Congenital Heart Defects
Precision Panel

Overview

Congenital Heart Defects (CHD) are the most common type of birth defect. They include abnormalities in heart structure that occur before birth. These defects occur in the foetus while it is developing in the uterus during pregnancy. Chromosomal abnormalities can be a cause of CHD, although other causes include excessive alcohol consumption during pregnancy, the use of medications, maternal viral infections such as Rubella or measles during the first trimester, the presence of CHD in a parent or sibling and maternal illness (diabetes mellitus, phenylketonuria). The inheritance of these diseases follows an autosomal dominant pattern, although exceptions can be found. CHD encompasses a variety of defects that are commonly grouped based on the nature of the structural heart defect, resulting blood flow patterns, observed familial recurrence risks and shared susceptibility genes. According to the resulting blood pattern they can be classified as:

1. Acyanotic conditions ("pink babies"): Have left-to-right shunt in which oxygenated blood from the lungs is shunted back into the pulmonary circulation. Examples of these include septal defects (Ventricular Septal Defect, Atrial Septal Defect), Patent Ductus Arteriosus, Coarctation of the Aorta etc.
2. Cyanotic conditions ("blue babies"): Have right-to-left shunt in which deoxygenated blood is shunted into the systemic circulation. Examples of these include Transposition Of Great Vessels, Tetralogy Of Fallot, Truncus Arteriosus, Tricuspid Atresia, Total Anomalous Pulmonary Venous Return etc.

The Igenomix Congenital Heart Disease Precision Panel can be used as a diagnostic and screening tool ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes.

Indications

The Igenomix Comprehensive Cardiology Precision Panel is indicated in those cases where there is a clinical suspicion or ultrasound finding with or without the following manifestations:

- Blue-tinted nails or lips
- Fast or troubled breathing (shortness of breath)
- Tiredness when feeding
- Sleepiness, tiredness and/or fatigue
- Tachycardia
- Ankle, leg or eye swelling

- Loss of consciousness during exertion

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular diagnosis for an accurate clinical diagnosis.
- Early initiation of treatment with a multidisciplinary team for appropriate surgical repair and interventional procedures to prevent further complications such as endocarditis, pulmonary hypertension, respiratory tract infections, arrhythmias, heart failure and sudden cardiac death.
- Appropriate prenatal diagnosis and close communication between obstetric, genetic and paediatric providers for optimization of neonatal outcomes.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.

