Blueprint Genetics

Aorta Panel

Test code: CA1001

Is a 53 gene panel that includes assessment of non-coding variants.

Is ideal for patients who have isolated or syndromic aortic disease presenting with ascending aortic dilatation, aneurysm or dissection.

About Aortic Diseases

Aortic dilatation is defined by a diameter larger than 110% of reference value determined by age, sex, and body surface area. Progressing aortic dilatation eventually fulfills the definition of aortic aneurysm, which is a local aortic diameter higher than 150% of reference value. Usually aortic aneurysm formation is driven by reduced elastin content and fragmentation with concomitant smooth muscle cell loss, a process called cystic medial degeneration. Although this process is seen normally as a consequence of aging, it is accelerated in aortic aneurysm diseases. Most aortic aneurysms are associated with non-syndromic dilatation. However, at least 20% of aortic aneurysms are in the context of syndromic diseases such as Marfan syndrome (MfS), Loeys-Dietz syndrome (LDS), Shprintzen-Goldberg syndrome (SGS) and Ehlers-Danlos syndromes (EDS). Individuals with aortic aneurysms are at risk of sudden cardiac death due to rupture and dissection.

Availability

4 weeks

Gene Set Description

Genes in the Aorta Panel and their clinical significance

Gene	Associated phenotypes	Inheritance	ClinVar	HGMD
ABCC6*	Pseudoxanthoma elasticum	AR	352	377
ABL1	Congenital heart defects and skeletal malformations syndrome (CHDSKM)	AD	30	5
ACTA2	Aortic aneurysm, familial thoracic, Moyamoya disease, Multisystemic smooth muscle dysfunction syndrome	AD	20	76
ADAMTS10	Weill-Marchesani syndrome	AR	8	14
ADAMTS17	Weill-Marchesani-like syndrome	AR	6	7
ADAMTS2	Ehlers-Danlos syndrome	AR	8	11
ADAMTSL4	Ectopia lentis, isolated	AR	11	27
ALDH18A1	Spastic paraplegia, Cutis laxa	AD/AR	22	30
ATP7A	Menkes disease, Occipital horn syndrome, Spinal muscular atrophy, distal, X-linked 3	XL	116	354
B3GAT3*	Multiple joint dislocations, short stature, craniofacial dysmorphism, and congenital heart defects	AR	6	13
BGN	Spondyloepimetaphyseal dysplasia, X-linked, Meester-Loeys syndrome	XL	8	7

CBS	Homocystinuria due to cystathionine beta-synthase deficiency	AR	88	205
COL1A1	Ehlers-Danlos syndrome, Caffey disease, Osteogenesis imperfecta type 1, Osteogenesis imperfecta type 2, Osteogenesis imperfecta type 3, Osteogenesis imperfecta type 4	AD	352	962
COL1A2	Ehlers-Danlos syndrome, cardiac valvular form, Osteogenesis imperfecta type 1, Osteogenesis imperfecta type 2, Osteogenesis imperfecta type 3, Osteogenesis imperfecta type 4	AD/AR	186	509
COL2A1	Avascular necrosis of femoral head, Rhegmatogenous retinal detachment, Epiphyseal dysplasia, with myopia and deafness, Czech dysplasia, Achondrogenesis type 2, Platyspondylic dysplasia Torrance type, Hypochondrogenesis, Spondyloepiphyseal dysplasia congenital (SEDC), Spondyloepimetaphyseal dysplasia (SEMD) Strudwick type, Kniest dysplasia, Spondyloperipheral dysplasia, Mild SED with premature onset arthrosis, SED with metatarsal shortening, Stickler syndrome type 1	AD	180	561
COL3A1	Ehlers-Danlos syndrome	AD	520	631
COL4A5	Alport syndrome	XL	704	992
COL5A1	Ehlers-Danlos syndrome	AD	101	154
COL5A2	Ehlers-Danlos syndrome	AD	24	35
COLGALT1	Brain small vessel disease	AR		
EFEMP2	Cutis laxa	AR	14	16
ELN	Cutis laxa, Supravalvular aortic stenosis	AD	78	113
ENPP1	Arterial calcification, Hypophosphatemic rickets	AD/AR	22	72
FBLN5	Cutis laxa, Macular degeneration, age-related	AD/AR	13	22
FBN1	MASS syndrome, Marfan syndrome, Acromicric dysplasia, Geleophysic dysplasia 3	AD	1465	2679
FBN2	Congenital contractural arachnodactyly (Beals syndrome)	AD	50	97
FKBP14	Ehlers-Danlos syndrome with progressive kyphoscoliosis, myopathy, and hearing loss	AR	5	6
FLNA	Frontometaphyseal dysplasia, Osteodysplasty Melnick-Needles, Otopalatodigital syndrome type 1, Otopalatodigital syndrome type 2, Terminal osseous dysplasia with pigmentary defects, Periventricular nodular heterotopia 1, Melnick-Needles syndrome, Intestinal pseudoobstruction, neuronal, X-linked/Congenital short bowel syndrome, Cardiac valvular dysplasia, X-linked	XL	133	257
FOXE3	Aphakia, congenital primary, Anterior segment mesenchymal dysgenesis, Cataract 34, Aortic aneurysm, familial thoracic	AR/AD	9	29
GATA5	Familial atrial fibrillation, Tetralogy of Fallot, Single ventricular septal defect	AD	5	32
HCN4	Sick sinus syndrome, Brugada syndrome, Left ventricular non-compaction cardiomyopathy (LVNC)	AD	8	34
LOX	Aortic aneurysm, familial thoracic 10	AD	6	7

