Overview

Useful For

Diagnostic or predictive testing for specific conditions when a DNA sequence variant of interest has been previously identified in a family member, and follow-up testing for this specific variant in other family members is desired

Carrier screening for individuals at risk for having a DNA sequence variant that was previously identified in a family member

Segregation analysis for a single familial DNA sequence variant

Genetics Test Information

Documentation of the specific familial variant is required and must be provided with the specimen in order to perform this test.

This test should be used for targeted (site-specific) testing for a single sequence variant identified in any of the genes listed: *ABCC9, ABCG5, ABCG8, ACTA2, ACTC1, ACTN2, ACVRL1 (ALK1), ADA (ADA1), ADA2 (CERC1), ADAM17, ADAMTS13, ADAMTS2, AICDA, AK1, AK2, AKAP9, ALDOA, ANK1, ANK2, ANKRD1, ANKRD26,Â AP3B1, APOB, ATM, ATP7A, BLNK, BPGM,Â BRAF, BTK, C15ORF41, C3, CACNA1C, CACNA2D1, CACNB2, CARD11, CARD14, CARD15, CAV3, CBL, CBS, CD19, CD247 (CD3Z), CD27, CD3D, CD3E, CD3G, CD40, CD40LG, CD46 (MCP), CD59, CD79A, CD79B (B29), CD81, CD8A, CDAN1, CEBPA, CEBPE, CFB, CFD,CFH CFHR1, CFHR3, CFHR5, CFI, CHD7, CHST14, CIITA, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, CORO1A, CR2 (CD21), CRYAB, CSF2RA, CSF3R, CSRP3, CTC1, CTLA4, CTPS1, CTSC, CXCR4, CYBA, CYB5A, CYB5R3, CYBB, DCLRE1C (ARTEMIS), DDX41, DES, DGKE, DKC1, DOCK8, DSC2, DSG2, DSP, DTNA, EGLN1, ELANE (ELA2), ENG, EPAS1, EPB41, EPB42, EPOR, ETV6, F8, FBN1, FBN2, FERMT3, FLNA, FKBP14, FOXN1, FOXP3, FPR1, G6PC3, G6PD, GATA1, GATA2, GCLC, GDF2 (BMP9), GFI1, GLA, GPD1L, GPI, GSR, GSS, GYPC, HAX1, HK1, HMOX1, HRAS, ICOS, IGHM, IGLL1 (LAMDA5), IKBKB, IKBKG (NEMO), IKZF1 (IKAROS), IL10, IL10RA, IL10RB, IL1RN, IL21, IL21R, IL2RA (CD25), IL2RG, IL36RN, IL7R, ISG15, ITK, ITGB2, JAK2, JAK3, JUP, KCNE1, KCNE2, KCNE3, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNN4, KCNQ1, KIF23, KLF1, KRAS, LAMA4, LAMP2, LAMTOR2 (MAPBPIP),LCK, LDB3, LDLR, LDLRAP1, LIG4, LMNA, LPIN2, LRBA, LRRC8A, MAGT1, MALT1,MAP2K1, MAP2K2, MEFV, MFAP5, MPL, MPO, MS4A1 (CD20), MTHFD1, MVK, MYBPC3, MYH11, MYH6, MYH7, MYL2, MYL3, MYLK, MYLK2, MYOZ2, MYPN, NCF2, NCF4, NEXN, NFKB2, NFKBIA (IKBA), NHEJ1, NHP2, NLRC4, NLRP12, NLRP3 (C1AS1), NOD2 (CARD15), NOP10, NOTCH1, NRAS, NT5C3A, ORAI1, PCSK9, PFKM, PGK1, PIEZO1, PIK3CD, PIK3R1, PKP2, PLCG2, PLG, PLN,PLOD1, PMM2 (CDG1), PNP, PRKAG2, PRKCD, PRKDC, PRKG1, PROC, PROS1, PSMB8, PSTPIP1 (CD2BP1), PTPN11, PTPRC (CD45), RAC2, RAF1, RAG1, RAG2, RASA1, RASGRP2, RBCK1 (HOIL1), RBM20, RBM8A, RFX5, RFXANK, RFXAP,Â RHAG, RHOH, RMRP, RNF168, RTEL1, RUNX1, RYR2, SBDS, SCN1B, SCN3B, SCN4B, SCN5A, SEC23B, SEMA3E, SERPINC1, SGCD, SH2B3, SH2D1A, SH3BP2, SHOC2, SKI, SKIV2L, SLC2A1, SLC2A10, SLC37A4, SLC39A13, SLC4A1, SLC46A1, SMAD3, SMAD4, SNTA1, SOS1, SPINK5, SPTA1, STAT1, STAT3, STAT5B, SPTB, SRP72, STIM1, STK4, STXBP2, TAP1, TAP2, TAPBP, TAZ,TBX1,TCAP, TCF3 (E47), TERC, TERT, TGFB2, TGFB3, TGFBR1, TGFBR2, THBD, TINF2, TMEM43, TNFAIP3, TNFRSF13B (TACI), TNFRSF13C, TNFRSF1A, TNFRSF4 (OX40), TNFSF12 (TWEAK),TNNC1, TNNI3, TNNT2, TP53, TPI1, TPM1, TRAC, TTC37, TTC7A, TTN, TTR, UNG, USB1 (C16ORF57), VCL, VPS13B (COH1), VPS45, VWF, WAS, WIPF1, WRAP53, XIAP (BIRC4), ZAP70*.

