tests based on a new, efficient and very accurate technology that makes use of a specific allelic PCR reaction with MALDI-TOF mass spectrometry.

Based on a DNA MICROCHIP array platform for genetic analysis, our team of investigators has developed genetic tests for eleven cardiac pathologies, e.g.: Hypertrophic cardiomyopathy, Dilated cardiomyopathy, Arrhythmogenic Right Ventricular Cardiomyopathy, Long and Short QT syndromes, Brugada Syndrome, genetic risk factors for thrombophilia, molecular markers of genetic risk for arterial hypertension, among others.

On top of our core competences on the subject of cardiovascular genetic testing, we are developing new high-tech bioinformatics technologies that support highly accurate analysis and integration of both genetic and clinical data. We plan to launch by the end of 2014 an innovative clinical decision support system, allowing physicians and practitioners to perform a more accurate diagnosis, prognosis and risk stratification.

## WITCH KIND OF SAMPLE IS TESTED IN A GENETIC TEST?

The biological samples that can be tested for DNA alterations include blood and bucal ephitelium (present in saliva)

## HOW IS A GENETIC TEST PERFORMED??

To perform a genetic test it is necessary to have an Order Form requested by the physician, to the genetic laboratory. The physician will explain to the patient the context of the requested genetic test. Patients that perform a genetic test must sign an Informed Consent document.

A blood sample is collected and sent to the genetic laboratory, for DNA extraction. The laboratory will analyze the genetic alterations that could be responsible or that could be considered molecular risk factors that predispose to a certain disease.

The test results will be made available to the physician or genetic counsellor, which are responsible to discuss them with the patient.

HeartGenetics's genetic diagnosis method makes use of a methodology that enables the analysis of a very large number of genetic alterations in a reliable manner. The genetic test is performed using a new DNA MICROCHIP that allows the detection of the most relevant genetic risk factors and / or genetic mutations associated with inherited cardiac diseases.

This diagnosis method is very accurate, with a sensitivity and specificity of 80% and 99%, respectively. The DNA MICROCHIP is able to test 100% of the mutations that has been associated to the cardiac disease under evaluation.

HeartGenetics implemented an efficient working protocol outlined in the following items:

- The biological samples and the Order Form are received at HearthGenetics laboratory. The samples are labelled with an adequate code to ensure reliability and traceability of the results.
- The DNA is extracted from the blood or saliva, quantified and analyzed for its purity and integrity.
- The genetic test is performed using a new DNA MICROCHIP.
- The genetic report, harboring the result of the genetic test, is delivered to the physician. This report contains information about the genetic alterations in the DNA of the sample that has been evaluated.

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# GENETIC COUNSELING

## WHAT IS THE IMPORTANCE OF GENETIC COUNSELING?

Genetic counselling is the process by which patients or relatives are given information about a genetic disorder.

Genetic counselling helps an individual to understand the medical facts, how heredity is involved, the risk for family members, and what options are available to deal with the risk, including available therapeutics.

In the presence of a negative result, predictive genetic testing of family members will not be informative and is therefore not warranted.

Individuals who undergo a genetic test should also undergo counselling by someone knowledgeable in the genetics of cardiovascular disease, so that results and their clinical significance can be appropriately reviewed and discussed.

Evaluation of familial inheritance and genetic counselling is recommended as part of the assessment of patients with inherited cardiac genetic diseases.

When the causal genetic alteration is detected in a patient, his or her relatives can then choose to have a genetic test.

Genetic testing associated with the clinical screening of all first-degree family members of patients is important to identify those individuals that are asymptomatic but have the genetic alterations.

Pre-symptomatic genetic testing can tell whether someone is at risk of developing the condition in the future.

## HOW LONG DOES IT TAKE TO GET AN ANSWER?

Genetic testing for inherited cardiac conditions usually takes 1 (one) month since the sample is accepted at the laboratory till the medical doctor receives the result.

In an emergency it can take 5 (five) days or less.

The results can only be of two forms: POSITIVE or NEGATIVE.

## WHAT TYPE OF RESULTS ARE EXPECTED?

A positive result indicates that a genetic alteration was found in one (or more) of the analyzed genes associated with the tested condition. These findings contribute to the accurate clinical diagnosis, influence therapeutics and life style management and provide valuable information to family members.

A negative result indicates that no mutation was found in the analyzed genes associated with the tested condition. If clinical symptoms exist, the patient should be kept under surveillance.

A possible reason for a negative result associated with clinical symptoms, is the presence of a genetic alteration in a gene or part of a gene that is still unknown or has not been associated with the condition under evaluation.