MAT2A*	Complement system	AD/AR		2
MED12	Ohdo syndrome, Mental retardation, with Marfanoid habitus, FG syndrome, Opitz-Kaveggia syndrome, Lujan-Fryns syndrome	XL	29	30
MFAP5	Aortic aneurysm, familial thoracic	AD	2	3
MYH11	Aortic aneurysm, familial thoracic	AD/AR	16	48
MYLK	Aortic aneurysm, familial thoracic 7	AD	16	28
NOTCH1	Aortic valve disease, Adams-Oliver syndrome	AD	56	96
PLOD1	Ehlers-Danlos syndrome	AR	30	41
PLOD3	Bone fragility with contractures, arterial rupture, and deafness	AR	3	3
PRKG1	Aortic aneurysm, familial thoracic 8	AD	2	3
SKI	Shprintzen-Goldberg syndrome	AD	20	23
SLC2A10	Arterial tortuosity syndrome	AR	23	34
SLC39A13	Spondylodysplastic Ehlers-Danlos syndrome	AR	2	9
SMAD2	Loeys-Dietz syndrome, Congenital heart defects, nonsyndromic	AD	4	13
SMAD3	Aneurysms-osteoarthritis syndrome, Loeys-Dietz syndrome	AD	48	82
SMAD4	Juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome, Polyposis, juvenile intestinal, Myhre dysplasia, Hereditary hemorrhagic telangiectasia	AD	179	143
SMAD6	Craniosynostosis 7	AD	5	38
TGFB2	Loeys-Dietz syndrome	AD	36	38
TGFB3	Loeys-Dietz syndrome (Reinhoff syndrome), Arrhythmogenic right ventricular dysplasia	AD	19	26
TGFBR1	Loeys-Dietz syndrome	AD	40	69
TGFBR2	Loeys-Dietz syndrome	AD	58	139
ZDHHC9	Mental retardation, syndromic, Raymond	XL	9	14

*Some regions of the gene are duplicated in the genome. Read more.

The gene has suboptimal coverage (means <90% of the gene's target nucleotides are covered at >20x with mapping quality score (MQ>20) reads), and/or the gene has exons listed under Test limitations section that are not included in the panel as they are not sufficiently covered with high quality sequence reads.

The sensitivity to detect variants may be limited in genes marked with an asterisk (*) or number sign (#). Due to possible limitations these genes may not be available as single gene tests.