Note: If testing is needed for a gene not on this list, see 1 of the following:

-PKLRG / Pyruvate Kinase Liver and Red Blood Cell (*PKLR*), Full Gene Sequencing and Large Deletion Detection, Varies testing for known familial large deletions in the *PKLR* gene

-*PKLR* single gene variant may be requested by ordering this test (KVAR1).

-UGTFG / UDP-Glucuronosyl Transferase 1A1 (UGT1A1), Full Gene Sequencing, Varies

-FMTT / Familial Mutation, Targeted Testing, Varies which includes targeted and site-specific and deletion or duplication testing for additional genes

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
MATCC	Maternal Cell Contamination, B	Yes	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
FIBR	Fibroblast Culture	Yes	No
CRYOB	Cryopreserve for Biochem Studies	No	No

Testing Algorithm

For prenatal specimens only: If amniotic fluid (nonconfluent cultured cells) is received, CULAF / Amniotic Fluid Culture for Genetic Testing will be added and charged separately. If chorionic villus specimen (nonconfluent cultured cells) is received, CULFB / Fibroblast Culture for Genetic Testing will be added and charged separately. For any prenatal specimen that is received, MATCC / Maternal Cell Contamination, Molecular Analysis, Varies studies will be added.

For skin biopsy or cultured fibroblast specimens, FIBR / Fibroblast Culture, Tissue and CRYOB / Cryopreservation for Biochemical Studies will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

Special Instructions

- Informed Consent for Genetic Testing
- Known Variant Analysis Required Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Genes Available for Known Variant Analysis Testing (KVAR1, KVAR2, KVAR3)
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name

Polymerase Chain Reaction (PCR) followed by DNA Sequencing Analysis or PCR

NY State Available

Yes

Specimen

Specimen Type

Varies

Advisory Information

This test can **only** be performed if 1 variant needs to be tested. If 2 variants need to be tested, order KVAR2 / Known Variant Analysis-2 Variants, Varies. If 3, 4, or 5 variants need to be tested, order KVAR3 / Known Variant Analysis-3+ Variants, Varies.

Additional Testing Requirements

All prenatal specimens and cord blood specimens must be accompanied by a maternal blood specimen; order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

If the familial variant was previously identified at an outside laboratory, sending DNA from a family member with a positive genetic test result to be used as a positive control is strongly recommended to ensure that the specific familial variant can be detected by our laboratory. Proband samples should be sent as a separate (KVAR1) order, under the proband's identifiers (ie, do not send the patient and proband samples under the same order). If a positive control is not provided, negative results will be reported with a stated limitation that the laboratory's ability to detect the familial variant has not been confirmed and a false-negative result cannot be ruled out.

Shipping Instructions

Prenatal specimens can be sent Monday through Thursday and **must be received by 5 p.m. CST on Friday** in order to be processed appropriately.

Necessary Information

The identification of a specific DNA sequence variant in an affected family member is required before this test can be performed for additional family members. If a familial variant has not been previously identified, call 800-533-1710 to discuss testing options.

Known Variant Analysis: Required Patient Information **form (T768) with documentation of the specific familial variant is required.** See Special Instructions. Testing will be held until information is received. If information is not received within 14 days of sample receipt, testing may be canceled.

Specimen Required

Submit only 1 of the following specimen types:

Preferred:

Specimen Type: Whole blood

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions: Send specimen in original tube.

Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 14 days

Specimen Type: Blood spot

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: Whatman FTA Classic paper, Ahlstrom 226 filter paper, or Blood Spot Collection Card

Specimen Volume: 2 to 5 blood spots on collection card

Collection Instructions:

1. An alternative blood collection option for a patient <1 year of age is finger stick.

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.

3. Do not expose specimen to heat or direct sunlight.

4. Do not stack wet specimens.

5. Keep specimen dry.

Additional Information:

1. For collection instructions, see Blood Spot Collection Instructions in Special Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Peripheral blood mononuclear cells (PBMCs)

Container/Tube: Cell pellet

Collection Instructions: Send as a suspension in freezing medium or cell pellet frozen on dry ice.

