MEDGENOME

Cardiogenetics

INTRODUCING

For the first time in India, a genetic test

to predict your risk of developing

Coronary Artery Disease

Cardiogenetics

Cardiovascular diseases are the single most common cause of death worldwide

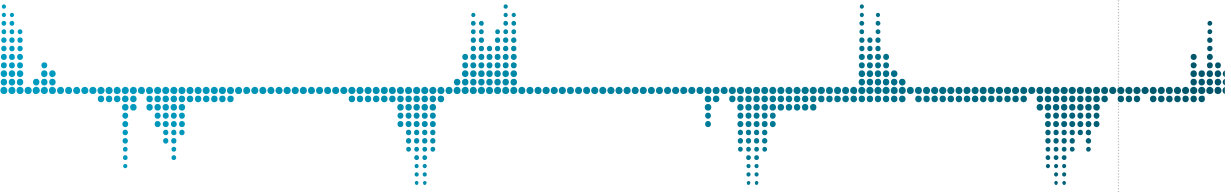
Genetic causes of Cardiovascular disease can be divided into two types:

Monogenic	Polygenic
Inherited monogenic forms can be autosomal dominant, autosomal recessive, or X-linked with genetic and clinical heterogeneity	Coronary artery disease is a multifactorial disease caused by a combination of several genetic and non-genetic factors. Predicted additive effect of genetic variants can be used to determine the risk of developing disease based on polygenic risk score (PRS)

2018 Heart Failure Society of America guideline on cardiomyopathies, a conjoint publication sharing the ACMG clinical practice resource (Hershberger RE et al., 2018)

"Genetic testing is recommended for the most clearly affected family member followed by cascade testing for pathogenic and likely pathogenic variants in at-risk family members, to facilitate patient management and family screening."

Genetic screening can help identify the causal genetic variant in monogenic forms, which will enable better disease management, cascade testing and timely intervention in at-risk relatives.



Inherited monogenic heart diseases

Inherited Arrhythmias (Sudden cardiac death)

- Brugada syndrome (BS)*
- Lev-Lenègre syndrome
- Atrial fibrillation (AF)
- Catecholaminergic polymorphic ventricular tachycardia (CPVT)*
- Timothy syndrome (TS)
- Long QT syndrome (LQTS)*
- Short QT syndrome (SQTS)
- Progressive Cardiac Conduction Disease (CCD)#

Cardiac Channelopathies develop as a result of mutations in genes encoding ion channel proteins, involved in cardiac conduction, impairing channel function. Significant variants may contribute to increased risk of ventricular arrhythmia and sudden death.

Test Code	Test Name	Methodology
MGM001	Cardiac channelopathy gene panel	NGS

Inherited Cardiomyopathy

- Hypertrophic cardiomyopathy (HCM)*
- Dilated cardiomyopathy (DCM)*
- Restrictive cardiomyopathy (RCM)*
- Arrhythmogenic Right Ventricular Dysplasia (ARVD)*
- Left ventricular non-compaction (LVNC)

Cardiomyopathies are disease of the heart muscle, characterized by the muscle becoming enlarged, abnormally thick or rigid. This may result in shortness of breath, arrhythmias or sudden death.

Test Code	Test Name	Methodology
MGM002	Cardiomyopathy gene panel	NGS

Note: Single gene may be associated with the different cardiac conditions (clinical heterogeneity), or variants in different genes may cause a similar cardiac phenotype (genetic heterogeneity).Reduced penetrance and variable expressivity, even among individuals in the same family is reported in literature.

Hypercholesterolemia and Dyslipidemia

- Familial hypercholesterolaemia (FH)*
- Lysosomal acid lipase deficiency
- Sitosterolaemia
- Dysbetalipoproteinaemia
- Familial Chylomicronemia Syndrome

Familial hypercholesterolaemia can be caused by genetic variants in lipid metabolism genes resulting in high levels of LDL cholesterol. Its deposition in the arteries leads to atherosclerosis and increased risk for coronary heart disease. Abnormal lipid levels LDL/HDL cholesterol and/or triglycerides (lipidemias) increase the risk for cardiovascular events

Test Code	Test Name	Methodology
MGM1291	Familial Hypercholesterolemia Gene Panel (PCSK9, LDLR, APOB, LDLRAP1)	NGS
MGM085	Hypercholesterolemia gene panel	NGS

Recommendations for FH Genetic Testing

Genetic testing for FH should be offered to individuals of any age in whom a strong clinical index of suspicion for FH exists on the basis of an examination of the patient's clinical and family histories.