Genes & Diseases

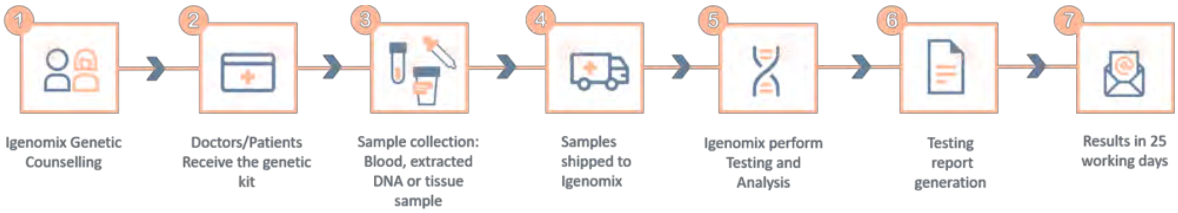
GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
A2ML1	Noonan Syndrome	AD,MU,P	100%	23 of 23
ABL1	Congenital Heart Defects And Skeletal Malformations Syndrome	AD	99.93%	8 of 8
ACTC1	Atrial Septal Defect Ostium Secundum Type, Dilated Cardiomyopathy, Left Ventricular Noncompaction, Familial Hypertrophic Cardiomyopathy	AD	99.93%	72 of 74
AFF4	Chops Syndrome	AD	99.42%	6 of 6
ARVCF	22q11.2 Deletion Syndrome	-	99.95%	2 of 2
B3GAT3	Multiple Joint Dislocations, Short Stature, Craniofacial Dysmorphism, With Or Without Congenital Heart Defects	AR	99.86%	15 of 15
BAZ1B	Williams Syndrome	-	99.05%	5 of 5
BCOR	Oculofaciocardiodental Syndrome	X,XD,G	99.87%	NA of NA
BMPR2	Pulmonary Hypertension, Pulmonary Venoocclusive Disease	AD	99.99%	590 of 600
BRAF	Cardiofaciocutaneous Syndrome, Leopard Syndrome, Noonan Syndrome	AD	100%	80 of 80
CBL	Noonan Syndrome	AD	100%	46 of 47
CDK13	Congenital Heart Defects, Dysmorphic Facial Features, And Intellectual Developmental Disorder	AD	92.37%	31 of 32
CHD7	Charge Syndrome,Omenn Syndrome	AD	96.25%	823 of 896
CHST3	CHST3-Related Skeletal Dysplasia, Multiple Joint Dislocations, Short Stature, Craniofacial Dysmorphism, With Or Without Congenital Heart Defects	AR	99.97%	38 of 38
COMT	22q11.2 Deletion Syndrome	AD	99.98%	5 of 5
CRELD1	Atrioventricular Septal Defect	AD	100%	14 of 14
CRKL	Distal 22q11.2 Microdeletion Syndrome		99.93%	5 of 6
DGCR2	Velocardiofacial Syndrome	AD	99.94%	3 of 3
DGCR6	Velocardiofacial Syndrome	AD	94.78%	NA of NA
DGCR8	Velocardiofacial Syndrome	AD	99.98%	2 of 2
DYNC2H1	Jeune Syndrome	AR,MU,D	99.78%	214 of 221
EHMT1	Kleefstra Syndrome	AD	98.58%	58 of 75
ELN	Familial Thoracic Aortic Aneurysm And Aortic Dissection, Supravalvular Aortic Stenosis, Williams Syndrome, Williams-beuren Syndrome	AD	99.99%	95 of 96
ESS2	Velocardiofacial Syndrome	AD	99.91%	NA of NA
FBN1	Familial Thoracic Aortic Aneurysm And Aortic Dissection, Marfan Lipodystrophy Syndrome, Marfan Syndrome, Shprintzen-Goldberg Syndrome, Weill-Marchesani Syndrome	AD	100%	2836 of 2845
FGFRL1	Wolf-Hirschhorn Syndrome	AD	99.94%	1 of 1
FLT4	Congenital Heart Defects, Tetralogy Of Fallot	AD	100%	119 of 120
GATA4	8p23.1 Microdeletion Syndrome, Atrial Septal Defect Ostium Secundum Type, Atrioventricular Septal Defect, Testicular Anomalies With Or Without Congenital Heart Disease, Tetralogy Of Fallot, Ventricular Septal Defect	AD	94.69%	108 of 130