In order to provide the most accurate answer to a patient with a NEGATIVE result but with clinical symptoms, the HeartGenetics's laboratory is equipped to perform a genome scan in order to find new unknown mutations.

The laboratory process for genetic testing was optimized to provide the most accurate test and reduce almost to zero the number of FALSE POSITIVES.

All POSITIVE results are double-checked.

# PATHOLOGIES

## THROMBOPHILIA

Thrombophilia is a disease characterized by an increased tendency of the blood to clot, leading to sometimes serious and/or life-threatening complications.

It is considered a multifactorial disease due to the interaction of genetic and environmental risk factors.

Venous Thromboembolism (VTE) is a common associated consequence with an annual age-dependent incidence of 1-3 individuals per 1000 per year. About one-third of the population with thrombophilia has experienced a pulmonary embolism and one-third develops VTE again within ten years of the initial diagnosis. It is believed that a number of genetic factors contribute to the development of thrombophilia.

HeartGenetics has developed an accurate and reliable genetic test that allows the detection of the most relevant genetic risk factors (genetic alterations) associated with thrombophilia.

This test allows physicians to predict the risk of increased tendency to form abnormal blood clots in blood vessels providing to each individual a personalized interpretation of the associated genetic risk for developing this pathology.

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# ARTERIAL HYPERTENSION

Arterial Hypertension (HTA) or high blood pressure is common, but too often goes undetected and constitutes a major risk factor for stroke, heart attack and heart failure.

An estimated 1 billion people worldwide have hypertension, and this number is expected to increase to 1.56 billion people by the year 2025. About 35-50% percent of hypertension is thought to be hereditary.

Determining the genetic cause of arterial hypertension has been difficult, because the level of blood pressure is the result of the interplay between heredity and environmental factors.

HeartGenetics has developed, to the best of our knowledge, the most complete and informative genetic test in the market.

This new test is an important tool to support physicians in their diagnosis of arterial hypertension, as genetic risk markers can predispose to HTA.

The integration of the test results with clinical data regarding physiopathological and biochemical features provides an opportunity to establish a more accurate therapeutic.

Moreover, this arterial hypertension genetic test will provide guidance to patients with a family history of HTA who wish to know if they should modify their lifestyles to help prevent the debilitating consequences of high blood pressure such as heart failure and stroke.

## HYPERTROPHIC CARDIOMYOPATHY

Cardiomyophathies are an important group of cardiovascular pathological conditions prevalent in the World population.

These pathologies are associated with heart dysfunction, which can vary from an asymptomatic course to heart failure.

Hypertrophic Cardiomyopathy (HCM) is a primary disorder of the myocardium that can present with mild symptoms as well as sudden cardiac death.

As the prevalence of HCM in the general US population is estimated to approach 1 in 500, HCM is a very common genetic cardiovascular disorder. Moreover, considerable interest has been raised regarding the athletes screening for early identification of cardiovascular diseases that are responsible for athletic field deaths and for disqualification of athletes at risk.

HeartGenetics has developed a very accurate and sensitive diagnosis test based on a DNA MICROCHIP specially designed for HCM evaluation. This test is the most accurate test in the market, evaluating 100% of the genetic alterations associated to this disease and described in the literature.

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# GLOSSARY OF GENETIC TERMS

- **DNA or deoxyribonucleic acid:** Is the hereditary material in humans. The information in DNA is stored as a code made up of four chemical bases: adenine (A), guanine (G), cytosine (C), and thymine (T). Human DNA consists of about 3 billion bases, and more than 99% of those bases are equal in all people. The order, or sequence, of these bases determines the information available for building and maintaining an organism, similar to the way in which letters of the alphabet appear in a certain order to form words and sentences.

- **DNA alteration or genetic alteration:** A change in a DNA sequence.

- **Gene:** A sequence of DNA that contains the message for a cell product, typically some type of protein. The human genome has approximately 25,000 genes.

- **Gene mutation:** A change in the DNA sequence that makes up a gene.

- **Gene mutation consequences – Genetic diseases:** To function correctly, each cell depends on thousands of proteins to do their jobs in the right places at the right times. Sometimes, gene mutations prevent one or more of these proteins from working properly. By changing a gene's instructions for making a protein, a mutation can cause the protein to malfunction or to be missing entirely. When a mutation alters a protein that plays a critical role in the body, it can disrupt normal development or cause a medical condition. A condition caused by mutations in one or more genes is called a genetic disorder.

## CONTACTS

For further information, please contact the HeartGenetics Laboratory.

Email:
lab_contact@heartgenetics.com

www.heartgenetics.com

In Genetics Home reference, http://ghr.nlm.nih.gov/handbook/basics/dna

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