Gene refers to the HGNC approved gene symbol; Inheritance refers to inheritance patterns such as autosomal dominant (AD), autosomal recessive (AR), mitochondrial (mi), X-linked (XL), X-linked dominant (XLD) and X-linked recessive (XLR); ClinVar refers to the number of variants in the gene classified as pathogenic or likely pathogenic in this database (ClinVar); HGMD refers to the number of variants with possible disease association in the gene listed in Human Gene Mutation Database (HGMD). The list of associated, gene specific phenotypes are generated from CGD or Mitomap databases.

Non-coding disease causing variants covered by the panel

Gene	Genomic location HG19	HGVS	RefSeq	RS-number
ABCC6	Chr16:16244424	c.4403+11C>G	NM_001171.5	rs72664215
ABCC6	Chr16:16256835	c.3506+15G>A	NM_001171.5	rs72664302
ABCC6	Chr16:16281097	c.1780-29T>A	NM_001171.5	rs72664206
ABCC6	Chr16:16284246	c.1432-22C>A	NM_001171.5	rs72664297
ATP7A	ChrX:77279056	c.2916+2480T>G	NM_000052.5	
ATP7A	ChrX:77287843	c.3294+763C>G	NM_000052.5	
CBS	Chr21:44496326	c.-86_-85+8delAGGTAGAAGA	NM_001178008.1	
COL1A1	Chr17:48266910	c.2668-11T>G	NM_000088.3	rs786205505
COL1A1	Chr17:48267594	c.2451+94G>T	NM_000088.3	
COL1A1	Chr17:48267611	c.2451+77C>T	NM_000088.3	rs72651665
COL1A1	Chr17:48268147	c.2343+31T>A	NM_000088.3	
COL1A1	Chr17:48272201	c.1354-12G>A	NM_000088.3	rs72648337
COL1A1	Chr17:48273368	c.1003-43_1003-32delTGCCATCTCTTC	NM_000088.3	rs72645359
COL1A1	Chr17:48273574	c.958-18_958-15delTTCC	NM_000088.3	rs72645351
COL1A1	Chr17:48273742	c.904-14G>A	NM_000088.3	
COL1A1	Chr17:48273743	c.904-15T>A	NM_000088.3	
COL1A2	Chr7:94025130	c.70+717A>G	NM_000089.3	rs72656354
COL1A2	Chr7:94030856	c.226-22_226-11delTTTTTTTTTTTT	NM_000089.3	
COL2A1	Chr12:48379984	c.1527+135G>A	NM_001844.4	
COL3A1	Chr2:189872183	c.3256-43T>G	NM_000090.3	rs587779667
COL4A5	ChrX:107813924	c.385-719G>A	NM_033380.2	rs104886396
COL4A5	ChrX:107816792	c.466-12G>A	NM_033380.2	rs104886414
COL4A5	ChrX:107820077	c.609+875G>T	NM_033380.2	
COL4A5	ChrX:107821295	c.646-12_646-11delTT	NM_033380.2	rs104886436
COL4A5	ChrX:107834930	c.1423+57dupC	NM_033380.2	rs104886328
COL4A5	ChrX:107838719	c.1424-20T>A	NM_033380.2	rs281874668
COL4A5	ChrX:107842994	c.1948+894C>G	NM_033380.2	
COL4A5	ChrX:107845097	c.2042-18A>G	NM_033380.2	rs104886341