GATA5	Congenital Heart Defects, Familial Bicuspid Aortic Valve, Tetralogy Of Fallot	AD,AR	87.02%	26 of 32
GATA6	Atrial Septal Defect Ostium Secundum Type, Atrioventricular Septal Defect, Conotruncal Heart Malformations, Truncus Arteriosus Communis, Pancreatic Hypoplasia-Diabetes-Congenital Heart Disease Syndrome, Tetralogy of Fallot	AD,AR	84.19%	66 of 84
GDF1	Asplenia With Cardiovascular Anomalies, Congenital Heart Defects, Tetralogy Of Fallot	AD,AR	75.72%	11 of 14
GJA5	Familial Atrial Fibrillation, Chromosome 1q21.1 Deletion Syndrome, Tetralogy Of Fallot	AD	99.88%	13 of 13
GP1BB	22q11.2 Deletion Syndrome	AR	74.08%	26 of 50
HAND1	Congenital Heart Disease, Hypoplastic Left Heart Syndrome	-	99.89%	9 of 9
HAND2	Familial Isolated Dilated Cardiomyopathy	-	99.19%	5 of 6
HDAC8	Cornelia De Lange Syndrome, Wilson-Turner Syndrome	X,XD,G	99.78%	NA of NA
HIRA	22q11.2 Deletion Syndrome	-	99.99%	5 of 5
JAG1	Tetralogy Of Fallot	AD	99.98%	640 of 641
JMJD1C	22q11.2 Deletion Syndrome	-	99.09%	27 of 27
KIFBP	Goldberg-Shprintzen Syndrome	AR	99.27%	NA of NA
KMT2A	Cornelia De Lange Syndrome, Wiedemann-Steiner Syndrome	AD	98.14%	144 of 149
KRAS	Cardiofaciocutaneous Syndrome, Noonan Syndrome, Toriello-Lacassie-Droste Syndrome	AD	100%	38 of 38
LZTR1	Noonan Syndrome	AD	99.99%	136 of 136
MAP2K1	Cardiofaciocutaneous Syndrome, Noonan Syndrome	AD	100%	31 of 31
MAP2K2	Cardiofaciocutaneous Syndrome, Neurofibromatosis-noonan Syndrome	AD	100%	37 of 37
MAPK1	Distal 22q11.2 Microdeletion Syndrome	-	96.91%	1 of 1
MRAS	Noonan Syndrome	AD	100%	3 of 3
MYRF	Cardiac-Urogenital Syndrome	AD	99.83%	27 of 27
NF1	Neurofibromatosis-Noonan Syndrome	AD	97.97%	3082 of 3166
NIPBL	Cornelia De Lange Syndrome	AD	99.32%	409 of 426
NKX2-5	Atrial Septal Defect With Or Without Atrioventricular Conduction Defects, Atrial Septal Defect, Ostium Secundum Type, Conotruncal Heart Malformations, Truncus Arteriosus Communis, Familial Bicuspid Aortic Valve, Familial Progressive Cardiac Conduction Defect, Hypoplastic Left Heart Syndrome, Tetralogy Of Fallot, Ventricular Septal Defect	AD,AR	99.98%	112 of 116
NKX2-6	Conotruncal Heart Malformations, Truncus Arteriosus Communis, Tetralogy Of Fallot	AR	99.83%	8 of 8
NOTCH1	Adams-Oliver Syndrome, Aortic Valve Disease, Familial Bicuspid Aortic Valve	AD	99.83%	178 of 179
NOTCH2	Acroosteolysis Dominant Type	AD	99.88%	91 of 91
NR2F2	Congenital Heart Defects, Partial Atrioventricular Septal Defect	AD	97.37%	16 of 18
NRAS	Noonan Syndrome, Schimmelpenning-Feuerstein-Mims Syndrome	AD	100%	15 of 15
NSD1	5q35 Microduplication Syndrome, Sotos Syndrome, Weaver Syndrome	AD	99.80%	451 of 459
NSD2	Wolf-Hirschhorn Syndrome	AD	99.91%	NA of NA
PPP1CB	Noonan Syndrome-like Disorder With Loose Anagen Hair	AD	99.87%	12 of 12
PRDM16	1p36 Deletion Syndrome, Familial Isolated Dilated Cardiomyopathy, Left Ventricular Noncompaction, Dilated Cardiomyopathy	AD	98.81%	20 of 20
PRDM6	Patent Ductus Arteriosus	AD	99.63%	4 of 4
PRKD1	Congenital Heart Defects And Ectodermal Dysplasia	AD	97.39%	8 of 9
PTPN11	Leopard Syndrome, Noonan Syndrome	AD	100%	150 of 151
RAD21	Cornelia De Lange Syndrome, Mungan Syndrome	AD,AR	99.80%	16 of 17
RAF1	Dilated Cardiomyopathy, Leopard, Noonan Syndrome	AD	100%	64 of 64
RASA2	Noonan Syndrome	-	99.82%	5 of 5
RBM10	Tarp Syndrome	X,XR,G	100%	NA of NA
RBPJ	Adams-Oliver Syndrome	AD	99.98%	8 of 8
RIT1	Noonan Syndrome	AD	99.85%	27 of 27
RRAS	Noonan Syndrome	-	95.86%	3 of 3
RRAS2	Noonan Syndrome	AD	99.80%	6 of 6
RREB1	22q11.2 Deletion Syndrome		99.92%	8 of 8
SEC24C	22q11.2 Deletion Syndrome	-	99.98%	NA of NA
SETD5	Cornelia De Lange Syndrome	AD	99.77%	37 of 37
SHOC2	Noonan Syndrome-like Disorder With Loose Anagen Hair	AD	99.98%	8 of 8
SKI	1p36 Deletion Syndrome, Shprintzen-Goldberg Craniosynostosis Syndrome	AD	99.66%	39 of 39
SMC1A	Cornelia De Lange Syndrome, Wiedemann-Steiner Syndrome	X,XR,XD,G	100%	NA of NA

