

Cardiovascular Diseases Genetic Testing Program

Description:

We offer comprehensive gene panels designed to diagnose the most common genetic causes of hereditary cardiovascular diseases. Testing is available for congenital heart malformation, cardiomyopathy, arrhythmia, thoracic aortic aneurysm, pulmonary arterial hypertension, Marfan syndrome, and RASopathy/Noonan spectrum disorders. Hereditary cardiovascular disease is caused by variants in many different genes, and may be inherited in an autosomal dominant, autosomal recessive, or X-linked manner. Other than condition-specific panels, we also offer single gene sequencing for any gene on the panels, targeted variant analysis, and targeted deletion/duplication analysis.

Tests Offered:

Arrhythmia Panels

- Comprehensive Arrhythmia Panel (81 genes)
- Atrial Fibrillation (A Fib) Panel (28 genes)
- Atrioventricular Block (AV Block) Panel (7 genes)
- Brugada Syndrome Panel (21 genes)
- Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Panel (11 genes)
- Long QT Syndrome Panel (19 genes)
- Short QT Syndrome Panel (6 genes)

Connective Tissue Disorders Panel

- Thoracic Aortic Aneurysm Panel (49 genes)
- Marfan Syndrome and MFS Related Disorders Panel (3 genes)

Cardiomyopathy Panels

- Comprehensive Cardiomyopathy Panel (135 genes)
- Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) Panel (18 genes)
- Dilated Cardiomyopathy (DCM) Panel (73 genes)
- Hypertrophic Cardiomyopathy (HCM) Panel (98 genes)
- Left Ventricular Noncompaction (LVNC) Panel (36 genes)
- Restrictive Cardiomyopathy (RCM) Panel (9 genes)

Congenital Heart Disease Panels

- Congenital Heart Disease Panel (187 genes)
- Heterotaxy Panel (114 genes)
- RASopathy/Noonan Spectrum Disorders Panel (31 genes)

Other Panels

- Pulmonary Arterial Hypertension (PAH) Panel (20 genes)

Indications:

Panels:

- Confirmation of genetic diagnosis in a patient with a clinical diagnosis of cardiovascular disease
- Carrier or pre-symptomatic diagnosis identification in individuals with a family history of cardiovascular disease of unknown genetic basis

Gene Specific Sequencing:

- Confirmation of genetic diagnosis in a patient with cardiovascular disease and in whom a specific gene associated diagnosis is suspected

Variant Specific Analysis:

- Pre-symptomatic testing of at-risk siblings and parents for medical management
- Carrier identification in individuals in whom specific variant(s) have been identified in the proband
- Prenatal diagnosis of an at-risk fetus, after confirmation of variant(s) in the parent(s) and by prior arrangement only

Deletion/Duplication Analysis:

- Completion of the diagnostic evaluation in a patient with a clinical diagnosis of cardiovascular disease who has had a negative panel or who is heterozygous for a variant in a gene associated with an autosomal recessive condition.

Specimen:

Provide at least 3 mL of whole blood in a lavender top (EDTA) tube or saliva in an Oragene saliva kit. Please call the lab at 513-636-4474 for a free saliva collection kit. Label the tube with the patient's name, birth date, and date of collection. Alternatively, 10 mcg of high quality DNA may be submitted.

For prenatal samples, at least 20 mL of amniotic fluid or at least 30 mg chorionic villi or 2 flasks of cultured cells is needed. 3 mL of maternal blood in lavender top (EDTA) tube is needed for maternal cell contamination studies.

Testing Methodology:

Panels: Our panels utilize Exome Sequencing (ES) technology to detect variants in predefined lists of clinically relevant genes to identify inherited forms of cardiovascular diseases. Our panels use the Human Comprehensive Exome kit from Twist Bioscience to capture the exonic regions of genes from the genomic DNA extracted from the patient. Targeted regions are sequenced using the Illumina sequencing system with paired-end reads. Sequence reads are aligned to reference genome (build UCSC hg19). Variants within exons and flanking sequences are identified and evaluated by a validated in-house developed bioinformatics analysis pipeline and Fabric software packages. Data quality is assessed to confirm it has a minimum coverage of 20X for >95% of targets of interest,

Gene Specific Sequencing: PCR-based or NGS-based sequencing of entire coding region, intron/exon boundaries of the specified gene

Variant Specific Analysis: Sanger sequencing following PCR amplification of the targeted variant(s) of the specified gene

Deletion/Duplication Analysis: Copy number variant analysis of the gene by comparative genomic hybridization

Results:

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for the clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

Test Sensitivity:

Analytical Sensitivity: The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed.

