INVITAE

INVITAE PROACTIVE TESTING RESULTS

Patient name: **DOB:** **Sex assigned at birth:** **Gender:** **Patient ID (MRN):**	**Sample type:** **Sample collection date:** **Sample accession date:**	**Report date:** **Invitae #:** **Clinical team:**

Test performed

Sequence analysis and deletion/duplication testing of the 83 genes listed in the Genes Analyzed section.

- Invitae Cardio Screen

RESULT: POSITIVE

A clinically significant genetic change was found in the MYLK gene, which is associated with a heart-related condition.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
MYLK	c.3072dup (p.Pro1025Thrfs*9)	heterozygous	PATHOGENIC

About this test

This test evaluates 83 genes for variants (genetic changes) that indicate a significantly increased risk of developing certain heart-related conditions. These are disorders for which effective medical interventions and preventive measures are known and available. Genetic changes of uncertain significance are not included in this report; however, if additional evidence becomes available to indicate that a previously uncertain genetic change is clinically significant, Invitae will update this report and provide notification.

Next steps

- This is a medically important result that should be discussed with an appropriate healthcare provider. Genetic counseling is recommended to discuss the implications of this result and potential next steps.
- Please see PMID: 36322642, 32860028, 25173340, 26621648, and 28225426 for management guidelines regarding MYLK-related condition(s).
- Consider sharing this result with relatives as they may also be at risk. Details on our Family Variant Testing program can be found at **www.invitae.com/family**.
- Register your test at **www.invitae.com/patients** to download a digital copy of your results. You can also access educational resources about how your results can help inform your health.

Laboratory Director: Qing Zhang, MD, PhD, FACMG, NYCQ, CGMB
Invitae 1400 16th Street, San Francisco, CA 94103 · clientservices@invitae.com · 800.436.3037

Clinical summary

A Pathogenic variant, c.3072dup (p.Pro1025Thrfs*9), was identified in MYLK.

- Certain genetic changes in the MYLK gene significantly increase the risk for an autosomal dominant condition known as thoracic aortic aneurysms and dissections (TAAD). If a person carries two clinically significant genetic changes, one in each copy of the MYLK gene, this may increase the risk for an autosomal recessive condition known as megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS).
- This is a clinically significant result that increases the risk to develop autosomal dominant MYLK-related conditions.
- Individuals with TAAD have an increased risk for enlargement (aneurysm) and tearing or rupture (dissection) of the arteries, particularly the main blood vessel that carries blood from the heart out to the rest of the body, which is known as the aorta. Screening and management guidelines exist to help identify, treat, and prevent aortic aneurysms and dissections. It is important to recognize that this result is not a diagnosis of aortic aneurysm or dissection and that not all individuals with a genetic change in MYLK will develop aortic aneurysms and dissections.

  MMIHS is characterized by a distended bladder, small colon (microcolon), and decreased intestinal muscle movements (intestinal peristalsis) that is typically evident in infancy.
- Since genetic changes are often shared within families, there is a chance that biological relatives may be at risk for the autosomal dominant MYLK-related conditions. Additionally, being a carrier for the autosomal recessive MYLK-related conditions means there is a chance of having children with autosomal recessive MYLK-related conditions.

Variant details

MYLK, Exon 18, c.3072dup (p.Pro1025Thrfs*9), heterozygous, PATHOGENIC

- This sequence change creates a premature translational stop signal (p.Pro1025Thrfs*9) in the MYLK gene. This variant occurs within the aortic-specific isoform of MYLK. Loss-of-function variants in the aortic-specific isoform of MYLK are known to be pathogenic for thoracic aortic dissections (PMID: 21055718).
- This variant is not present in population databases (gnomAD no frequency).
- This variant has not been reported in the literature in individuals affected with MYLK-related conditions.
- For these reasons, this variant has been classified as Pathogenic.

