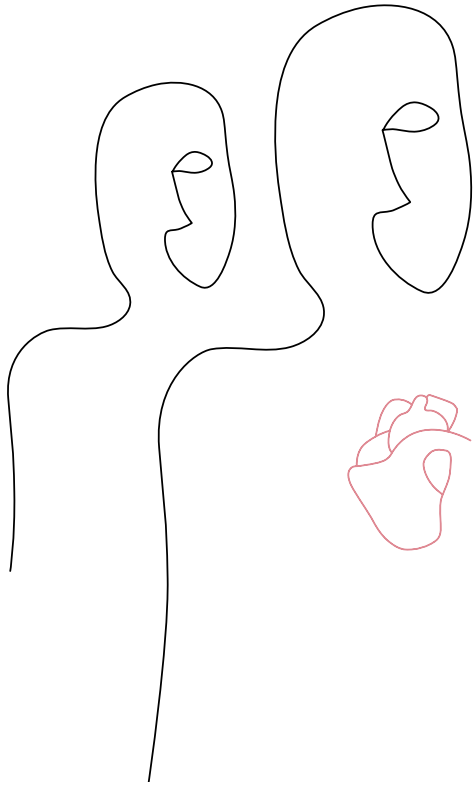
Cordis DX

Physician's Booklet



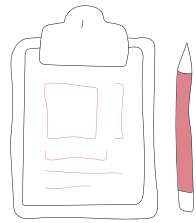
"Your Genes Speak, We Translate"

Genekor

Committed to Biotechnological Innovation

Genekor Medical S.A. presents the new **Cordis DX®** tests, a new line of thorough and clinically verified molecular multi-gene tests, with high specificity and sensitivity, which analyze the genes that are related to hereditary cardiovascular diseases such as:

- Cardiomyopathies
- Channelopathies
- Aortopathies
- Pulmonary arterial hypertension
- Congenital Heart Disease
- Hyperlipidemia - Dyslipidemia (ex. Familial Hypercholesterolemia)
- and others ...
- Long-QT & Short QT syndromes
- Brugada Syndrome
- CPVT Syndrome
- Marfan Syndrome
- Noonan Syndrome
- Loeys-Dietz Syndrome
- Ehlers Danlos Syndrome
- and others



Why Cordis DX® molecular analyses are important

DIAGNOSIS:

They confirm the clinical diagnosis in a reliable and fast way and reduce the need for more invasive procedures. Accurate diagnosis of inherited cardiovascular disease is now possible with the use of genetic analysis, which minimizes dilemmas regarding the management and prognosis of the disease and assists the physician in estimating the time for surgery.

The test is very important in diagnosis of hereditary arrhythmogenic diseases, such as channelopathies, that are linked to a high risk of sudden death in normally built hearts (ex Long QT Syndrome, Brugada Syndrome etc..)

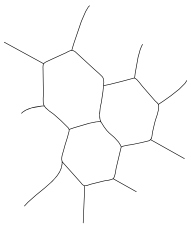
PROGNOSIS:

By knowing in detail the genetic mutations that are responsible for a patient's disease, we can predict its progress, taking into account all the factors that concern the specific patient.

We can also identify relatives who carry the same mutation and are at increased risk of developing the same disease and thus be properly managed. The test's contribution is particularly important in families that carry genes associated with sudden death.

MANAGEMENT:

The proper management of the patient and his/her family is based on the correct diagnosis and prognosis of the disease, so that the physician is oriented towards the most appropriate treatment and patient-regulation.



It informs about the avoidance of certain medications and guides lifestyle modifications to avoid causing heart attacks as much as possible.
It assists in the decision for early surgery and / or placement of an implantable cardiac defibrillator or pacemaker.

It identifies appropriate control intervals and possible interventions for at-risk family members.