COL4A5	ChrX:107849932	c.2245-40A>G	NM_033380.2	
COL4A5	ChrX:107849958	c.2245-14T>A	NM_033380.2	
COL4A5	ChrX:107852872	c.2395+2750A>G	NM_033380.2	
COL4A5	ChrX:107908726	c.3374-11C>A	NM_033380.2	rs104886387
COL4A5	ChrX:107933678	c.4529-2300T>G	NM_033380.2	
COL4A5	ChrX:107935633	c.4529-345A>G	NM_033380.2	
COL4A5	ChrX:107938272	c.4821+121T>C	NM_033380.2	rs104886423
COL4A5	ChrX:107938337	c.4822-152dupT	NM_033380.2	
COL4A5	ChrX:107938346	c.4822-151_4822-150insT	NM_033380.2	rs397515494
COL5A1	Chr9:137645685	c.1720-11T>A	NM_000093.4	rs863223444
COL5A1	Chr9:137680989	c.2647-12A>G	NM_000093.4	
COL5A1	Chr9:137686903	c.2701-25T>G	NM_000093.4	rs765079080
COL5A1	Chr9:137726806	c.5137-11T>A	NM_000093.4	rs183495554
COL5A2	Chr2:189927655	c.1924-11T>C	NM_000393.3	
ELN	Chr7:73480347	c.2272+20C>G	NM_001278939.1	
FBN1	Chr15:48707358	c.8051+375G>T	NM_000138.4	
FBN1	Chr15:48720682	c.6872-14A>G	NM_000138.4	
FBN1	Chr15:48721629	c.6872-961A>G	NM_000138.4	
FBN1	Chr15:48739106	c.5672-87A>G	NM_000138.4	
FBN1	Chr15:48739107	c.5672-88A>G	NM_000138.4	
FBN1	Chr15:48764885	c.4211-32_4211-13delGAAGAGTAACGTGTGTTTCT	NM_000138.4	
FBN1	Chr15:48786466	c.2678-15C>A	NM_000138.4	
FBN1	Chr15:48802380	c.1589-14A>G	NM_000138.4	
FBN1	Chr15:48818478	c.863-26C>T	NM_000138.4	
FBN2	Chr5:127670560	c.3974-24A>C	NM_001999.3	
FBN2	Chr5:127670562	c.3974-26T>G	NM_001999.3	
FBN2	Chr5:127671284	c.3725-15A>G	NM_001999.3	
FLNA	ChrX:153581587	c.6023-27_6023-16delTGACTGACAGCC	NM_001110556.1	
GATA5	Chr20:61051165	c.-201A>G	NM_080473.4	
GATA5	Chr20:61051462		NM_080473.4	rs1193866928
SMAD2	Chr18:45396947	c.237-12A>G	NM_005901.5	

TGFB3	Chr14:76425035	c.*495C>T	NM_003239.2	rs387906514
TGFB3	Chr14:76447266	c.-30G>A	NM_003239.2	rs770828281
TGFBR2	Chr3:30648317	c.-59C>T	NM_001024847.2	

Test Strengths

The strengths of this test include:

- CAP accredited laboratory
- CLIA-certified personnel performing clinical testing in a CLIA-certified laboratory
- Powerful sequencing technologies, advanced target enrichment methods and precision bioinformatics pipelines ensure superior analytical performance
- Careful construction of clinically effective and scientifically justified gene panels
- Some of the panels include the whole mitochondrial genome (please see the Panel Content section)
- Our Nucleus online portal providing transparent and easy access to quality and performance data at the patient level
- Our publicly available analytic validation demonstrating complete details of test performance
- ~2,000 non-coding disease causing variants in our clinical grade NGS assay for panels (please see 'Non-coding disease causing variants covered by this panel' in the Panel Content section)
- Our rigorous variant classification scheme
- Our systematic clinical interpretation workflow using proprietary software enabling accurate and traceable processing of NGS data
- Our comprehensive clinical statements

Test Limitations

The following exons are not included in the panel as they are not sufficiently covered with high quality sequence reads: *ADAMTS2* (NM_021599:11), *B3GAT3* (NM_001288722:5). Genes with suboptimal coverage in our assay are marked with number sign (#) and genes with partial, or whole gene, segmental duplications in the human genome are marked with an asterisk (*) if they overlap with the UCSC pseudogene regions. Gene is considered to have suboptimal coverage when >90% of the gene's target nucleotides are not covered at >20x with mapping quality score (MQ>20) reads. The technology may have limited sensitivity to detect variants in genes marked with these symbols (please see the Panel content table above).

This test does not d etect the following:

- Complex inversions
- Gene conversions
- Balanced translocations
- Some of the panels include the whole mitochondrial genome (please see the Panel Content section)
- Repeat expansion disorders unless specifically mentioned
- Non-coding variants deeper than ±20 base pairs from exon-intron boundary unless otherwise indicated (please see above Panel Content / non-coding variants covered by the panel).