Children with persistent* LDL-C levels ≥160 mg/dL or adults with persistent** LDL-C levels ≥190 mg/dL without an apparent secondary cause of hypercholesterolemia† and with at least 1 first-degree relative similarly affected or with premature CAD‡ or when family history is not available (eg, adoption)

Children with persistent* LDL-C levels ≥190 mg/dL or adults with persistent** LDL-C levels ≥250 mg/dL without an apparent secondary cause of hypercholesterolemia,† even in the absence of a positive family history

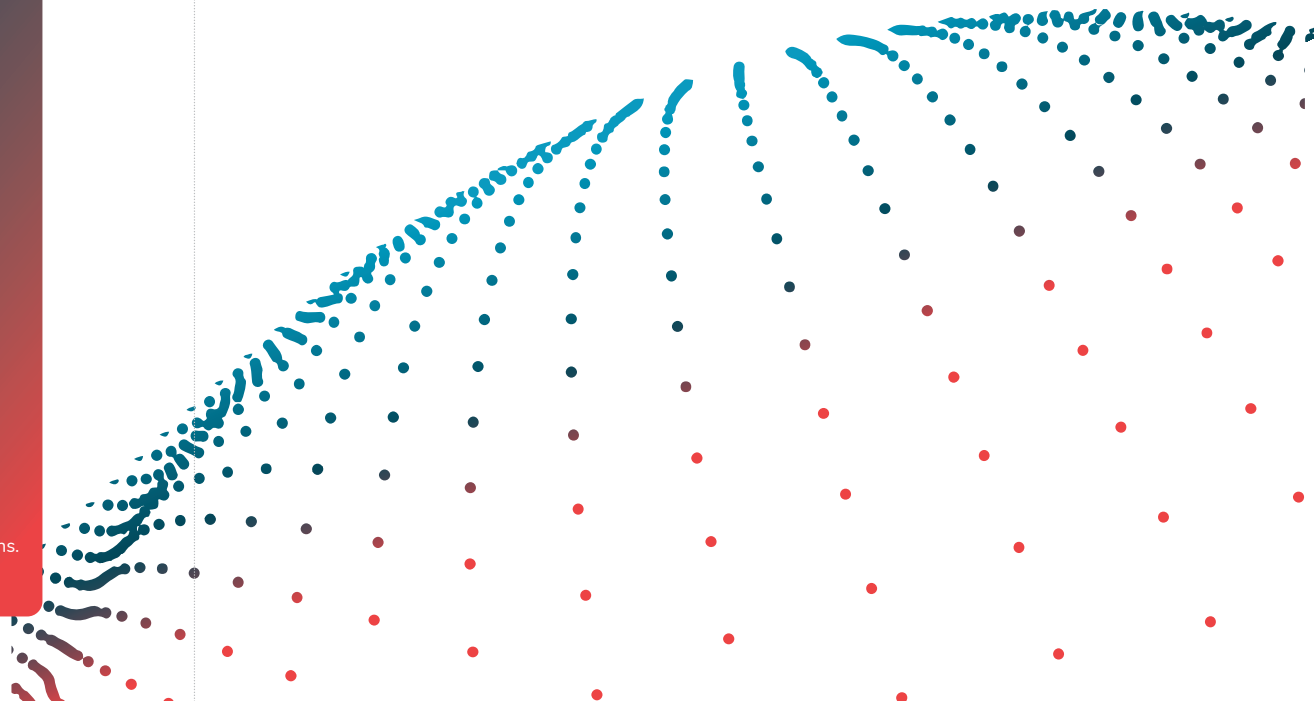
LDL-C, low-density lipoprotein cholesterol.
**Two or more measurements, including assessment after intensive lifestyle modification.
†Hypothyroidism, diabetes mellitus, renal disease, nephrotic syndrome, liver disease, and medications.
(Adapted from Sturm et al., 2018)

Aortopathy

- Familial thoracic aortic aneurysms and dissections*
- Loey-Deitz*; Marfan syndrome*; Ehlers Danlos

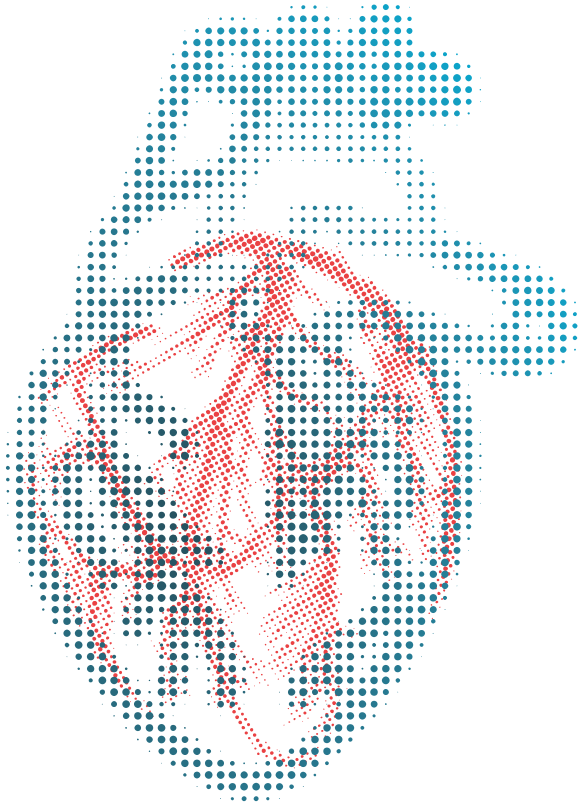
Aneurysms involving the aortic root and/or ascending aorta without concomitant aortic valve disease. Usually progressive and the individual may be asymptomatic, diagnosed during imaging studies