Examples of clinical use Cordis DX®

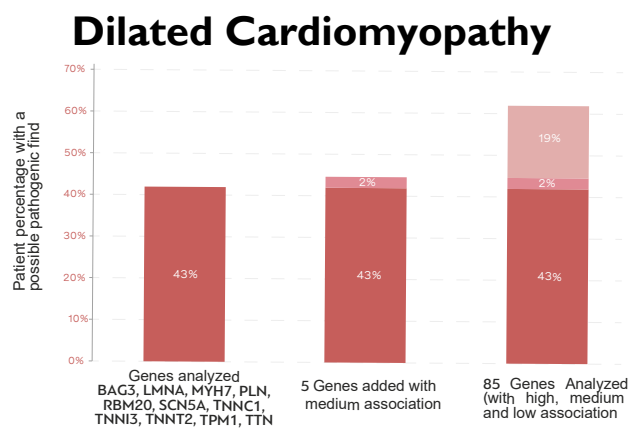
Channelopathies: They help shape lifestyle recommendations and choice of the right medication, as well as make decisions about using an implantable defibrillator (ICD).

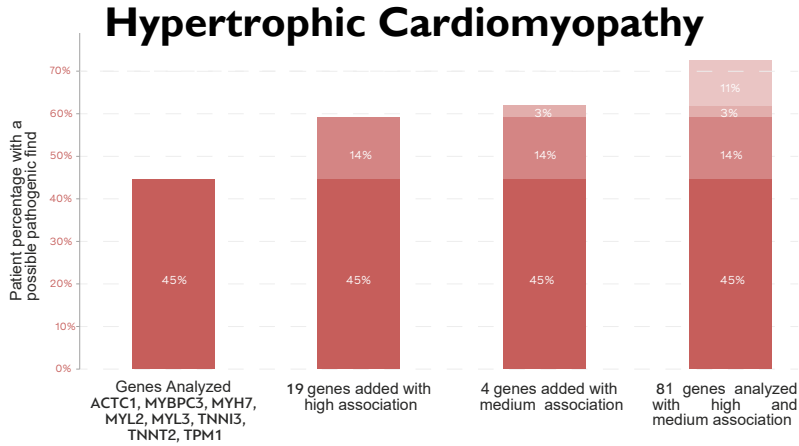
Aortic Diseases: Aortic diseases manifested by aneurysms and separation (Marfan syndrome, familial thoracic aortic aneurysms, Loeys-Dietz syndrome, Ehlers-Danlos syndrome). Detection of pathological mutation helps determine the time of surgery.

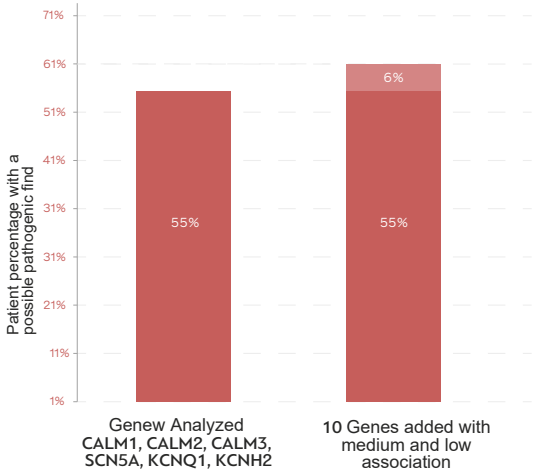
Hypertrophic Cardiomyopathy (HCM): The gene mutations that are often detected are directly related to the patient's phenotype. Genetic analysis can contribute to the differential diagnosis between classic sarcoma disease and various syndromes with hypertrophy on ultrasound (such as Fabry disease, Danon disease, etc.)

Dilated Cardiomyopathy (DCM): Genetic analysis has prognostic value, and the detection of specific genetic findings may contribute to better patient management. For example, mutations in the LMNA gene are associated with a high risk of sudden cardiac death, and defibrillator implantation is required.

The extra value of a multi-gene NGS test

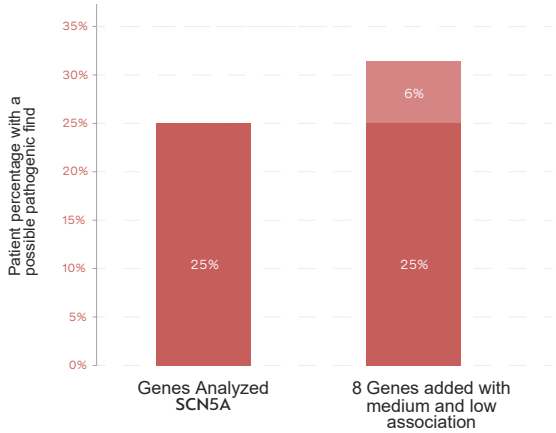






Long QT Syndrome

Brugada Syndrome



Molecular Tests are recommended by validated international organizations of Cardiology