SMC3	Cornelia De Lange Syndrome	AD	100%	30 of 30
SOS1	Noonan Syndrome	AD	100%	103 of 104
SOS2	Noonan Syndrome	AD	99.48%	6 of 7
STAG2	Xq25 Microduplication Syndrome	X,XR,G	99.09%	NA of NA
TAB2	Congenital Heart Defects, Polyvalvular Heart Disease Syndrome	AD	99%	13 of 13
TBX1	22q11.2 Deletion Syndrome, Conotruncal Heart Malformations, Truncus Arteriosus Communis, DiGeorge Syndrome, Tetralogy Of Fallot, Velocardiofacial Syndrome	AD,AR	88.70%	35 of 42
TBX20	Atrial Septal Defect Ostium Secundum Type	AD	99.98%	33 of 34
TBX5	Holt-Oram Syndrome	AD	100%	143 of 152
TFAP2B	Char Syndrome, Patent Ductus Arteriosus	AD	100%	19 of 19
TKT	Short Stature, Developmental Delay, And Congenital Heart Defects	AR	99%	6 of 6
TLL1	Atrial Septal Defect Ostium Primum Type, Atrial Septal Defect Ostium Secundum Type	AD	99.96%	8 of 8
TMEM94	Intellectual Developmental Disorder With Cardiac Defects And Dysmorphic Facies	AR	98%	NA of NA
UFD1	22q11.2 Deletion Syndrome	-	99.98%	NA of NA
VPS33A	Mucopolysaccharidosis-like Syndrome With Congenital Heart Defects And Hematopoietic Disorders	AR	97.86%	1 of 1
WDPCP	Bardet-Biedl Syndrome, Congenital Heart Defects	AR	99.30%	8 of 8
ZFPM2	Tetralogy Of Fallot	AD	99.40%	44 of 46
ZIC3	X-linked Visceral Heterotaxy	X,XR,G	99.98%	NA of NA

* Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial
** HGMD: Number of clinically relevant mutations according to HGMD

Methodology



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Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

- Get more information about the test.
- Request your kit.
- Request a pick up of the kit after collecting the sample.

References

1. Baumgartner, H., & De Backer, J. (2020). The ESC Clinical Practice Guidelines for the Management of Adult Congenital Heart Disease 2020. *European Heart Journal*, *41*(43), 4153-4154. doi: 10.1093/eurheartj/ehaa701
2. What are Congenital Heart Defects? | CDC. (2021). Retrieved 18 February 2021, from https://www.cdc.gov/ncbddd/heartdefects/facts.html
3. Sun, R., Liu, M., Lu, L., Zheng, Y., & Zhang, P. (2015). Congenital Heart Disease: Causes, Diagnosis, Symptoms, and Treatments. *Cell biochemistry and biophysics*, *72*(3), 857–860. https://doi.org/10.1007/s12013-015-0551-6
4. Williams, K., Carson, J., & Lo, C. (2019). Genetics of Congenital Heart Disease. *Biomolecules*, *9*(12), 879. https://doi.org/10.3390/biom9120879
5. Saliba, A., Figueiredo, A., Baroneza, J., Afiune, J., Pic-Taylor, A., Oliveira, S., & Mazzeu, J. (2020). Genetic and genomics in congenital heart disease: a clinical review. *Jornal De Pediatria*, *96*(3), 279-288. doi: 10.1016/j.jped.2019.07.004
6. Linglart, L., & Gelb, B. D. (2020). Congenital heart defects in Noonan syndrome: Diagnosis, management, and treatment. *American journal of medical genetics. Part C, Seminars in medical genetics*, *184*(1), 73–80. https://doi.org/10.1002/ajmg.c.31765

7. Calcagni, G., Unolt, M., Digilio, M. C., Baban, A., Versacci, P., Tartaglia, M., Baldini, A., & Marino, B. (2017). Congenital heart disease and genetic syndromes: new insights into molecular mechanisms. *Expert review of molecular diagnostics*, *17*(9), 861–870. https://doi.org/10.1080/14737159.2017.1360766
8. Hopkins, M. K., Dugoff, L., & Kuller, J. A. (2019). Congenital Heart Disease: Prenatal Diagnosis and Genetic Associations. *Obstetrical & gynecological survey*, *74*(8), 497–503. https://doi.org/10.1097/OGX.0000000000000702