Test Code	Test Name	Methodology
MGM013	Ehler Danlos syndrome gene panel	NGS
MGM015	Marfan syndrome (FBN1) gene analysis	NGS
MGM014	Marfan syndrome (FBN1) deletion/duplication analysis	MLPA
MGM272	Clinical exome sequencing	NGS



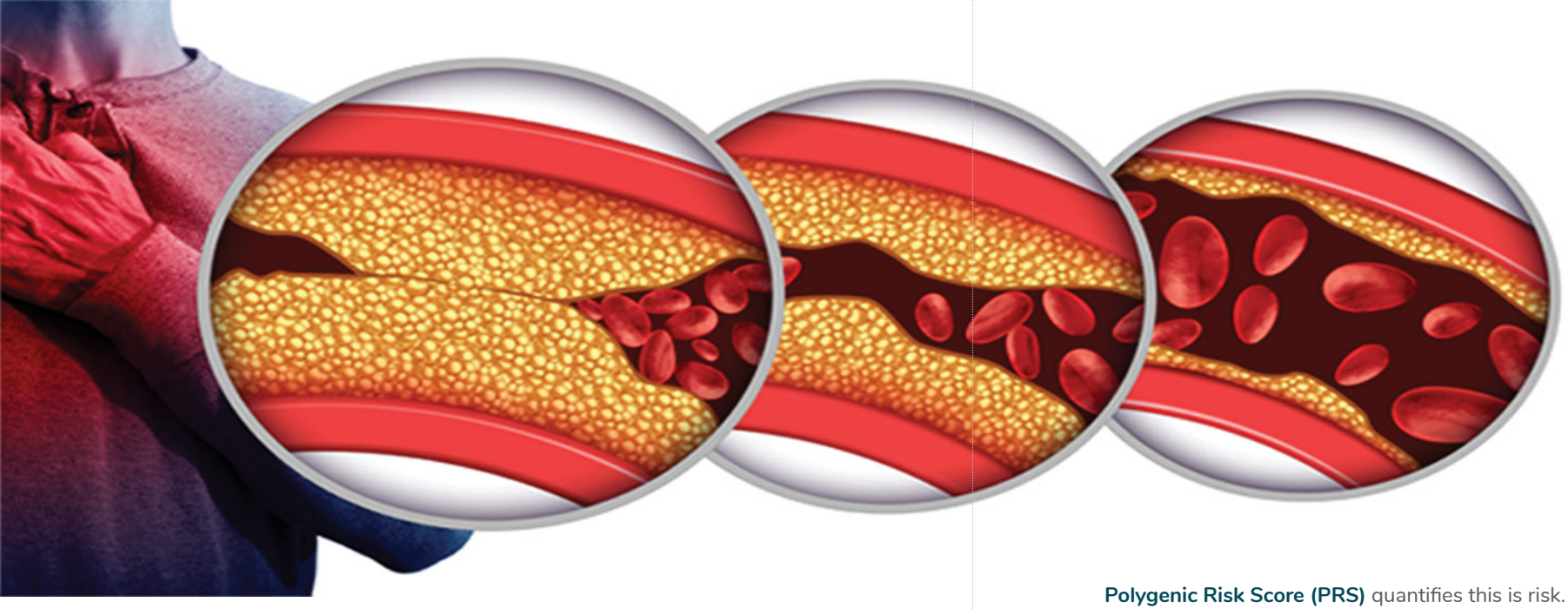
Other Inherited Cardio Vascular Diseases with Genetic Basis

- Syndromic and non-syndromic congenital structural and functional heart defects e.g. ***RASopathy syndromes****,
- Cardiomyopathies in ***Duchenne/Becker muscular dystrophy*, Congenital muscular dystrophies****,
- Pulmonary arterial hypertension (PAH)
- Pulmonary veno-occlusive disease (PVOD)
- Hereditary hemorrhagic telangiectasia (HHT)
- Ischiocoxopodopatellar syndrome (ICPPS)
- Hereditary Hemochromatosis