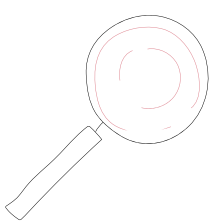
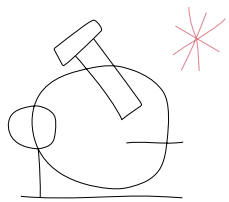
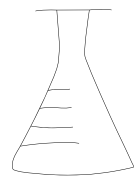
International Guidelines

- Recommended by **Heart Rhythm Society (HRS) & European Heart Rhythm Association (EHRA**) for the diagnosis and management of Channelopathies
- Recommended by the American Association of Cardiologists for the diagnosis and the management of Arrhythmias
- Recommended by the **Heart Failure Society of America** and the **European Society of Cardiology** for the diagnosis and management of cardiomyopathies
- Recommended by the **European Society of Cardiology** and the **European Respiratory Society** for the diagnosis and the management of Pulmonary arterial hypertension

CordisDX *257 Genes*	A2ML1 - ABCC6 - ABCC8 - ABCC9 - ABL1 - ACAD9 - ACTA1 ACTA2 -ACTC1 - ACTN2 - ACVRL1 - ADAMTS10 - ADAMTS17 ADAMTSL4 - AGK - AGL - AKAP9 - ALDH18A1 - ALMS1 - ALPK3 ANK2 - ANKRD1 - APOA1 - AQP1 - ATP7 - AB3GAT3 BAG3 - BGN - BMPR1B - BMPR2 - BRAF CACNA1C - CACNA2D1 - CACNB2 - CALM1 - CALM2 - CALM3 CALR3 - CASQ2 - CAS21 - CAV1 - CAV3 - CBL - CBS - CDH2 CHRM2 - CHST14 - COL1A1 - COL1A2 - COL2A1 - COL3A1 - COL4A5 - COL5A1 - COL5A2 - COX15 - CRYAB - CSRP3 - CTC1 CTNNA3 DBH - DEPDC5 - DES - DMD - DOLK - DPM3 - DSC2 - DSG2 - DSP - DTNA - DYSF - EEF1A2 EFEMP2 EIF2AK4 - ELAC2 - ELN - EMD - ENG - ENPP1 - EPG5 - ETFA - ETFB - ETFDH - EYA4 FBLN5 - FBN1 - FBN2 - FBXL4 - FHL1 - FHL2 - FHOD3 - FKBP14 FKRP - FKTN - FLNA - FLNC - FOXE3 - FXN GAA - GATA4 - GATA5 - GATAD1 - GBE1 - GDF2 - GJA5 - GLA GLB1 - GPD1L - GSK3B - GYS1 HADHA - HAND1 - HCN4 - HFE - HRAS ILK JPH2 - JUP KCNA1 - KCNA5 - KCND3 - KCNE1 - KCNE2 - KCNE3 - KCNE5 KCNH2 - KCNJ2 - KCNJ5 - KCNJ8 - KCNK3 - KCNQ1 - KCNQ2 KCNQ3 - KCNT1 - KLHL24 - KRAS LAMA4 - LAMP2 - LDB3 - LMNA - LOX - L2TR1 MAP2K1 - MAP2K2 - MAT2A - MED12 - MEF2A - MFAP5 MIB1 - MLYCD - MRAS - MYBPC3 - MYH11 - MYH6 - MYH7 MYL2 - MYL3 - MYL4 - MYLK - MYLK2 - MYOT - MYO22 MYPN NDUFAF2 - NEBL - NEXN - NF1 - NFU1 - NKX2-5 - NOS1AP NOTCH1 - NOTCH3 - NPPA - NRAS - NUP155 PCCA - PCCB - PCDH19 - PDLIM3 - PKP2 -PLEC - PLN - PLOD1 PRDM16 - PRKAG2 - PRKG1 - PTPN11 RAF1 - RANGRF - RASA1 - RASA2 - RBCK1 - RBM20 - RIT1 RMND1 - RYR1 - RYR2 SALL4 - SARS2 - SCN10A - SCN1A - SCN1B - SCN2B - SCN3B SCN4B - SCN5A- SCN8A - SCN9A - SDHA - SGCD - SHOC2 SKI- SLC25A4 - SLC2A1 - SLC2A10 - SLC39A13 - SLMAP - SMAD2 SMAD3 - SMAD4 - SMAD6 - SMAD9 - SNTA1 - SOS1 - SOS2 SOX17 - SPRED1 - STRA6 - SYNE1 - SYNE2 TAB2 - TA2 - TBX20 - TBX4 - TBX5 - TCAP - TECRL - TGFB2 TGFB3 - TGFBR1 - TGFBR2 - TMEM43 - TMPO - TNNC1 - TNNI3 TNNI3K - TNNT2 - TPM1 - TRDN - TRPM4 - TTN - TTR - TXNRD2 VCL - VPS13A XK ZDHHC9 - ZNF469
CordisDX Select *43 Genes*	ABCC9 - AKAP9 - ANK2 - APOB CACNA1C - CACNA2D1 - CACNB2 - CALM1 - CALM2 - CALM3 CASQ2 - CAV3 GPD1L HAMP - HCN4 - HFE - HFE2 KCND3- KCNE1- KCNE2- KCNE3 - KCNH2 - KCNJ2 - KCNJ5 KCNJ8 - KCNQ1 LDLR - LDLRAP1 - LMNA PCSK9- PKP2 - RYR2 - SCN10A - SCN1B- SCN2B - SCN3B SCN4B - SCN5A - SLC40A1 - SNTA1 TFR2 - TRDN - TRPM4
CordisDX LDL *4 Genes*	APOB LDLR - LDLRAP1 PCSK9

