Washington University CardioGene Set

GENOMICS AND PATHOLOGY SERVICES
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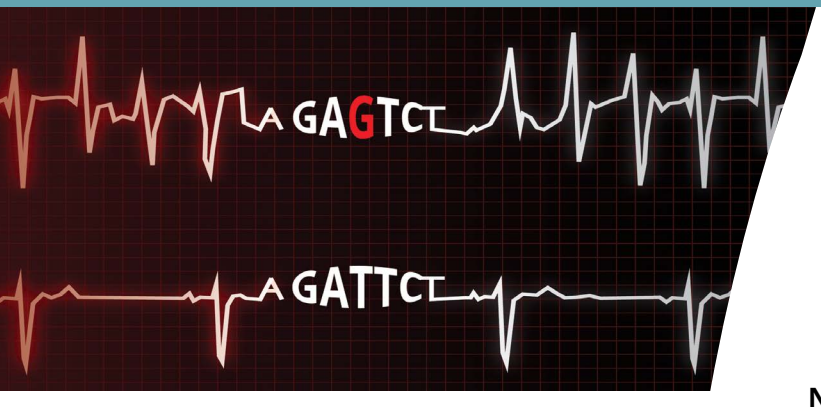
CLINICAL TESTING • RESEARCH • EDUCATION



Genomic profiling for cardiac disease

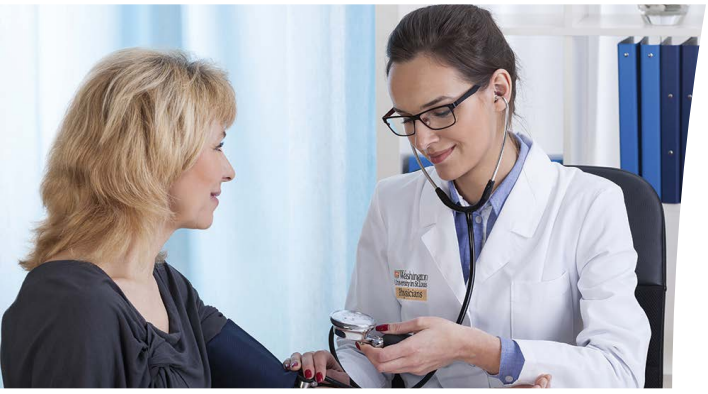
Developed in collaboration with **leading cardiologists** from Washington University School of Medicine

Next-generation sequencing of key genes implicated in arrhythmias and cardiomyopathies for efficient, cost-effective and robust germline variant detection

Concise, expert interpretations by board-certified clinical genomicists, reported back to the ordering physician

Personal support for physicians in result interpretation by our highly-trained genomicists and genetic counselor

Testing covered by most insurance; preauthorization performed by GPS



Orderable gene sets include:

Arrhythmia

- **Brugada** *(10 genes)*
- **CPVT** *(5 genes)*
- **LQTS** *(13 genes)*
- **SQTS** *(5 genes)*

Cardiomyopathy

- **ARVC** *(8 genes)*
- **DCM** *(32 genes)*
- **HCM** *(31 genes)*
- **LVNC** *(10 genes)*

Clinical utility

The **Washington University CardioGene Set** is designed to identify causative genetic variation within patients affected with cardiomyopathy or arrhythmia syndromes.

The identification of a pathogenic genetic alteration may be used to solidify a **diagnosis**, allowing for more appropriate patient **management** and surveillance. It also enables tailored genetic counseling in both the patient and at-risk family members.

Targeted next-generation sequencing provides clinicians with a powerful tool to enrich patient care and enables the analysis of multiple genes with clinical relevance to enhance the diagnostic yield of testing. Such analysis opens the potential for **disease specific therapies** over time and may enable genotype-phenotype correlations to be drawn.

Washington University Physicians®
Washington University School of Medicine in St. Louis

Washington University CardioGene Set

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Indications for testing

Indications for testing include symptoms of a variety of arrhythmias and cardiomyopathies:

- Brugada syndrome (BrS)
- Catecholaminergic polymorphic ventricular tachycardia (CPVT)
- Long QT syndrome (LQTS)
- Short QT syndrome (SQTS)
- Arrhythmogenic right ventricular cardiomyopathy (ARVC)
- Dilated cardiomyopathy (DCM)
- Hypertrophic cardiomyopathy (HCM)
- Noonan syndrome
- Left ventricular noncompaction (LVNC)

Genes tested

Arrhythmia Gene Set: Includes all genes from the following four gene sets.