Genes analyzed

This table represents a complete list of genes analyzed for this individual. Genes listed in this table may also have additional reported clinical associations outside of the conditions listed. Additional information about gene-condition associations can be found at http://www.omim.org. An asterisk (*) indicates that this gene has a limitation. Please see the Limitations section for details.

Cardiovascular-related genes

GENE	TRANSCRIPT	ASSOCIATED CONDITION(S)
ACTA2	NM_001613.2	Aortopathy
ACTC1*	NM_005159.4	Cardiomyopathy, Congenital Heart Disease
ACTN2*	NM_001103.3	Arrhythmia, Cardiomyopathy
ACVRL1	NM_000020.2	Hereditary Hemorrhagic Telangiectasia, Pulmonary Arterial Hypertension
APOB	NM_000384.2	Familial Hypercholesterolemia, Familial Hypobetalipoproteinemia
BAG3	NM_004281.3	Cardiomyopathy, Neuromuscular Condition
BMPR2	NM_001204.6	Pulmonary Arterial Hypertension
CACNA1C*	NM_000719.6;NM_001129840.1	Arrhythmia, Cardiomyopathy, Congenital Heart Disease
CACNB2	NM_201590.2	Arrhythmia
CALM1	NM_006888.4	Arrhythmia
CALM2	NM_001743.4	Arrhythmia
CALM3	NM_005184.2	Arrhythmia
CASQ2	NM_001232.3	Arrhythmia
CAV1	NM_001753.4	Pulmonary Arterial Hypertension
CAV3	NM_033337.2	Arrhythmia, Cardiomyopathy, Neuromuscular Condition
COL3A1*	NM_000090.3	Connective tissue disorder
COL5A1	NM_000093.4	Connective tissue disorder
COL5A2	NM_000393.3	Connective tissue disorder
CRYAB	NM_001885.2	Cardiomyopathy, Neuromuscular Condition
CSRP3	NM_003476.4	Cardiomyopathy
DES	NM_001927.3	Arrhythmia, Cardiomyopathy, Neuromuscular Condition
DMD	NM_004006.2	Cardiomyopathy, Neuromuscular Condition
DSC2	NM_024422.4	Arrhythmia, Cardiomyopathy
DSG2	NM_001943.3	Arrhythmia, Cardiomyopathy
DSP	NM_004415.2	Arrhythmia, Cardiomyopathy
EMD	NM_000117.2	Arrhythmia, Cardiomyopathy, Neuromuscular Condition
ENG*	NM_000118.3	Hereditary Hemorrhagic Telangiectasia, Pulmonary Arterial Hypertension
F2	NM_000506.3	Hemophilia, Hereditary Thrombophilia
F5	NM_000130.4	Hemophilia, Hereditary Thrombophilia
F9	NM_000133.3	Hemophilia, Hereditary Thrombophilia
FBN1	NM_000138.4	Connective tissue disorder
FHL1	NM_001449.4	Cardiomyopathy, Neuromuscular Condition
FLNC*	NM_001458.4	Cardiomyopathy, Neuromuscular Condition
GDF2	NM_016204.2	Hereditary Hemorrhagic Telangiectasia, Pulmonary Arterial Hypertension
GLA	NM_000169.2	Cardiomyopathy, Lysosomal Storage Disease
GPD1L	NM_015141.3	Arrhythmia
HCN4	NM_005477.2	Arrhythmia, Cardiomyopathy
JUP	NM_002230.2	Arrhythmia, Cardiomyopathy
KCNE1	NM_000219.5	Arrhythmia
KCNE2	NM_172201.1	Arrhythmia
KCNH2	NM_000238.3	Arrhythmia
KCNJ2	NM_000891.2	Arrhythmia
KCNQ1	NM_000218.2	Arrhythmia
LAMP2	NM_002294.2	Cardiomyopathy, Arrhythmia, Glycogen Storage Disease
LDLR	NM_000527.4	Familial Hypercholesterolemia
LDLRAP1	NM_015627.2	Familial Hypercholesterolemia
LMNA	NM_170707.3	Arrhythmia, Cardiomyopathy, Neuromuscular Condition
MYBPC3	NM_000256.3	Cardiomyopathy
MYH11	NM_001040113.1	Aortopathy
MYH7	NM_000257.3	Cardiomyopathy, Neuromuscular Condition
MYL2	NM_000432.3	Cardiomyopathy
MYL3	NM_000258.2	Cardiomyopathy
MYLK	NM_053025.3	Aortopathy
NKX2-5	NM_004387.3	Arrhythmia, Congenital Heart Disease
PCSK9*	NM_174936.3	Familial Hypercholesterolemia
PKP2	NM_004572.3	Arrhythmia, Cardiomyopathy
PLN	NM_002667.3	Arrhythmia, Cardiomyopathy
PRKAG2	NM_016203.3	Arrhythmia, Cardiomyopathy
PRKG1	NM_006258.3	Aortopathy
PROC	NM_000312.3	Hereditary Thrombophilia
PROS1	NM_000313.3	Hereditary Thrombophilia