CordisDX® tests offer to the physician maximum differential diagnosis with high percentage of specificity and sensitivity, saving precious time and cost per patient case.

Cordis DX Focus	GENES
Cardiomyopathies 147 Genes	A2ML1- ACTC1 - ABCC6 - ABCC9 - ACAD9 - ACADVL - ACTA1 ACTN2 - AGK - AGL - ALMS1 - ANKRD1 - APOA1 BAG3 - BRAF CACNA1C - CACNB2- CALM3 - CALR3 CASQ2 - CAS21 - CAV3 CBL CDH2 - CHRM2 - COX15 - CRYAB - CSRP3 -CTC1- CTNNA3 DBH - DES - DMD - DOLK - DPM3 - DSC2 - DSG2 - DSP DTNA- DYSF EEF1A2 - ELAC2 - EMD - EPG5 - ETFA - ETFB - ETFDH - EYA4 FBXL4 - FHL1 - FHL2 - FHOD3 - FKRP - FKTN - FLNC - FXN GAA - GATA4 - GATAD1 - GBE1 - GLA - GLB1 - GSK3B HADHA - HAND1 - HCN4 - HFE - HRAS ILK JPH2 - JUP KCNQ1 -KLHL24 - KRAS LAMA4 - LAMP2 - LDB3 - LMNA - LZTR1 MAP2K1 - MAP2K2 - MED12 - MIB1 -MLYCD - MYBPC3 -MYH6 MYH7 - MYL2 - MYL3 - MYL4 - MYLK2 - MYOT - MYO22 MYPN NDUFAF2 - NEBL - NEXN - NF1 - NKX2-5 - NPPA - NRAS PCCA - PCCB - PDLIM3 - PKP2 - PLEC - PLN - PRDM16 PRKAG2 - PTPN11 RAF1 - RASA1 - RASA2 - RBCK1 - RBM20 - RIT1 - RMND1 - RYR2 SCN5A- SDHA- SGCD - SHOC2 - SLC25A4 - SOS1 - SOS2 - SPRED1 TAB2 -TA2 - TBX20 - TBX5 - TCAP - TGFB3 - TMEM43 - TMPO TNNC1 - TNNI3 - TNNI3K - TNNT2 - TPM1 - TTN - TTR - TXNRD2 VCL - VPS13A XK