This test may not reliably detect the following:

- Low level mosaicism in nuclear genes (variant with a minor allele fraction of 14.6% is detected with 90% probability)
- Stretches of mononucleotide repeats
- Low level heteroplasmy in mtDNA (>90% are detected at 5% level)
- Indels larger than 50bp
- Single exon deletions or duplications
- Variants within pseudogene regions/duplicated segments
- Some disease causing variants present in mtDNA are not detectable from blood, thus post-mitotic tissue such as skeletal muscle may be required for establishing molecular diagnosis.

The sensitivity of this test may be reduced if DNA is extracted by a laboratory other than Blueprint Genetics.

For additional information, please refer to the Test performance section and see our Analytic Validation.

Test Performance

The genes on the panel have been carefully selected based on scientific literature, mutation databases and our experience.

Our panels are sectioned from our high-quality, clinical grade NGS assay. Please see our sequencing and detection performance table for details regarding our ability to detect different types of alterations (Table).

Assays have been validated for various sample types including EDTA-blood, isolated DNA (excluding from formalin fixed paraffin embedded tissue), saliva and dry blood spots (filter cards). These sample types were selected in order to maximize the likelihood for high-quality DNA yield. The diagnostic yield varies depending on the assay used, referring healthcare professional, hospital and country. Plus analysis increases the likelihood of finding a genetic diagnosis for your patient, as large deletions and duplications cannot be detected using sequence analysis alone. Blueprint Genetics' Plus Analysis is a combination of both sequencing and deletion/duplication (copy number variant (CNV)) analysis.

The performance metrics listed below are from an initial validation performed at our main laboratory in Finland. The performance metrics of our laboratory in Seattle, WA, are equivalent.

Performance of Blueprint Genetics high-quality, clinical grade NGS sequencing assay for panels.

	Sensitivity % (TP/(TP+FN)	Specificity %
Single nucleotide variants	99.89% (99,153/99,266)	>99.9999%
Insertions, deletions and indels by sequence analysis		
1-10 bps	99.2% (7,745/7,806)	>99.9999%
11-50 bps	99.13% (2,524/2,546)	>99.9999%
Copy number variants (exon level dels/dups)		
1 exon level deletion (heterozygous)	100% (20/20)	NA
1 exon level deletion (homozygous)	100% (5/5)	NA
1 exon level deletion (het or homo)	100% (25/25)	NA
2-7 exon level deletion (het or homo)	100% (44/44)	NA
1-9 exon level duplication (het or homo)	75% (6/8)	NA
Simulated CNV detection		
5 exons level deletion/duplication	98.7%	100.00%
Microdeletion/-duplication sdrs (large CNVs, n=37))		
Size range (0.1-47 Mb)	100% (25/25)	

The performance presented above reached by Blueprint Genetics high-quality, clinical grade NGS sequencing assay with the following coverage metrics

Mean sequencing depth	143X
Nucleotides with >20x sequencing coverage (%)	99.86%

Performance of Blueprint Genetics Mitochondrial Sequencing Assay.

	Sensitivity %	Specificity %
ANALYTIC VALIDATION (NA samples; n=4)		
Single nucleotide variants		
Heteroplasmic (45-100%)	100.0% (50/50)	100.0%
Heteroplasmic (35-45%)	100.0% (87/87)	100.0%
Heteroplasmic (25-35%)	100.0% (73/73)	100.0%
Heteroplasmic (15-25%)	100.0% (77/77)	100.0%
Heteroplasmic (10-15%)	100.0% (74/74)	100.0%
Heteroplasmic (5-10%)	100.0% (3/3)	100.0%
Heteroplasmic (<5%)	50.0% (2/4)	100.0%
CLINICAL VALIDATION (n=76 samples)		
All types		
Single nucleotide variants n=2026 SNVs		
Heteroplasmic (45-100%)	100.0% (1940/1940)	100.0%
Heteroplasmic (35-45%)	100.0% (4/4)	100.0%
Heteroplasmic (25-35%)	100.0% (3/3)	100.0%
Heteroplasmic (15-25%)	100.0% (3/3)	100.0%
Heteroplasmic (10-15%)	100.0% (9/9)	100.0%
Heteroplasmic (5-10%)	92.3% (12/13)	99.98%
Heteroplasmic (<5%)	88.9% (48/54)	99.93%
Insertions and deletions by sequence analysis n=40 indels		
Heteroplasmic (45-100%) 1-10bp	100.0% (32/32)	100.0%
Heteroplasmic (5-45%) 1-10bp	100.0% (3/3)	100.0%
Heteroplasmic (<5%) 1-10bp	100.0% (5/5)	99,997%
SIMULATION DATA /(mitomap mutations)		
Insertions, and deletions 1-24 bps by sequence analysis; n=17		