Sequencing Test Limitations: Pathogenic variants may be present in a portion of the genes not covered by this test or in regions with suboptimal data due to homologous issue, polynucleotides, or nucleotide repeats, and therefore may not be identified. Thus, the absence of identified pathogenic variants does not exclude the possibility of a genetic etiology for the patient's symptoms. Certain types of mutations are not detected. Only single base pair changes or small insertions or deletions of DNA are detected. Large deletions, duplications, or rearrangements, mitochondrial genome mutations, repeat expansions, low level mosaicism and many epigenetic defects may not be detected by this test.

Regions of Homology

These gene regions with homology may generate

| GENE | TRANSCRIPT | EXON | CHROM | EXON_START | EXON_END |
|--------|--------------|------|-------|------------|-----------|
| ARMC4 | NM_001290020 | 9 | 10 | 28257851 | 28257947 |
| CDC42 | NM_001791 | 6 | 1 | 22417920 | 22418010 |
| FLNC | NM_001458 | 47 | 7 | 128498061 | 128498271 |
| LEFTY2 | NM_001172425 | 3 | 1 | 226127455 | 226127571 |
| SDHA | NM_004168 | 14 | 5 | 254507 | 254621 |
| TBX20 | NM_001166220 | 6 | 7 | 35271111 | 35271192 |

Low coverage (<20X) regions

| GENE | TRANSCRIPT | EXON | CHROM | EXON_START | EXON_END |
|---------|--------------|---------|-------|------------|-----------|
| ADAMTS2 | NM_021599 | 11 | 5 | 178578129 | 178578201 |
| ARMC4 | NM_001290021 | 13 | 10 | 28142170 | 28142292 |
| B3GAT3 | NM_001288722 | 5 | 11 | 62383657 | 62383708 |
| B3GAT3 | NM_001288723 | 5 | 11 | 62383673 | 62383712 |
| HYDIN | NM_001270974 | 76-79 | 16 | 70867789 | 70874136 |
| HYDIN | NM_001270974 | 81-84 | 16 | 70852244 | 70863733 |
| MTO1 | NM_133645 | 7 | 6 | 74190015 | 74190090 |
| MTO1 | NM_001123226 | 8 | 6 | 74190719 | 74190839 |
| NOTCH2 | NM_024408 | 2-4 | 1 | 120539619 | 120572610 |
| PKP2 | NM_004572 | 6 | 12 | 32996115 | 32996247 |
| TNXB | NM_019105 | 32-34 | 6 | 32011783 | 32013103 |
| TNXB | NM_019105 | 36-40 | 6 | 32010231 | 32011333 |
| TNXB | NM_019105 | 2-44 | 6 | 32009125 | 32009950 |
| TTN | NM_001267550 | 173-193 | 2 | 179518934 | 179528076 |
| TTN | NM_001267550 | 195-198 | 2 | 179517964 | 179518624 |

Please note: These regions represent the low coverage (<20X) regions identified during our test validation. For specific patient cases, these regions may vary slightly.

Turn-Around Time:

Gene panels: up to 6 weeks

Individual/custom gene sequencing: up to 6 weeks

Targeted analysis: up to 2 weeks

Deletion/Duplication analysis: up to 4 weeks

CPT Codes:

- *APOB* (R3500Q/R3500W) Sequencing Analysis: **81401**
- Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) Panel, Dilated Cardiomyopathy (DCM) Panel, Hypertrophic Cardiomyopathy (HCM) Panel, Left Ventricular Noncompaction (LVNC) Panel, Restrictive Cardiomyopathy (RCM) Panel: **81439**
- Atrial Fibrillation (A Fib) Panel, Brugada Syndrome Panel, Congenital Heart Disease Panel (CHD), Heterotaxy Panel, Long QT Syndrome Panel, Pulmonary Arterial Hypertension (PAH) Panel: **81443**
- Atrioventricular Block (AV Block) Panel: **81404, 81405, 81406**
- Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Panel: **81403, 81405, 81408**
- Comprehensive Arrhythmia Panel: **8141**
- Comprehensive Cardiomyopathy Panel: **81439**

- FBN1 Full Mutation Analysis: **81408**
- LDLR Gene Sequencing: **81406**
- Marfan Syndrome and MFS Related Disorders Panel: **81405 x2, 81408**
- RASopathy/Noonan Spectrum Disorders Panel: **81442**
- Short QT Syndrome Panel: **81403, 81406, 81479 x2**
- Thoracic Aortic Aneurysm Panel: **81410**
- TTN Full Mutation Analysis: **81479**
- Targeted variant analysis and deletion/duplication: **call for information.**

Please call 1-866-450-4198 for current pricing, insurance preauthorization or with any billing questions.