Hypertrophic Cardiomyopathy (HCM) 81 Genes	A2ML1 - ABCC9 - ACAD9 - ACADVL- ACTA1 - ACTC1 - ACTN2 AGK - AGL- ANKRD1 - APOA1 BAG3 - BRAF CACNA1C - CACNB2 - CALM3 - CALR3 - CASQ2 - CAV3 - CBL COX15 - CRYAB - CSRP3 - CTC1 DES - DSP - DTNA ELAC2 - EPG5 FBXL4 - FHL1 - FHOD3 - FLNC - FXN GAA - GATA4 - GLA - GSK3B HRAS JPH2 KCNQ1 - KLHL24 - KRAS LAMP2 - LDB3 MAP2K1 - MAP2K2 - MYBPC3 - MYH6 - MYH7 - MYL2 - MYL3 MYLK2 - MYO22 - MYPN NDUFAF2 - NEXN - NF1 - NRAS PDLIM3 - PLN - PRKAG2 - PTPN11 RAF1 - RASA1 - RIT1 - RYR2 SHOC2 - SLC25A4 - SOS1 - SOS2 - SPRED1 TCAP - TMPO - TNNC1 - TNNI3 - TNNT2 - TPM1 - TTN - TTR VCL
Dilated Cardiomyopathyθεια (DCM) 85 Genes	ABCC6 - ABCC9 - ACTA1 - ACTC1 - ACTN2 - ANKRD1 -APOA1 BAG3 - ALMS1 CAS21 - CHRM2 DMD - CRYAB - CSRP3 - DES - DOLK- DSC2 - DSG2 - DSP DTNA - DPM3 - DYSF EEF1A2 - EMD - EPG5 - ETFA - ETFB - ETFDH FHOD3 - FKTN - FLNC GATA4 - GATAD1 - GBE1 - GSK3B HAND1 - HCN4 GLB1 - ILK - JPH2 - JUP KLHL24 LAMA4 - LAMP2 - LDB3 - LMNA MIB1 - MLYCD - MYBPC3 - MYH6 - MYH7 - MYL4 - MYPN NEBL - NEXN - NKX2-5 PKP2 - PCCA - PCCB - PRDM16 - PLN RAF1 - RBCK1 - RBM20 - RMND1 - RYR2 SGCD - SCN5A TA2 - TNNI3K - TBX20 - TBX5 - TCAP - TMEM43 - TMPO - TNNC1 - TNNI3 - TNNT2 - TAB2 - TPM1 - TTN - TTR - TXNRD2 VCL - VPS13A
Right ventricular arrhythmia (ARVC) 28 Genes	ACTC1 BAG3 CDH2 - CTNNA3 DES - DSC2 - DSG2 - DSP FLNC JUP LDB3 - LMNA MYBPC3 - MYH7 - MYL2 - MYL3 NKX2-5 PKP2 - PLN RYR2 SCN5A TGFB3 - TMEM43 - TTN - TNNC1 - TNNI3 - TNNT2 - TPM1

Left Ventricular Non-Compaction Cardiomyopathy 32 Genes	ABCC9 - ACTC1 BAG3 CTNNA3 DES - DMD - DSC2 - DSG2 - DSP - DTNA EMD FLNC HCN4 JPH2 - JUP LAMP2 - LMNA MYBPC3 - MYH6 - MYH7 PKP2 - PLN RAF1 - RBM20 - RYR2 SCN5A TAZ - TCAP - TNNT2 - TPM1 - TTN VCL
Atrial Fibrillation 18 Genes	CACNB2 HCN4 KCNA5 - KCNE1 - KCNE2 - KCNH2 - KCNJ2 - KCNJ5 - KCNQ1 LDB3 - LMNA NUP155 RYR2 SCN10A - SCN1B - SCN3B - SCN5A TBX5
Arrhythmias 84 Genes	ABCC9 - ACTN2 - AKAP9 - ANK2 BAG3 CACNA1C - CACNA2D1 - CACNB2 - CALM1 - CALM2 - CALM3 CASQ2 - CAV3 - CDH2 - CTNNA3 DBH - DEPDC5 - DES - DSC2 - DSG2 - DSP EMD FLNC GJA5 - GPD1L HCN4 JUP KCNA1 - KCNA5 - KCND3 - KCNE1 - KCNE2 - KCNE3 - KCNE5 KCNH2 - KCNJ2 - KCNJ5 - KCNJ8 - KCNK3 - KCNQ1 - KCNQ2 KCNQ3 - KCNT1 LDB3 - LMNA MYH6 - MYH7 - MYL4 NKX2-5 - NOS1AP - NPPA - NUP155 PCDH19 - PDLIM3 - PKP2 - PLN - PRKAG2 RANGRF - RBM20 - RYR2 SALL4 - SCN10A - SCN1A - SCN1B - SCN2B - SCN3B - SCN4B SCN5A - SCN8A - SCN9A - SLC2A1 - SLMAP - SNTA1 TBX5 - TECRL - TGFB3 - TMEM43 - TNNI3 - TNNI3K - TNNT2 TRDN - TRPM4 - TTN
Brugada syndrome 9 Genes	CACNA1C - CACNB2 - CAV3 HCN4 KCNH2 SCN1B - SCN3B - SCN5A TRPM4