Homoplasmic (100%) 1-24bp	100.0% (17/17)	99.98%
Heteroplasmic (50%)	100.0% (17/17)	99.99%
Heteroplasmic (25%)	100.0% (17/17)	100.0%
Heteroplasmic (20%)	100.0% (17/17)	100.0%
Heteroplasmic (15%)	100.0% (17/17)	100.0%
Heteroplasmic (10%)	94.1% (16/17)	100.0%
Heteroplasmic (5%)	94.1% (16/17)	100.0%
Copy number variants (separate artifical mutations; n=1500)		
Homoplasmic (100%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (50%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (30%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (20%) 500 bp, 1kb, 5 kb	99.7%	100.0%
Heteroplasmic (10%) 500 bp, 1kb, 5 kb	99.0%	100.0%
The performance presented above reached by following coverage metrics at assay level (n=66)		
	Mean of medians	Median of medians
Mean sequencing depth MQ0 (clinical)	18224X	17366X
Nucleotides with >1000x MQ0 sequencing coverage (%) (clinical)	100%	
rho zero cell line (=no mtDNA), mean sequencing depth	12X	

Bioinformatics

The target region for each gene includes coding exons and ±20 base pairs from the exon-intron boundary. In addition, the panel includes non-coding variants if listed above (Non-coding variants covered by the panel). Some regions of the gene(s) may be removed from the panel if specifically mentioned in the 'Test limitations" section above. The sequencing data generated in our laboratory is analyzed with our proprietary data analysis and annotation pipeline, integrating state-of-the art algorithms and industry-standard software solutions. Incorporation of rigorous quality control steps throughout the workflow of the pipeline ensures the consistency, validity and accuracy of results. Our pipeline is streamlined to maximize sensitivity without sacrificing specificity. We have incorporated a number of reference population databases and mutation databases such as, but not limited, to 1000 Genomes Project, gnomAD, ClinVar and HGMD into our clinical interpretation software to make the process effective and efficient. For missense variants, *in silico* variant prediction tools such as SIFT, PolyPhen, MutationTaster are used to assist with variant classification. Through our online ordering and statement reporting system, Nucleus, the customer has an access to details of the analysis, including patient specific sequencing metrics, a gene level coverage plot and a list of regions with inadequate coverage if present. This reflects our mission to build fully transparent diagnostics where customers have easy access to crucial details of the analysis process.

Clinical Interpretation

We provide customers with the most comprehensive clinical report available on the market. Clinical interpretation requires a fundamental understanding of clinical genetics and genetic principles. At Blueprint Genetics, our PhD molecular geneticists,

medical geneticists and clinical consultants prepare the clinical statement together by evaluating the identified variants in the context of the phenotypic information provided in the requisition form. Our goal is to provide clinically meaningful statements that are understandable for all medical professionals regardless of whether they have formal training in genetics.

Variant classification is the corner stone of clinical interpretation and resulting patient management decisions. Our classifications follow the ACMG guideline 2015.