Shipping Instructions:

Please enclose test requisition with sample. All information must be completed before sample can be processed. Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Saturday.

Ship to:

Genetics and Genomics Diagnostic Laboratory
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

Note: Cardiovascular diseases panel cases with negative or uncertain findings can be reflexed to Whole Exome Sequencing (WES). A separate test order and a signed consent form is required for all WES testing. In addition, including biological parental samples is strongly encouraged to assist with the analysis of WES and to increase test yield. Reflex to WES orders can either be placed simultaneously or separately. Separate reflex to WES orders are subject to review prior to the initiation of testing. Please see our website at www.cincinnatichildrens.org/exome to obtain a WES test requisition and consent form.

Arrhythmia Disorders:

| Panel Name | # of Genes | Genes |
|---|------------|---|
| Comprehensive Arrhythmia Panel | 81 | <i>ABCC9, ACTN2, AKAP9, ANK2, ANKRD1, BAG3, CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CALM3, CASQ2, CAV3, CDH2, CPT1A, CTNNA3, DES, DSC2, DSG2, DSP, EMD, FLNC, GATA4, GATA5, GATA6, GJA5, GNB5, GPD1L, GYG1, HCN4, JUP, KCNA5, KCND3, KCNE1, KCNE1L, KCNE2, KCNE3, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNK3, KCNQ1, KCNQ3, LDB3, LMNA, MYH6, MYH7, MYL4, NKX2-5, NOS1AP, NPPA, NUP155, PDLIM3, PKP2, PLN, PPA2, PRKAG2, RANGRF, RBM20, RYR2, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, SLC25A20, SLMAP, SNTA1, TBX5, TECRL, TGFB3, TMEM43, TNNI3, TNNI3K, TNNT2, TRDN, TRPM4, TTN</i> |
| Atrial Fibrillation (A Fib) Panel | 28 | <i>ABCC9, CACNB2, GATA4, GATA6, GJA5, HCN4, KCNA5, KCND3, KCNE1, KCNE1L, KCNE2, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNQ1, LDB3, LMNA, NPPA, NUP155, RYR2, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, TBX5</i> |
| Atrioventricular Block (AV Block) Panel | 7 | <i>DES, EMD, LMNA, NKX2-5, SCN1B, SCN5A, TRPM4</i> |
| Brugada Syndrome Panel | 21 | <i>ABCC9, CACNA1C, CACNA2D1, CACNB2, CAV3, GPD1L, HCN4, KCND3, KCNE1L, KCNE3, KCNH2, KCNJ8, PKP2, RANGRF, SCN10A, SCN1B, SCN2B, SCN3B, SCN5A, SLMAP, TRPM4</i> |

Arrhythmia Disorders (cont.):

| Panel Name | # of Genes | Genes |
|--|------------|---|
| Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Panel | 11 | ANK2, CALM1, CALM2, CALM3, CASQ2, KCNJ2, KCNQ1, RYR2, SCN5A, TECRL, TRDN |
| Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) Panel | 19 | AKAP9, ANK2, CACNA1C, CALM1, CALM2, CALM3, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNJ5, KCNQ1, NOS1AP, SCN4B, SCN5A, SNTA1, TECRL, TRDN |
| Short QT Syndrome Panel | 6 | CACNA1C, CACNA2D1, CACNB2, KCNH2, KCNJ2, KCNQ1 |

Connective Tissue Disorders:

| Panel Name | # of Genes | Genes |
|---|------------|--|
| Thoracic Aortic Aneurysm Panel | 49 | ABL1, ACTA2, ADAMTS10, ADAMTS2, ADAMTSL4, ALDH18A1, BGN, CBS, CHST14, COL1A1, COL1A2, COL2A1, COL3A1, COL5A1, COL5A2, EFEMP2, ELN, FBLN5, FBN1, FBN2, FKBP14, FLNA, FOXE3, GATA5, LOX, LTBP3, MAT2A, MED12, MFAP5, MYH11, MYLK, NOTCH1, PLOD1, PRKG1, SKI, SLC2A10, SLC39A13, SMAD2, SMAD3, SMAD4, SMAD6, TAB2, TGFB2, TGFB3, TGFBRI, TGFBRI2, TGFBRI3, TNXB, ZNF469 |
| Marfan Syndrome and MFS Related Disorders Panel | 3 | FBN1, TGFBRI, TGFBRI2 |

