This comprehensive genetic test is affordable, accurate, and helps future generations identify their own risk for cardiac disease.

GENESYS Diagnostics INC.

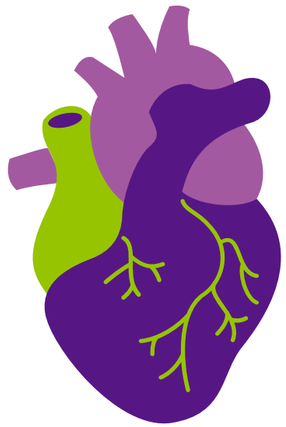
CAP ACCREDITED COLLEGE of AMERICAN PATHOLOGISTS

CLIA Clinical Laboratory Improvement Amendments

HEREDITARY CARDIOLOGY NEXT GENERATION SEQUENCING

Genesys' Cardiac Disease Panel analyzes variants within exons in 174 genes for 17 inherited cardiac conditions.

AT LEAST 25% OF SUDDEN CARDIAC ARRESTS HAVE A COMPONENT OF INHERITANCE



TEST INFORMATION

Description	Hereditary Cardiac Disease Panel
Method	Next Generation Sequencing
Specimen Type	Buccal swab
Turnaround Time	3-6 weeks
Testing Performed	Mon-Sat
Shipping	Pickup service available Mon-Fri

Genetic testing provides useful information for your patients' cardiac health

- Identifies patient's risk
- Identifies the risk for the patient's close relatives
- Helps patients make informed healthcare decisions and lifestyle changes

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GENESYS OFFERS 5 CARDIAC SEQUENCING PANELS COVERING A VAST RANGE OF CARDIAC CONDITIONS:

1 **The Full Cardiac Panel (174 genes) covers all conditions outlined below.**

2 **The Arrhythmia & Cardiomyopathy Comprehensive Panel (134 genes) includes genes involved in the following cardiac conditions:**

- **Arrhythmic Right Ventricular Cardiomyopathy (ARVC)** is commonly caused by genetic abnormalities in genes encoding desmosomal proteins such as the DSP, DSG2, and DSC2 genes. The prevalence of ARVC is estimated to be about 1 in 5,000 for the general population, with symptoms usually presenting between the second and fifth decades of life. ARVC damages the myocardium, leading to symptoms of lightheadedness, syncope, and death in extreme cases.
- **Brugada Syndrome** is mainly caused by mutations in the SCN5A gene, though other genes may be involved as well. The mutations disrupt sodium ion channels, resulting in an arrythmia characterized by difficulty breathing, loss of consciousness, and sudden death. The prevalence is estimated to be 5 in 10,000 people worldwide with symptoms generally arising around the age of 40.
- **Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)** is commonly caused by mutations in the RYR2 and CASQ2 genes. These genes are responsible for controlling calcium movement within myocytes and are essential for normal cardiac muscle contraction. The prevalence of CPVT is estimated to be about 1 in 10,000 and symptoms usually begin in childhood. Symptoms include light-headedness, dizziness, fainting, and death if untreated.
- **Dilated Cardiomyopathy (DCM)** is a disease that causes the ventricles to thin and stretch, causing the heart difficulty in pumping blood throughout the body. Mutations in more than 30 genes impacting cardiomyocytes have been linked to dilated cardiomyopathy. The incidence rate of dilated cardiomyopathy is about 6 cases per 100,000 individuals a year with symptoms mainly arising in adults younger than 50 years. Symptoms generally include irregular heartbeat, shortness of breath, fatigue, and swelling in the legs and feet.
- **Familial Atrial Fibrillation (FAF)** can be caused by mutations in multiple genes including ABCC9, KCNH2, and SCN5A. The disease is a result of uncoordinated electrical activity in the atria of the heart and results in a fast, irregular heartbeat. Symptoms include dizziness, chest pain, fluttering or pounding in the chest, shortness of breath, fainting, and sometimes death. Complications can arise at any age, though some individuals may never present with health problems. The incidence rate is unknown, but it is the most common form of current arrythmia, affecting more than 3 million people in the United States.
- **Hypertrophic Cardiomyopathy (HCM)** is generally caused by mutations in genes that affect the development of the heart muscle such as MYH7, MYBPC3, TNNT2, TNNI3, and others. HCM is characterized by thickening of the heart muscle, usually in the interventricular septum. Common symptoms include chest pain, shortness of breath, chest palpitations, fainting, and an increased risk of sudden death. HCM is estimated to affect 1 in 500 people worldwide and is the most common genetic heart disease in the United States.
- **Left Ventricular Non-Compaction (LVNC)** is mainly caused by mutations in the MYH7 and MYBPC3 genes. LVNC is characterized by a thickening and spongy appearance of the left ventricle, impairing the ability to pump blood properly throughout the body. Symptoms include abnormal blood clots, irregular heart rhythm, palpitations, fatigue, fainting, trouble laying fat, and death in extreme cases. An estimated 10 million individuals are diagnosed with LVNC each year.
- **Long QT Syndrome (LQTS)** has been linked to variants in more than 12 genes coding for ion channels of the heart such as ANK2, SCN5A, SCN4B, and others. The incidence rate is approximately 1 in 2,000 live births and the condition is characterized by prolongation of the QT interval corresponding to the repolarization of the heart muscle. Symptoms of long QT syndrome include fainting, blurred vision, lightheadedness, palpitations, weakness, and seizures in some people. Most individuals will develop symptoms by age 40, and some may experience symptoms weeks after birth.
- **Noonan Syndrome (NS)** is mainly caused by mutations in the PTPN11, SOS1, RAF1, and RIT1 genes which are important in the RAS/MAPK signaling pathway. Noonan Syndrome is characterized by unusual facial features, short stature, heart defects, bleeding problems, skeletal malformations, and pulmonary valve stenosis. The incidence rate is about 1 in 2,000 people and symptoms usually present at birth, though they may be undiagnosed in mild cases.
- **Restrictive Cardiomyopathy (RCM)** is caused by mutations in several genes including the TNNI3 gene. The condition arises due to heart muscle stiffness and impairment of muscle relaxation after contraction. As a result, not enough blood enters the ventricles and instead builds up in the atria and lungs. Symptoms of RCM include failure to gain weight, extreme tiredness, fainting, and sudden death if untreated. RCM is present at birth and its prevalence is unknown due to its rarity. It is estimated to account for 5% of all cases of cardiomyopathy.
- **Short QT Syndrome (SQTS)** is caused by mutations in the KCNH2, KCNJ2, and KCNQ1 genes, which provide instructions for making potassium ion channels. Deficiencies in these channels shorten the QT interval, which corresponds to a decrease in repolarization time. The condition is considered rare with many cases being undiagnosed or misdiagnosed, though some have estimated the incidence rate to be 1 in 10,000. Individuals diagnosed with short QT syndrome can have a variety of symptoms such as dizziness, fainting, cardiac arrest and sudden death.
- **Transthyretin Amyloidosis (ATTR)** is caused by mutations in the TTR gene and is characterized by the buildup of abnormal deposits of a protein called amyloid (amyloidosis) in the body's organs and tissues. Its incidence rate is estimated to be 1:100,000, and symptoms typically develop between age 20 and 70. People with cardiac amyloidosis may have an abnormal heartbeat (arrhythmia), an enlarged heart (cardiomegaly), or orthostatic hypertension. These abnormalities can lead to progressive heart failure and death.