The final step in the analysis of sequence variants is confirmation of variants classified as pathogenic or likely pathogenic using bi-directional Sanger sequencing. Variant(s) fulfilling the following criteria are not Sanger confirmed: the variant quality score is above the internal threshold for a true positive call, and visual check-up of the variant at IGV is in-line with the variant call. Reported variants of uncertain significance are confirmed with bi-directional Sanger sequencing only if the quality score is below our internally defined quality score for true positive call. Reported copy number variations with a size <10 exons are confirmed by orthogonal methods such as qPCR if the specific CNV has been seen less than three times at Blueprint Genetics.

Our clinical statement includes tables for sequencing and copy number variants that include basic variant information (genomic coordinates, HGVS nomenclature, zygosity, allele frequencies, in silico predictions, OMIM phenotypes and classification of the variant). In addition, the statement includes detailed descriptions of the variant, gene and phenotype(s) including the role of the specific gene in human disease, the mutation profile, information about the gene's variation in population cohorts and detailed information about related phenotypes. We also provide links to the references used, congress abstracts and mutation variant databases used to help our customers further evaluate the reported findings if desired. The conclusion summarizes all of the existing information and provides our rationale for the classification of the variant.

Identification of pathogenic or likely pathogenic variants in dominant disorders or their combinations in different alleles in recessive disorders are considered molecular confirmation of the clinical diagnosis. In these cases, family member testing can be used for risk stratification within the family. In the case of variants of uncertain significance (VUS), we do not recommend family member risk stratification based on the VUS result. Furthermore, in the case of VUS, we do not recommend the use of genetic information in patient management or genetic counseling.

Our interpretation team analyzes millions of variants from thousands of individuals with rare diseases. Thus, our database, and our understanding of variants and related phenotypes, is growing by leaps and bounds. Our laboratory is therefore well positioned to re-classify previously reported variants as new information becomes available. If a variant previously reported by Blueprint Genetics is re-classified, our laboratory will issue a follow-up statement to the original ordering health care provider at no additional cost.

CPT code(s) *

81410(1), 81411(1)

* The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

ICD Codes

Refer to the most current version of ICD-10-CM manual for a complete list of ICD-10 codes.

Sample Requirements

- Blood (min. 1ml) in an EDTA tube
- Extracted DNA, min. 2 µg in TE buffer or equivalent
- Saliva (Please see Sample Requirements for accepted saliva kits)

Label the sample tube with your patient's name, date of birth and the date of sample collection.

We do not accept DNA samples isolated from formalin-fixed paraffin-embedded (FFPE) tissue. In addition, if the patient is

affected with a hematological malignancy, DNA extracted from a non-hematological source (e.g. skin fibroblasts) is strongly recommended.

Please note that, in rare cases, mitochondrial genome (mtDNA) variants may not be detectable in blood or saliva in which case DNA extracted from post-mitotic tissue such as skeletal muscle may be a better option.

Read more about our sample requirements here.

For Patients

Other

- Aortic Dissection Association Scandinavia
- Ashley EA et al. Genetics and cardiovascular disease: a policy statement from the American Heart Association. Circulation. 2012 Jul 3;126(1):142-57.
- Boodhwani M et al. Canadian Cardiovascular Society position statement on the management of thoracic aortic disease. Can J Cardiol. 2014 Jun;30(6):577-89.
- Erbel R et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. Eur Heart J. 2014 Nov 1;35(41):2873-926.
- GeneReviews - Arterial Tortuosity Syndrome
- GeneReviews - Loeys-Dietz Syndrome
- GeneReviews - Marfan Syndrome
- GeneReviews - Shprintzen-Goldberg Syndrome
- GeneReviews - Thoracic Aortic Aneurysms and Aortic Dissections
- GeneReviews - Vascular Ehlers-Danlos Syndrome
- Genetic Aortic Disorders Association Canada
- Hiratzka LF et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: Circulation. 2010 Apr 6;121(13):e266-369
- Loeys-Dietz Syndrome Foundation
- Marfan Association UK
- Marfan Foundation
- NORD - Arterial Tortuosity Syndrome
- NORD - Ehlers Danlos Syndrome
- NORD - Marfan Syndrome
- Tinkle BT et al. Health supervision for children with Marfan syndrome. Pediatrics. 2013 Oct;132(4):e1059-72.