Long QT (LQT) Syndrome *16 Genes*	AKAP9 - ANK2 - ASCN5A CACNA1C - CALM1 - CALM2 - CALM3 - CAV3 KCNE1 - KCNE2 - KCNH2 - KCNJ2 - KCNJ5 - KCNQ1 NOS1AP - SCN5A TECRL
Short QT (SQT) Syndrome *5 Genes*	CACNA1C -CACNB2 KCNH2 - KCNJ2 - KCNQ1
CPVT Syndrome *10 Genes*	ANK2 CALM1 - CALM2 - CALM3 - CASQ2 KCNJ2 LMNA RYR2 TRDN - TECRL
Pulmonary arterial hypertension *20 Genes*	ABCC8 - ACVRL1 - AQP1 BMPR1B - BMPR2 CAV1 EIF2AK4 - ENG GDF2 KCNA5 - KCNK3 NFU1 - NOTCH3 RASA1 SARS2 - SMAD4 - SMAD9 - SOX17 - STRA6 TBX4
Aortic Anomalies *50 Genes*	ABCC6 - ABL1 - ACTA2 - ADAMTS10 - ADAMTS17 - ADAMTSL4 ALDH18A1 - ATP7A B3GAT3 - BGN CBS - COL1A1 - COL1A2 - COL2A1 - COL3A1 - COL4A5 COL5A1 - COL5A2 EFEMP2 - ELN ENG ENPP1 FBN1 - FBN2 - FKBP14 - FLNA - FOXE3 GATA5 HCN4 LOX MAT2A - MED12 - MFAP5 - MYH11 - MYLK NOTCH1 PLOD1 - PRKG1 SKI - SLC2A10 - SLC39A13 - SMAD2 - SMAD3 - SMAD4 SMAD6 TGFB2 - TGFB3 - TGFBR1 - TGFBR2 ZNF469
Ehlers Danlos Syndrome *26 Genes*	ABCC6 - ALDH18A1 - ATP7A BGN CBS - CHST14 - COL1A1 - COL1A2 - COL2A1 - COL3A1 COL5A1 COL5A2 EFEMP2 - ELN FBLN5 - FBN1 - FBN2 - FKBP14 - FLNA PLOD1 SLC39A13 - SMAD3 TGFB2 - TGFBR1 - TGFBR2 ZNF469

2 BLOOD EDTA TUBES - 15 WORKING DAYS

Noonan Syndrome 20 Genes	A2ML1 BRAF CBL HRAS KRAS LZTR1 MAP2K1 - MAP2K2 - MRAS NF1 - NRAS PTPN11 RAF1 - RASA1 - RASA2 - RIT1 SHOC2 - SOS1 - SOS2 - SPRED1
Marfan Syndrome 28 Genes	ABL1 - ADAMTS10 - ADAMTS17 - ADAMTSL4 B3GAT3 - BGN CBS - COL1A1 - COL1A2 - COL2A1 - COL3A1 - COL5A1 - COL5A2 EFEMP2 FBN1 - FBN2 LOX MAT2A - MED12 PLOD1 SKI - SLC2A10 - SMAD3 - SMAD6 TGFB2 - TGFB3 - TGFBR1 - TGFBR2

MyTheragene

Pharmacogenomics

MyTheragene® is an innovative multi-gene test, with high sensitivity and specificity, which is based on pharmacogenomic science and analyzes 40 genes related to the metabolic pathway for over 500 drugs.