GENE	TRANSCRIPT	ASSOCIATED CONDITION(S)
RBM20	NM_001134363.2	Arrhythmia, Cardiomyopathy
RYR2	NM_001035.2	Arrhythmia, Cardiomyopathy
SCN5A	NM_198056.2	Arrhythmia, Cardiomyopathy
SERPINC1	NM_000488.3	Hereditary Thrombophilia
SGCD	NM_000337.5	Cardiomyopathy, Neuromuscular Condition
SMAD3	NM_005902.3	Aortopathy
SMAD4	NM_005359.5	Hereditary Hemorrhagic Telangiectasia
SMAD9	NM_001127217.2	Pulmonary arterial hypertension (PAH)
TCAP	NM_003673.3	Cardiomyopathy, Neuromuscular Condition
TGFB2	NM_003238.3	Aortopathy
TGFB3	NM_003239.3	Aortopathy, Arrhythmia, Cardiomyopathy
TGFBR1	NM_004612.2	Aortopathy
TGFBR2	NM_003242.5	Aortopathy
TMEM43	NM_024334.2	Arrhythmia, Cardiomyopathy
TNNC1	NM_003280.2	Cardiomyopathy
TNNI3	NM_000363.4	Arrhythmia, Cardiomyopathy
TNNT2	NM_001001430.2	Arrhythmia, Cardiomyopathy
TPM1	NM_001018005.1	Cardiomyopathy
TRDN	NM_006073.3	Arrhythmia
TTN*	NM_001267550.2	Arrhythmia, Cardiomyopathy, Neuromuscular condition
TTR	NM_000371.3	Hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis)
VCL	NM_014000.2	Cardiomyopathy

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Methods

- Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol, and sequenced using Illumina technology. Unless otherwise indicated, all targeted regions are sequenced with ≥50x depth or are supplemented with additional analysis. Reads are aligned to a reference sequence (GRCh37), and sequence changes are identified and interpreted in the context of a single clinically relevant transcript, indicated in the Genes Analyzed table. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 20bp of flanking intronic sequence, and other specific genomic regions demonstrated to be causative of disease at the time of assay design. Promoters, untranslated regions, and other non-coding regions are not otherwise interrogated. For some genes only targeted loci are analyzed. Exonic deletions and duplications are called using an in-house algorithm that determines copy number at each target by comparing the read depth for each target in the proband sequence with both mean read-depth and read-depth distribution, obtained from a set of clinical samples. Markers across the X and Y chromosomes are analyzed for quality control purposes and may detect deviations from the expected sex chromosome complement. Such deviations may be included in the report in accordance with internal guidelines. Confirmation of the presence and location of reportable variants is performed as needed based on stringent criteria using one of several validated orthogonal approaches (PubMed ID 30610921). Sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778). Confirmatory sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778). RNA sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778).