3 **The Aortopathy Comprehensive Panel (24 genes) includes genes involved in the following cardiac conditions:**

- **Aortic Valve Disease** is commonly caused by mutations in the ACTA2, SMAD3, and TGFBR1 genes and consists of two subtypes: aortic valve stenosis and aortic valve regurgitation. Both subtypes are caused by improper functioning of the valve connecting the left ventricle and aorta. Aortic stenosis is present in 5% of the population aged 65 and older whereas aortic regurgitation is estimated to occur in about 10% of individuals 60 and older, though some cases present earlier. Symptoms of aortic valve disease include heart murmurs, chest pain, dizziness, fainting, arrhythmia, and shortness of breath.
- **Familial Thoracic Aortic Aneurysm** is caused mainly by mutations in the ACTA2 and TGFBR2 genes, though some other rare genetic variants have been identified in other genes. In this disease, the aorta becomes weakened and stretched, leading to a bulge in the vessel wall (aneurysm). Aortic aneurysms often present with no symptoms, but in severe cases swelling in the extremities, painful swallowing, shortness of breath, and coughing may occur. The incidence of the disease is unknown due to underdiagnosis, but ruptured aortic aneurysms are estimated to cause about 30,000 deaths in the United States each year.
- **Loeys-Dietz Syndrome (LDS)** is a disease that is commonly caused by mutations in the TGFBR1, TGFB2, TGFB3, and SMAD3 genes. The syndrome is characterized by weakening and enlargement of the aorta, increasing the risk of developing an aortic aneurysm. Symptoms of Loeys-Dietz syndrome include craniosynostosis, scoliosis, a sunken or protruding chest, and elongated limbs with joint deformities. This syndrome is very rare, with incidence rates of less than 1 in 100,000 people annually.
- **Marfan Syndrome (MFS)** is caused by mutations in the FBN1 gene, which is normally involved in providing strength and flexibility to connective tissue. In Marfan Syndrome, the aortic wall may weaken and stretch leading to the development of an aneurysm. Individuals with Marfan Syndrome are generally tall and slender, have elongated fingers and toes, loose joints, and large arm spans. Features of this syndrome may become apparent at any time between infancy and adulthood. The incidence of Marfan Syndrome is estimated to be 1 in 5,000 worldwide.

4 **The Congenital Heart Disease Panel (24 genes) includes genes involved in congenital heart defects. These heart defects can present at birth or may develop over time as the heart valves and vessels are affected by wear. Congenital heart defects affect 40,000 newborns per year in the United States.**

- ACTC1, ALMS1, BRAF, CBL, CRELD1, ELN, HRAS, JAG1, KRAS, MAPK2K1, MAPK2K2, MYH6, NKX2-5, NODAL, NOTCH1, NRAS, PTPN11, RAF1, SALL4, SCN5A, SHOC2, SOS1, TBX5, ZIC3

5 **The Familial Hypercholesterolemia Panel (15 genes) includes genes involved in Familial Hypercholesterolemia is an autosomal dominant disorder that affects 1:500 individuals.**

- APOA4, APOA5, APOB, CETP, CREB3L3, GCKR, GPIHBP1, HADHA, LDLR, LDLRAP1, LMF1, LPL, PCSK9, SREBF2, ZHX3

These panels identify germline variants in genes known to be involved in hereditary cardiac disease. Identification of variants may result in better outcomes for patients. Physicians can screen and monitor disease progression more closely, use therapies best suited for the patient's condition, and give patients the knowledge to make informed decisions regarding their health.