It is suitable for everyone who is taking or is about to take medication, but it is important that the following groups of patients undergo it:

- » Patients with complicated drug precriptions and multiple diseases
- » Patients who show little or no response to current medication
- » Patients who experience side effects from current treatment
- » Patients with chronic diseases
- » Patients with rare or severe disorders
- » Patients with allergies to drugs

MyTheragene® Gene Panel									
ABCB1	*ABCG2*	*ADRA2A*	*ANK1*	*APOE*	*COMT*	*CYP1A2*	*CYP2B6*	*CYP2C19*	*CYP2C8*
CYP2C9	*CYP2D6*	*CYP3A4*	*CYP3A5*	*DBH*	*DPYD*	*DRD1*	*DRD4*	*F2*	*F5*
FLOT1	*GABRA6*	*GABRP*	*GRIK4*	*HCP5*	*HLA-A*	*HTR2A*	*HTR2C*	*ITGB3*	*KIF6*
MTHFR	*OPRD1*	*OPRK1*	*OPRM1*	*SLCO1B1*	*TPMT*	*UGT1A1*	*UGT2B15*	*UGT2B7*	*VKORC1*

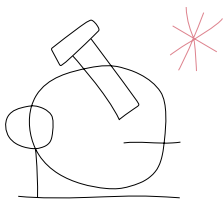
(10 WORKING DAYS)
(2 blood EDTA tubes)

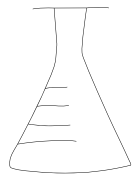
Thrombophilia Assays

Primary Genetic Analysis for Thrombophilia

GENES	MUTATION POLYMORPHISM
Factor V Leiden	*G1691A ή R508Q (Leiden)*
	H1299R (R2)
Prothrombin	*G20210A*
Methylene tetrahydrofolic acid reductase (MTHFR)	*C677T*

(10 WORKING DAYS**)**
1 BLOOD TUBE EDTA OR SALIVA SAMPLE





Complete Genetic Analysis for Thrombophilia

GENES	Mutation Polymorphism
Factor V Leiden	*G1691A ή R508Q (Leiden)*
	H1299R (R2)
Prothrombin	*G20210A*
Factor XIII (fibrin stabilizing factor)	*V34L*
B - fibrinogen	*455 G>A*
Plasminogen Activator Inhibitor (PAI-1)	*4G / 5G*
Human Platelet Antigens HPA	*1a / 1b*
Methylene tetrahydrofolic acid reductase (MTHFR)	*C677T*
	A1298C
Apolipoprotein B.(ApoB)	*R3500Q*
Apolipoprotein E (ApoE)	*codons 112 (Cys / Arg)*

(10 WORKING DAYS)
1 BLOOD TUBE EDTA OR SALIVA SAMPLE

The Company

Genekor Medical SA is a multinational company committed to biotechnology, that develops and conducts molecular analyses for the diagnosis, prediction and management of various diseases, such as cancer, cardiovascular disease and neurological diseases, in order to assist physicians in the application of medical precision by specialty.

Founded in 2007 and it is separated into 3 different Departments

- Department of Research and Development of Molecular Assays
- Department of Molecular Testing
- Department of Scientific Support and Consulting

Genekor is constantly evolving, developing and investing in state-of-the-art equipment, providing specialized services in the field of Genetics to the global market.

Our team consists of certified and internationally recognized and published scientists, who share the same vision for high quality health services and work to provide physicians with relevant, accurate and useful information as well as ongoing support for the selection of more effective individualized therapies for their patients.

Our mission is to revolutionize the personalized treatment of patients by developing and offering highly sensitive and specific molecular assays that are applicable in everyday clinical practice, incorporating state-of-the-art technology and assisting physicians in applying cutting edge tools for individualized medicine worldwide.

Genekor's clinical specialization focuses on the following:

- Response to targeted therapy
- Pharmacogenomics
- Identification of hereditary disease
- Scientific support and consulting

Genekor
Committed to Biotechnological Innovation

Certifications:

- Our specialized laboratories are accredited for a number of examinations according to ESYD ELOT EN ISO 15189:2012 (cer N. 822) as in corresponding sections EPED.
- We are certified with ISO 9001:2015 (Cer N.. 041150049) and with ELOT ISO / IEC 27001:2013 (cer N. 048190009) by TUV NORD HELLAS.
- We participate in external quality control programs to ensure the high quality of molecular assays EMQN - GenQA -CAP.

Genekor Medical S.A.

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