  The following additional analyses are performed if relevant to the requisition. For PMS2 exons 12-15, the reference genome has been modified to force all sequence reads derived from PMS2 and the PMS2CL pseudogene to align to PMS2, and variant calling algorithms are modified to support an expectation of 4 alleles. If a rare SNP or indel variant is identified by this method, both PMS2 and the PMS2CL pseudogene are amplified by long-range PCR and the location of the variant is determined by Pacific Biosciences (PacBio) SMRT sequencing of the relevant exon in both long-range amplicons. If a CNV is identified, MLPA or MLPA-seq is run to confirm the variant. If confirmed, both PMS2 and PMS2CL are amplified by long-range PCR, and the identity of the fixed differences between PMS2 and PMS2CL are sequenced by PacBio from the long-range amplicon to disambiguate the location of the CNV. For C9orf72 repeat expansion testing, hexanucleotide repeat units are detected by repeat-primed PCR (RP-PCR) with fluorescently labeled primers followed by capillary electrophoresis. Interpretation Reference Ranges: Benign (Normal Range): <25 repeat units, Uncertain: 25-30 repeat units, Pathogenic (Full Mutation): >=31 repeat units (PMID: 21944779, 22406228, 23111906, 28689190, 31315673, 33168078, 33575483). A second round of RP-PCR utilizing a non-overlapping set of primers is used to confirm the initial call in the case of suspected allele sizes of 22 or more repeats. For RNA analysis of the genes indicated in the Genes Analyzed table, complementary DNA is synthesized by reverse transcription from RNA derived from a blood specimen and enriched for specific gene sequences using capture hybridization. After high-throughput sequencing using Illumina technology, the output reads are aligned to a reference sequence (genome build GRCh37; custom derivative of the RefSeq transcriptome) to identify the locations of exon junctions through the detection of split reads. The relative usage of exon junctions in a test specimen is assessed quantitatively and compared to the usage seen in control specimens. Abnormal exon junction usage is evaluated as evidence in the Sherloc variant interpretation framework. If an abnormal splicing pattern is predicted based on a DNA variant outside the typical reportable range, as described above, the presence of the variant is confirmed by targeted DNA sequencing.

- A PMID is a unique identifier referring to a published, scientific paper. Search by PMID at **http://www.ncbi.nlm.nih.gov/pubmed**.
- An rsID is a unique identifier referring to a single genomic position, and is used to associate population frequency information with sequence changes at that position. Reported population frequencies are derived from a number of public sites that aggregate data from large-scale population sequencing projects, including ExAC (**http://exac.broadinstitute.org**), gnomAD (**http://gnomad.broadinstitute.org**), and dbSNP (**http://ncbi.nlm.nih.gov/SNP**).
- A MedGen ID is a unique identifier referring to an article in MedGen, NCBI's centralized database of information about genetic disorders and phenotypes. Search by MedGen ID at **http://www.ncbi.nlm.nih.gov/medgen**. An OMIM number is a unique identifier referring to a comprehensive entry in Online Mendelian Inheritance in Man (OMIM). Search by OMIM number at **http://omim.org/**.
- Invitae uses information from individuals undergoing testing to inform variant interpretation. If "Invitae" is cited as a reference in the variant details this may refer to the individual in this requisition and/or historical internal observations.

Limitations

Based on validation study results, this assay achieves >99% analytical sensitivity and specificity for single nucleotide variants, insertions and deletions <15bp in length, and exon-level deletions and duplications. Invitae's methods also detect insertions and deletions larger than 15bp but smaller than a full