Specimen Stability Information: Frozen

Specimen Type: Cultured fibroblasts

Container/Tube: T-75 or T-25 flask

Specimen Volume: 1 Full T-75 or 2 full T-25 flasks

Additional Information: Indicate the tests to be performed on the fibroblast culture cells. A separate culture charge will be assessed under FIBR / Fibroblast Culture, Tissue. An additional 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Stability Information: Ambient (preferred)/Refrigerated <24 hours

Specimen Type: Skin biopsy

Supplies: Fibroblast Biopsy Transport Media (T115)

Container/Tube: Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin. Tubes of culture media can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin).

Specimen Volume: 4-mm punch

Additional Information: A separate culture charge will be assessed under FIBR / Fibroblast Culture, Tissue. An additional 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Stability Information: Refrigerated (preferred)/Ambient

Specimen Type: Cord blood

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions:

1. Send specimen in original tube

2. Label specimen as cord blood

Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 14 days

Specimen Type: DNA

Container/Tube: 2 mL screw top tube

Specimen Volume: 100 mcL (microliters)

Collection Instructions:

1. The preferred volume is 100 mcL at a concentration of 250 ng/mcL.

2. Include concentration and volume on tube.

Specimen Stability Information: Frozen (preferred)/Ambient/Refrigerated

Prenatal Specimens

Due to the complexity of prenatal testing, consultation with the laboratory is requiredfor all prenatal testing.

Specimen Type: Amniotic fluid

Container/Tube: Amniotic fluid container

Specimen Volume: 20 mL

Specimen Stability Information: Refrigerated (preferred)/Ambient

Additional Information: A separate culture charge will be assessed under CULAF / Amniotic Fluid Culture for Genetic Testing.

Specimen Type: Cultured amniocytes

Container/Tube: T-25 flask

Specimen Volume: 2 Full flasks

Collection Instructions: Submit confluent cultured cells from another laboratory.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Chorionic villi

Container/Tube: 15-mL tube containing 15-mL of transport media

Specimen Volume: 20 mg

Specimen Stability Information: Refrigerated

Additional Information: A separate culture charge will be assessed under CULFB / Fibroblast Culture for Genetic Testing.

Specimen Type: Cultured chorionic villi

Container/Tube: T-25 flasks

Specimen Volume: 2 Full flasks

Collection Instructions: Submit confluent cultured cells from another laboratory.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

2. If not ordering electronically, complete, print, and send a Cardiovascular Test Request (T724) with the specimen.

Specimen Minimum Volume

Whole Blood: 1 mL
Cord Blood: 1 mL
Amniotic Fluid: 10 mL
Chorionic Villi: 5 mg

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

This test is available for the analysis of the presence of 1 genetic variant (nucleotide substitution, small insertion/deletion or large genomic deletion/duplication [also known as copy number variation]) previously identified in a family member. This targeted testing can be used for diagnostic or predictive testing in cases in which a variant has been previously identified in an affected family member. This testing may also be used for segregation analysis to determine whether a particular variant is segregating with the phenotype in an affected family. This test is used for a specific subset of genes only. Refer to Genes Available for Known Variant Analysis Testing (KVAR1, KVAR2, or KVAR3) in Special Instructions. If testing is needed for a gene not on the gene list, see FMTT / Familial Mutation, Targeted Testing, Varies which includes targeted/site-specific testing for additional genes.

Refer to the following resources for information regarding the listed gene targets. GeneReviews-NCBI Bookshelf, available at www.ncbi.nlm.nih.gov/books/NBK1116/ or OMIM, available at www.omim.org/

Testing may be delayed if required documentation (ie, patient information sheet) is not received.

Reference Values

An interpretive report will be provided.

Interpretation

Evaluation and categorization of variants is performed using the most recent published American College of Medical Genetics and Genomics recommendations as a guideline.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Test results should be interpreted in the context of clinical findings, family history, and other laboratory testing. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Rare variants may be present and, although unlikely, could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Blood samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from samples obtained under these circumstances may

not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

Analysis is performed for the familial variant provided only. This assay does not rule out the presence of other variants within the tested gene or within other genes.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 2015;17(5):405-424

Performance

Method Description

DNA sequencing or qPCR is utilized to test for the presence of a specific variant, deletion, or duplication previously identified in a family member.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Varies

Analytic Time

10 days

Maximum Laboratory Time

16 days

Specimen Retention Time

Extracted DNA: 2 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81403

81265 (if appropriate)

81266 (if appropriate)

88233-(if appropriate)

88240-(if appropriate)

88235-(if appropriate)

88240-(if appropriate)

88233-(if appropriate)

88240-(if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
KVAR1	Known Variant Analysis-1 Variant	95786-0

Result ID	Test Result Name	Result LOINC Value
43923	Variant Tested	36908-2
43544	Result Summary	50397-9
43545	Result Details	82939-0
43546	Interpretation	69047-9
43547	Additional Information	48767-8
43548	Method	49549-9
43549	Disclaimer	62364-5
43550	Reviewed by	18771-6