- **BrS Gene Set:** *CACNA1C, CACNB2, GPD1L, HCN4, KCND3, KCNE3, KCNJ8, PKP2, SCN1B, SCN3B, SCN5A*
- **CPVT Gene Set:** *ANK2, CALM1, CASQ2, KCNJ2, RYR2*
- **LQTS Gene Set:** *AKAP9, ANK2, CACNA1C, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNJ5, KCNQ1, SCN4B, SCN5A, SNTA1*
- **SQTS Gene Set:** *CACNA1C, CACNB2, KCNH2, KCNJ2, KCNQ1*

Cardiomyopathy Gene Set: Includes all genes from the following four gene sets.

- **ARVC Gene Set:** *DES, DSC2, DSG2, DSP, JUP, PKP2, RYR2, TMEM43*
- **DCM Gene Set:** *ABCC9, ACTC1, ACTN2, ANKRD1, BAG3, CSRP3, CTF1, DES, EMD, FHL1, FHL2, GATAD1, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, NEXN, PLN, RBM20, SCN5A, SGCD, TAZ, TCAP, TMPO, TNNC1, TNNI3, TNNT2, TPM1, TTN, VCL*
- **HCM Gene Set:** *ACTC1, ACTN2, BRAF, CSRP3, GLA, HRAS, KRAS, LAMP2, MAP2K1, MAP2K2, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYLK2, MYOZ2, NEXN, NRAS, PLN, PRKAG2, PTPN11, RAF1, RIT1, SHOC2, SOS1, TNNC1, TNNI3, TNNT2, TPM1, TTR*
- **LVNC Gene Set:** *ACTC1, CASQ2, DTNA, LDB3, LMNA, MYBPC3, MYH7, TAZ, TNNT2, VCL*

Testing methodology

Tests are performed using targeted hybridization capture coupled with next-generation sequencing (NGS) in our CAP/CLIA labs for comprehensive coverage of all coding exons of ordered genes. Types of variation detected include single nucleotide variants (SNVs) and small insertions and deletions (indels).

Results and interpretation

DNA sequence data are analyzed by GPS's clinically validated bioinformatics pipeline to identify and annotate genetic variants associated with arrhythmias or cardiomyopathies.

Variants are interpreted by a board-certified clinical genomicist in the context of the patient's disease. Those that are most likely to account for the observed clinical phenotype based on evidence from the medical literature are highlighted. Results are returned to the ordering physician in a concise report.

Specimen requirements

Specimen types accepted include 2-5 mL of peripheral blood in a lavender-top EDTA tube. Specimen kits are available upon request.

Turnaround time

The turnaround time for testing and interpretation is four to six weeks after a specimen arrives following pre-authorization.

Ordering

To order a test, submit a completed requisition form (available on our website) by fax or email. Tests are reimbursable, and GPS performs insurance preauthorization.

Selected references

Ackerman MJ, Priori SG, et al. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies. Heart Rhythm. 2011 Aug;8(8):1308-39.

Westaway SK, Reinier K, et al. Common variants in CASQ2,GPD1L, and NOS1AP are significantly associated with risk of sudden death in patients with coronary artery disease. Circ Cardiovasc Genet. 2011 Aug 1;4(4):397-402.

Jeff JM, Brown-Gentry K, et al. SCN5A variation is associated with electrocardiographic traits in the Jackson Heart Study. Circ Cardiovasc Genet. 2011 Apr;4(2):139-44.

Sedlacek K, Stark K, et al. Common genetic variants in ANK2 modulate QT interval: results from the KORA study. Circ Cardiovasc Genet. 2008 Dec;1(2):93-9.

Schwartz PJ. The congenital long QT syndromes from genotype to phenotype: clinical implications. J Intern Med. 2006 Jan;259(1):39-47.

Contact us to order a test or for more info

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