exon but sensitivity for these may be marginally reduced. Invitae's deletion/duplication analysis determines copy number at a single exon resolution at virtually all targeted exons. However, in rare situations, single-exon copy number events may not be analyzed due to inherent sequence properties or isolated reduction in data quality. Certain types of variants, such as structural rearrangements (e.g. inversions, gene conversion events, translocations, etc.) or variants embedded in sequence with complex architecture (e.g. short tandem repeats or segmental duplications), may not be detected. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity. Unless explicitly guaranteed, sequence changes in the promoter, non-coding exons, and other non-coding regions are not covered by this assay. Please consult the test definition on our website for details regarding regions or types of variants that are covered or excluded for this test. This report reflects the analysis of an extracted genomic DNA sample. While this test is intended to reflect the analysis of extracted genomic DNA from a referred patient, in very rare cases the analyzed DNA may not represent that individual's constitutional genome, such as in the case of a circulating hematolymphoid neoplasm, bone marrow transplant, blood transfusion, chimerism, culture artifact or maternal cell contamination. Invitae's RNA analysis is not designed for use as a stand-alone diagnostic method and cannot determine absolute RNA levels. Results from the RNA analysis may not be informative for interpreting copy number gains. CACNA1C: Deletion/duplication and sequencing analysis is not offered for exons 44-45. ACTC1: Sequencing analysis for exons 6 includes only cds +/- 10 bp. ACTN2: Deletion/duplication analysis is not offered for exon 9. ENG: Sequencing analysis for exons 7 includes only cds +/- 10 bp. PCSK9: Sequencing analysis for exons 9 includes only cds +/- 10 bp. TTN: Exons 45-46, 147, 149, 164, 172-201 (NM_001267550.2) are excluded from analysis. TTN variants are included in the primary report based on functional effect and/or location. A complete list of variants of uncertain significance, likely benign and benign variants in TTN is available upon request. Variants are named relative to the NM_001267550.2 (meta) transcript. Variants in the coding sequence and intronic boundaries of the clinically relevant NM_133378.4 (N2A) and fetal isoforms are reported (PMID: 25589632, 29598826, 29691892, 31660661), with the exception of the PEVK tandem repeat region (172-198) (PMID: 28040389). COL3A1: Deletion/duplication analysis is not offered for exons 23-24. FLNC: Deletion/duplication analysis is not offered for exon 47. Sensitivity and specificity for single nucleotide variants, insertions and deletions in exons 47-48 may be reduced due to the presence of segmental duplications overlapping the region.

Disclaimer

DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of many aspects used by the healthcare provider to help with a diagnosis and treatment plan, but it is not a diagnosis itself. This test was developed and its performance characteristics determined by Invitae. It has not been cleared or approved by the FDA. The laboratory is regulated under the Clinical Laboratory Improvement Act (CLIA) as qualified to perform high-complexity clinical tests (CLIA ID: 05D2040778). This test is used for clinical purposes. It should not be regarded as investigational or for research.

This report has been reviewed and approved by:

Matteo Vatta, Ph.D., FACMG
Clinical Molecular Geneticist

INVITAE

GENERAL GUIDELINES

POSITIVE RESULTS GUIDE: MYLK

This document is not part of Invitae's clinical report and does not represent medical advice. These are general guidelines that are not specific to your result and may not represent all relevant international recommendations. You can use this guide to talk to your healthcare provider about your test results, clinical history, and the most current guidelines. This guide may not be appropriate for results that are suspected to be blood-limited, possibly mosaic, or suggestive of a larger imbalance of genetic material. Invitae recognizes that individuals have diverse gender and sexual identities. In this guide, the terms female, male, women, and men refer to sex assigned at birth.

What is a positive MYLK result?

A positive test result means that a genetic change (variant) was found in the MYLK gene. A positive MYLK variant is considered "pathogenic" or "likely pathogenic" because it increases the chance for thoracic aortic aneurysm and dissection (TAAD), also referred to as familial thoracic aortic aneurysm and dissection (FTAAD).