Cardiomyopathy Disorders:

| Panel Name | # of Genes | Genes |
|--|------------|--|
| Comprehensive Cardiomyopathy Panel | 135 | AARS2, ABCC9, ACAD9, ACADVL, ACTA1, ACTC1, ACTN2, AGK, AGL, ALMS1, ALPK3, ANKRD1, BAG3, BRAF, CACNA1C, CALR3, CASQ2, CAV3, CAVIN4, CBL, CDH2, CHRM2, COX15, CPT2, CRYAB, CSRP3, CTNNA3, DES, DMD, DOLK, DSC2, DSG2, DSP, DTNA, ELAC2, EMD, EPG5, EYA4, FBXO32, FHL1, FHL2, FKRP, FKTN, FLNC, FXN, GAA, GATA4, GATA6, GATAD1, GBE1, GLA, GLB1, HAND1, HCN4, HRAS, ILK, JPH2, JUP, KRAS, LAMA4, LAMP2, LDB3, LMNA, LRRC10, LZTR1, MAP2K1, MAP2K2, MIB1, MTO1, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYL4, MYLK2, MYO6, MYOM1, MYOZ2, MYPN, NDUFAF2, NEBL, NEXN, NF1, NKX2-5, NPPA, NRAS, PCCA, PCCB, PDLIM3, PKP2, PLEKHM2, PLN, PPP1CB, PRDM16, PRKAG2, PSEN1, PSEN2, PTPN11, RAF1, RBM20, RIT1, RMND1, RYR2, SCN5A, SCO2, SDHA, SGCD, SHOC2, SLC22A5, SLC25A4, SOS1, SOS2, SPEG, SPRED1, SURF1, SYNE2, TAB2, TAZ, TBX20, TBX5, TCAP, TGFB3, TMEM43, TMPO, TNNC1, TNNI3, TNNI3K, TNNT2, TPM1, TRDN, TTN, TTR, TXNRD2, VCL |
| Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) Panel | 18 | CDH2, CTNNA3, DES, DSC2, DSG2, DSP, FLNC, JUP, LDB3, LMNA, MYH7, PKP2, PLN, RYR2, SCN5A, TGFB3, TMEM43, TTN |
| Dilated Cardiomyopathy (DCM) Panel | 73 | ABCC9, ACTC1, ACTN2, ALMS1, ALPK3, ANKRD1, BAG3, CAV3, CHRM2, CRYAB, CSRP3, DES, DMD, DOLK, DSC2, DSG2, DSP, DTNA, EMD, EYA4, FHL2, FKRP, FKTN, FLNC, GATA6, GATAD1, GLA, HCN4, ILK, JPH2, JUP, LAMA4, LAMP2, LDB3, LMNA, LRRC10, MIB1, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYPN, NEBL, NEXN, NKX2-5, PDLIM3, PKP2, PLN, PRDM16, PRKAG2, PTPN11, RAF1, RBM20, RYR2, SCN5A, SDHA, SGCD, SPEG, TAZ, TBX20, TCAP, TMEM43, TMPO, TNNC1, TNNI3, TNNT2, TPM1, TRDN, TTN, TTR, TXNRD2, VCL |
| Hypertrophic Cardiomyopathy (HCM) Panel | 98 | AARS2, ABCC9, ACAD9, ACADVL, ACTA1, ACTC1, ACTN2, AGK, AGL, ALPK3, ANKRD1, BAG3, BRAF, CACNA1C, CALR3, CAV3, CBL, COX15, CPT2, CRYAB, CSRP3, DES, DMD, DSC2, DSG2, DSP, DTNA, ELAC2, EMD, EPG5, FHL1, FKTN, FLNC, FXN, GAA, GATA4, GATAD1, GLA, HRAS, ILK, JPH2, JUP, KRAS, LAMA4, LAMP2, LDB3, LMNA, LZTR1, MAP2K1, MAP2K2, MTO1, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYLK2, MYO6, MYOM1, MYOZ2, MYPN, NDUFAF2, NEBL, NEXN, NF1, NRAS, PDLIM3, PKP2, PLN, PPP1CB, PRKAG2, PTPN11, RAF1, RBM20, RIT1, RYR2, SCN5A, SCO2, SDHA, SGCD, SHOC2, SLC22A5, SLC25A4, SOS1, SOS2, SPRED1, SURF1, TAZ, TCAP, TMEM43, TMPO, TNNC1, TNNI3, TNNT2, TPM1, TTN, TTR, VCL |
| Left Ventricular Noncompaction (LVNC) Panel | 36 | ABCC9, ACTC1, ACTN2, BAG3, CTNNA3, DES, DMD, DSC2, DSG2, DSP, DTNA, EMD, FBXO32, FLNC, HCN4, JPH2, JUP, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, PKP2, PLEKHM2, PLN, RAF1, RBM20, RYR2, SCN5A, TAZ, TCAP, TNNT2, TPM1, TTN, VCL |
| Restrictive Cardiomyopathy (RCM) Panel | 9 | ACTC1, BAG3, CRYAB, DES, MYBPC3, MYH7, TNNI3, TNNT2, TTR |