Next Generation Sequencing (NGS)			
MGM266	Noonan syndrome gene panel	MGM137	Duchenne muscular dystrophy (DMD) gene panel
MGM261	Alagille syndrome gene panel	MGM141	Muscular dystrophy and Congenital myopathy gene panel
MGM1031	Holt-Oram syndrome (TBX5) gene sequencing	MGM1518	Pulmonary arterial hypertension gene panel
MGM1261	CHARGE syndrome (SEMA3E and CHD7) gene sequencing	MGM083	Hemochromatosis gene Panel
MGM400	Rasopathy gene Panel		
Multiplex ligation-dependent probe amplification (MLPA)			
MGM552	Alagille syndrome 1 (JAG1) deletion/ duplication analysis	MGM140	Limb-girdle muscular dystrophy (SGCA, SGCB,SGCD, SGCG & FKRP) deletion/duplication analysis
MGM136	Duchenne muscular dystrophy (DMD) deletion/duplication analysis		

Note: *- Phenotypes that have been suggested by American Heart Association for Genetics-Guided Diagnosis and Management of Cardiovascular Conditions (PMID: 32698598)



Introducing KardioGen

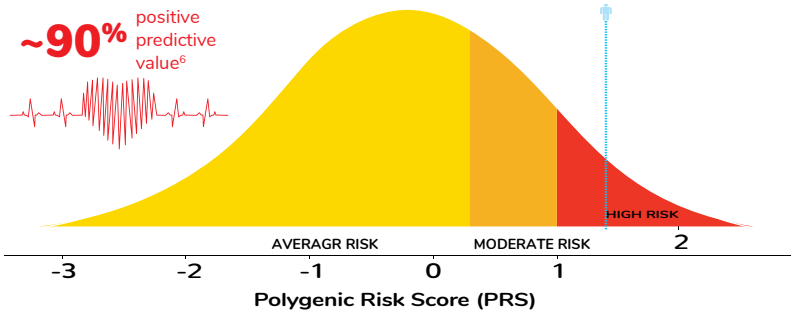
Polygenic Risk Score Test for Coronary Artery Disease Prediction

What is Polygenic Risk Score?

Genetic research over the past decade has realized that our risk for many common conditions such as heart disease and diabetes are not influenced by just one gene, or even a handful of them. Instead, multiple genes work in tandem to influence our risk for diseases. Many small-effect genetic variations contribute to a person's susceptibility to CAD.

Polygenic Risk Score (PRS) quantifies this is risk. A genome-wide PRS for CAD integrates information from 6 million sites of common DNA variation into a single metric-available from birth – of inherited risk. The risk is classified into High, Moderate or Average Risk.

This test can be taken only once at anytime during the person lifetime



MedGenome's KardioGen test is validated for the South Asian population#

Refer to our KardioGen brochure for more information

Minxian Wang, P. R. (2020). Development and testing of a genome-wide polygenic score for coronary artery disease in South Asians. Journal of the American College of Cardiology.

Why do you need Genetic Testing for Cardiac Diseases?

- To identify the genetic cause in families where multiple members are affected (family history)
- To confirm the diagnosis (both syndromic and non-syndromic)
- Cascade testing in related individuals to determine carrier status or risk
- Genetic diagnosis can guide informed treatment options and management strategies

When do you need to get tested?

- Congenital heart abnormalities
- cardiac arrest or sudden deaths in the family of unknown aetiology
- Enlarged heart or aorta or aortic aneurysm in the chest at less than 55 years of age
- Heart attack/Stroke at less than 55 years of age
- Unexplained Irregular heartbeat (arrhythmia)
- Very high cholesterol level
- Pulmonary hypertension
- Family history with symptoms of heart ailments

For any further technical queries please contact
techsupport@medgenome.com

Other Genetic Tests for Cardiology

Test Code	Test Methodology
	RT-PCR
MGM005	Clopidogrel dosage CYP2C19*2 & CYP2C19*3
MGM1033	Statin induced myopathy predisposition SLCO1B1 p.(Va-l174Ala)
MGM1034	Warfarin dosage-VKORC1 (c.-1639 G>A), CYP2C9*2,-CYP2C9*3,CYP2C9*13
	PCR
MGM1032	Cardiomyopathy predisposition - MYBPC3 (25bp dele-tion) by PCR-gel
	Microarray
MGM514/ MGM294	ANEUPLOIDIES
	NGS
MGM272	Clinical exome sequencing
MGM274	Whole exome sequencing
	FISH
MGM1104	Di George / VCF syndrome
MGM1063	FISH for Williams syndrome
	MLPA
MGM516	DiGeorge syndrome deletion/duplication analysis

Test Methodology	TAT (working days)
NGS	21 Working Days
MLPA	14 Working Days

Test Methodology	TAT (working days)
FISH	9 Working Days
PCR/RT PCR	7 Working Days

Test sample requirement

Blood
(3ml in EDTA tubes)

FREE GENETIC COUNSELLING

FREE Pre and post-test Counselling: To understand potential benefits, risks, and limitations of genetic testing

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