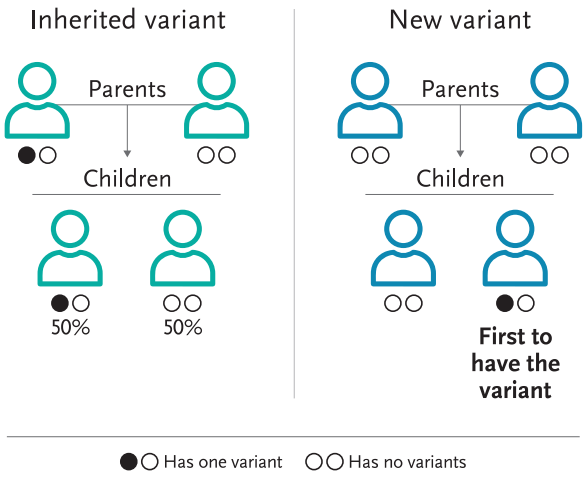
What does this mean?

Thoracic aortic aneurysm is characterized by dilation (ballooning) of the aorta, which is the artery that carries blood from the heart to the rest of the body. Thoracic aortic aneurysms can affect the aortic root, ascending, and/or descending aorta. In some cases an aneurysm can lead to dissection or rupture of the blood vessel causing rapid blood loss. As such, aortic dissection is considered a life-threatening medical emergency. Symptoms of aortic dissection may include sudden onset of severe chest, back, or abdominal pain, shortness of breath, fainting, heavy sweating, confusion, and/or loss of vision. However, symptoms, severity, and age of onset can vary. Some individuals may never develop TAAD. Individuals may have different conditions or symptoms depending on whether they inherit one or two variants in MYLK. Rarely, some people inherit two MYLK variants, which may cause megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS). See the table later in this guide for more information and possible next steps.

What does this mean for family members?

Relatives should be informed about these results. It is recommended that family members talk with their own healthcare provider about a plan for genetic testing and/or health screening. Genetic testing is a personal choice and some individuals may choose not to have genetic testing. Laws protecting employment and health insurance may apply to individuals undergoing genetic testing (for example, the Genetic Information Nondiscrimination Act in the United States).

Will family members have the same variant(s)?
The image shows where a MYLK variant may have come from. Any individual can inherit and pass on a MYLK variant, regardless of sex.



MYLK variants can be inherited from a parent or an individual may be the first person in the family to have a new MYLK variant. Siblings and other relatives may also have this MYLK variant. Individuals with a MYLK variant can pass it on to children.

For individuals who are planning a family, reproductive options may be available to help lower the chance of passing on a variant to children.

Create a plan with a healthcare provider

These options are a guide for an individual and their healthcare provider. They are meant to be used along with an individual's genetic test results and other health information as part of a discussion to make a personalized care plan. Each option may or may not be right for an individual. A positive test result on its own cannot predict how a condition may affect an individual. This guide may not be appropriate for results that are suspected to be blood-limited, possibly mosaic, or suggestive of a larger imbalance of genetic material.