Congenital Heart Disease Disorders:

| Panel Name | # of Genes | Genes |
|---|------------|--|
| Congenital Heart Disease Panel | 187 | <i>ABL1, ACTA2, ACTB, ACTC1, ACTG1, ACVR1, ACVR2B, ACVRL1, ADAMTS10, AK7, ALMS1, ANKS6, ARHGAP31, ARMC4, ATRX, B3GAT3, BBS1, BBS10, BBS2, BCL9L, BCOR, BMPR2, BRAF, C21ORF59, CACNA1C, CBL, CCDC103, CCDC11, CCDC114, CCDC151, CCDC39, CCDC40, CCDC65, CCNO, CDK13, CENPF, CFAP300, CHD4, CHD7, CITED2, COL2A1, CREBBP, CRELD1, CYR61, DHCR7, DNAAF1, DNAAF2, DNAAF3, DNAAF4, DNAAF5, DNAH1, DNAH11, DNAH5, DNAH8, DNAH9, DNAI1, DNAI2, DNAJB13, DNAL1, DRC1, DSG2, DSP, DTNA, EFTUD2, EIF2AK4, ELN, ENG, EVC, EVC2, FBN1, FBN2, FGFR2, FLNA, FLNB, FOXC1, FOXC2, FOXF1, FOXH1, G6PC3, GAS2L2, GAS8, GATA4, GATA5, GATA6, GDF1, GJA1, GJA5, GLI3, GPC3, HAND1, HES7, HRAS, HYDIN, INVS, JAG1, KCNJ2, KIF7, KRAS, LEFTY2, LMNA, LRRC56, LRRC6, MAP2K1, MAP2K2, MCIDAS, MED13L, MEGF8, MEIS2, MID1, MKKS, MKS1, MMP21, MRE11, MYCN, MYH6, NAT10, NEK8, NF1, NIPBL, NKX2-5, NKX2-6, NME8, NODAL, NOTCH1, NOTCH2, NPHP3, NR2F2, NRAS, NSD1, NTRK3, OFD1, PIH1D3, PIK3R2, PITX2, PKD1L1, PKD2, PPP1CB, PQBP1, PRKD1, PRKG1, PRRX1, PTPN11, RAF1, RAI1, RBM10, RIT1, RSPH1, RSPH3, RSPH4A, RSPH9, SALL4, SCN1B, SCN5A, SEMA3E, SHOC2, SHROOM3, SKI, SMAD2, SMAD6, SOS1, SOS2, SOX2, SOX7, SPAG1, SPEG, TAB2, TBX1, TBX20, TBX3, TBX5, TCAP, TCTN2, TFAP2B, TGDS, TGFB2, TGFB2, TLL1, TTC25, TWIST1, UBR1, VCL, WDR35, ZFPM2, ZIC3, ZMPSTE24, ZMYND10, ZNF469</i> |
| Heterotaxy Panel | 114 | <i>ACTC1, ACVR2B, AK7, ALMS1, ANKS6, ARMC4, BBS1, BBS10, BBS2, BCL9L, BCOR, BRAF, C21ORF59, CBL, CCDC103, CCDC11, CCDC114, CCDC151, CCDC39, CCDC40, CCDC65, CCNO, CENPF, CFAP300, CHD7, CRELD1, DNAAF1, DNAAF2, DNAAF3, DNAAF4, DNAAF5, DNAH1, DNAH11, DNAH5, DNAH8, DNAH9, DNAI1, DNAI2, DNAJB13, DNAL1, DRC1, ELN, EVC, EVC2, FOXF1, FOXH1, GAS2L2, GAS8, GATA4, GATA6, GDF1, GJA1, GPC3, HES7, HRAS, HYDIN, INVS, JAG1, KIF7, KRAS, LEFTY2, LMNA, LRRC56, LRRC6, MAP2K1, MAP2K2, MCIDAS, MED13L, MEGF8, MEIS2, MKS1, MMP21, MRE11, NAT10, NEK8, NF1, NKX2-5, NKX2-6, NME8, NODAL, NOTCH1, NOTCH2, NPHP3, NR2F2, NRAS, NSD1, OFD1, PIH1D3, PKD1L1, PKD2, PQBP1, PRRX1, PTPN11, RAF1, RIT1, RSPH1, RSPH3, RSPH4A, RSPH9, SCN5A, SHOC2, SHROOM3, SMAD2, SOS1, SPAG1, TBX1, TBX5, TCTN2, TTC25, UBR1, WDR35, ZIC3, ZMPSTE24, ZMYND10</i> |
| RASopathy/Noonan Spectrum Disorders Panel | 31 | <i>A2ML1, ACTB, ACTG1, BRAF, CBL, CDC42, HRAS, KAT6B, KRAS, LZTR1, MAP2K1, MAP2K2, NF1, NF2, NRAS, NSUN2, PPP1CB, PTEN, PTPN11, RAF1, RASA1, RASA2, RIT1, RRAS, SHOC2, SOS1, SOS2, SPRED1, TBCK, TSC1, TSC2</i> |