Options to consider

TOPIC	OPTION	MORE INFORMATION
TAAD	• Baseline imaging of the aorta is recommended. (1)	• Aortic imaging with transthoracic echocardiogram (TTE) should include measurement of the aortic valve, sinuses of Valsalva, sinotubular junction, and ascending aorta. (1,2) ◦ If the aortic root and/or ascending aorta are not visualized adequately on TTE, magnetic resonance imaging (MRI) or computed tomographic (CT) imaging is recommended. (1) • Imaging of the full arterial tree (including cerebral arteries) may be considered. (3)
	• For individuals who are unaffected by TAAD, ongoing annual imaging of the aorta is recommended. (1)	• Ongoing imaging intervals may be adjusted based on findings, as well as an individual's age, gene variant, and family history. (1)
	• For individuals affected by TAAD, management may involve establishing a healthcare team, such as cardiologists, cardiovascular surgeons, and others.	• Treatment for TAAD is individualized. Various treatment options including medication, surgical interventions, and/or lifestyle modifications may be considered to manage TAAD. (1,2,3)
	• Individuals who are currently affected by aortic aneurysm may consider elective operation at smaller diameters to avoid acute dissection or rupture. (1)	• Factors that may be considered to help inform elective operation decisions include aortic growth rate, aortic valve involvement, comorbid conditions, family history, and an individual's age. (1,2,3)
	• Discuss exercise recommendations and restrictions.	• Exercise guidance is focused on reducing the risk of major aortic complications, such as dissection or rupture. • Recommendations for exercise eligibility and disqualification for athletes with aortic diseases are available. (4) ◦ Individuals may be recommended to avoid certain forms of strenuous exercise based on medical and/or family history. (4) ◦ Individuals may require additional surveillance if participating in certain forms of exercise. (4)
Pregnancy considerations	• Genetic counseling and discussion of pregnancy-related risks of aortic dissection is recommended. (1) • For individuals with a MYLK variant, aortic imaging is recommended prior to pregnancy. (1) • For individuals with aortic diameter greater than or equal to 4.5cm and a positive MYLK variant, prophylactic aortic surgery is recommended prior to becoming pregnant. (1)	• Aortic dissection related to pregnancy has occurred at smaller diameters in individuals with a positive MYLK variant. Prophylactic aortic surgery before pregnancy at an even smaller aortic diameter may be reasonable depending on factors like family history and aortic growth rate. (1)
	• For individuals with a MYLK variant, pregnancy management should involve a multidisciplinary team, including a maternal-fetal medicine (MFM) specialist and cardiologists, ideally at a center that could facilitate emergency aortic repair. (1) ◦ Beta blocker therapy is recommended during pregnancy. (1)	

TOPIC	OPTION	MORE INFORMATION
	◦ Aortic imaging is recommended every trimester and in the postpartum period. (1) ◦ Cesarean delivery may be considered for some pregnant individuals. (1)	
Family planning	• Discuss reproductive risks. (5) • Individuals with a MYLK variant have a 50% chance to pass on the variant to a child.	• Preconception and prenatal reproductive options are available and could be discussed in more detail with a reproductive specialist.
	• Individuals with a MYLK variant may also have an increased chance to have a child with MMIHS, if their reproductive partner also has a positive MYLK variant.	• MMIHS is a condition characterized by congenital enlargement of the bladder (megacystis) due to the inability to empty and a smaller than normal colon (microcolon). MMIHS typically affects lifespan depending on an individual's symptoms and complications.
	• An individual's reproductive partner can consider genetic testing to help determine the risk of a child inheriting two MYLK variants and having MMIHS. (5)	• If an individual's reproductive partner also has a positive MYLK variant, there would be a 25% chance to have a child with MMIHS.

These options include recommendations from PMID: 36322642 (1), PMID: 32860028 (2), PMID: 25173340 (3), PMID: 26621648 (4), and PMID: 28225426 (5). More information about genetics and disease continues to be available, so please always refer to the current guidelines and recommendations when considering surveillance and treatment options. Information on this document may not include all relevant international recommendations and acts as a supplement to the Invitae result report. This information is not meant to replace a discussion with an individual's healthcare provider and should not be considered or interpreted as medical advice. Additional resources provided within this document do not indicate or imply any endorsement by Invitae with respect to any third party or any website or the products or services offered by any third party.

Resources

Genetic counseling can help individuals understand their genetic test results and options for next steps. Reviewing test results with a genetic counselor or other healthcare provider is recommended. Local or telehealth genetic counselors can be identified using the Find a Genetic Counselor search tool at nsgc.org (US and Canada). Individuals who had genetic testing through Invitae can also log in to their patient portal (invitae.com) to view their results, contact a genetic counselor, or join Invitae's Patient Insights Network (PIN), an online platform where individuals can share information about their health and experiences to help advance research and drug development.

Connect with advocacy groups and other resources

- GenTAC Alliance: www.gentacalliance.org
- The Marfan Foundation: www.marfan.org

Notes for personalized assessment