Other Panels:

| Panel Name | # of Genes | Genes |
|---|------------|---|
| Pulmonary Arterial Hypertension (PAH) Panel | 20 | <i>ACVRL1, BMPR2, CAV1, EIF2AK4, ENG, FOXF1, GDF2, GGCX, KCNA5, KCNK3, KLK1, NFU1, NOTCH1, NOTCH3, RASA1, SMAD4, SMAD9, SOX17, TBX4, TOPBP1</i> |

Note: Single gene sequencing is available for all genes listed in the next-generation panels through custom gene sequencing.

Targeted deletion and duplication analysis is available for all genes except *A2ML1, ABCC9, ABL1, ACTA1, ACTA2, ACTG1, ACTN2, ACVR1, ACVR2B, AKAP9, ALPK3, ANKRD1, APOB (R3500Q/R3500W), ARHGAP31, BCL9L, CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CALM3, CALR3, CAV1, CAVIN4, CCDC114, CDC42, CDH2, CDK13, CHD4, CHRM2, COL5A2, CRYAB, CSRP3, CTNNA3, CYR61, DSG2, DTNA, FBXO32, FHL2, FOXE3, FOXH1, FXN, GATA5, GA-TAD1, GDF1, GDF2, GNB5, GPD1L, HAND1, HCN4, ILK, JPH2, KCND3, KCNE1, KCNE1L, KCNE2, KCNE3, KCNJ5, KCNJ8, KCNK3, KCNQ3, KLK1, LAMA4, LDB3, LDLR, LEFTY2, LOX, LRRC10, LZTR1, MAP2K1, MAT2A, MCIDAS, MFAP5, MIB1, MID1, MRE11, MYH6, MYL2, MYL3, MYL4, MYLK2, MYOM1, MYPN, NAT10, NEBL, NOS1AP, NOTCH3, NTRK3, PDLIM3, PLEKHM2, PPA2, PPP1CB, PRKD1, PRKG1, PRRX1, PSEN1, PSEN2, RANGRF, RASA2, RBM20, RIT1, RRAS, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SDHA, SHROOM3, SKI, SLMAP, SMAD2, SMAD4, SMAD6, SMAD9, SNTA1, SOS2, SPEG, SYNE2, TCAP, TECRL, TFAP2B, TGFB3, TGFB3, TLL1, TMEM43, TMPO, TNNC1, TNNI3K, TNNT2, TOPBP1, TRPM4, TTN, TTR, TXNRD2, VCL, WDR35* and *ZMYND10* at an additional charge.