Helix

Helix Family Variant Testing

FAVT2 I Diagnostic Test

Overview

Test Description

Helix Family Variant Testing is a targeted test to identify the presence or absence of one or more specific variants previously identified as being present in a family member. The entire gene will be evaluated for each gene included in the order, based on the analytical and reportable range described below, and therefore additional variants determined to be pathogenic or likely pathogenic within the genes ordered will also be included in the report. Variants of uncertain significance (VUS) will not be included except in cases where the variant specified in the order is determined to be a VUS.

Genetics Information

This test utilizes next-generation sequencing to detect single nucleotide variants, insertions and deletions up to 20 bp, and copy number variants. This test includes the targeted variant or variants ordered for a given gene included in the order, along with any other pathogenic or likely pathogenic variants detected in the gene(s).

Indications For Testing

A family member of a proband who has received a genetic test result with a test result with an identified variant within the analytical and reportable range of this test.

Clinical Descriptions

Useful for diagnostic testing when the patient is at increased risk to carry a variant associated with a specific condition that has been previously identified in a family member.

Conditions

Dependent upon the specific gene(s) ordered.

Test Details

Genes Tested

Based on order.

Methods & Limitations

Extracted DNA is enriched for targeted regions and then sequenced using the Helix Exome+ (R) assay on an Illumina DNA sequencing system. Data is then aligned to a modified version of GRCh38 and all genes are analyzed using the MANE transcript and MANE Plus Clinical transcript, when available. Small variant calling is completed using a customized version of Sentieon's DNAseq software, augmented by a proprietary small variant caller for difficult variants. Copy number variants (CNVs) are then called using a proprietary bioinformatics pipeline based on depth analysis with a comparison to similarly sequenced samples. Reportable variants in *PMS2* exons 11-15 are confirmed by PacBio long reads. Both the *MSH2* Boland inversion (exons 1-7) and the *BRCA2* Alu insertion are detected by identifying discordant read-pairs spanning the presumed breakpoint. Interpretation is based upon guidelines published by the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) or their modification by ClinGen Variant Curation Expert Panels when available. Interpretation is limited to the transcripts indicated on the report, +/- 10 bp into intronic regions, except as noted below. Helix variant classifications include pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign. Variants classified as pathogenic, likely pathogenic, or VUS if the requested variant is classified as such, are included in the report. All reported variants (except for VUSs with limited evidence of pathogenicity) are confirmed through secondary manual inspection of DNA sequence data or orthogonal testing. Benign and likely benign variants are not reported but are available upon request. Risk estimations and management guidelines included in this report are based on analysis of primary literature and recommendations of applicable professional societies, and should be regarded as approximations.

Based on validation studies, this assay delivers > 99% sensitivity and specificity for single nucleotide variants and insertions and deletions (indels) up to 20 bp. Larger indels and complex variants are also reported but sensitivity may be reduced. Based on validation studies, this assay delivers > 99% sensitivity to multi-exon CNVs and > 90% sensitivity to single-exon CNVs. This test may not detect variants in challenging regions (such as short tandem repeats, homopolymer runs, and segmental duplications), sub-exonic CNVs, chromosomal aneuploidy, or variants in the presence of mosaicism. Phasing will be attempted and reported, when possible. Structural rearrangements such as inversions, translocations, complex rearrangements, and gene conversions are not tested in this assay unless explicitly indicated. Additionally, deep intronic, promoter, and enhancer regions may not be covered. It is important to note that this assay cannot detect all variants known to increase disease risk, and that a negative result does not guarantee that the tested individual does not carry a rare, undetectable variant in the genes analyzed. Any potential incidental findings outside of these genes and conditions will not be identified, nor reported. The results of a genetic test may be influenced by various factors, including bone marrow transplantation, blood transfusions, or in rare cases, hematolymphoid neoplasms.

Results do not rule out the presence of other variants related to this condition. Results may include incidental findings within the gene that are determined to be pathogenic or likely pathogenic.

Gene Specific Notes:
Gene specific notes vary by ordered gene. For details, visit helix.com/clinical-genomics/targeted-analyses/family-variant-testing. For questions, contact clinicalsupport@helix.com.

Disclaimer

This test was developed and validated by Helix, Inc. This test has not been cleared or approved by the United States Food and Drug Administration (FDA). The Helix laboratory is accredited by the College of American Pathologists (CAP) and certified under the Clinical Laboratory Improvement Amendments (CLIA #: 05D2117342) to perform high-complexity clinical tests. This test is used for clinical purposes. It should not be regarded as investigational use only or for research use only.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations. Variants are classified based on known, predicted, or possible pathogenicity; however, this test only reports pathogenic and likely pathogenic variants along with interpretive comments detailing the evidence applied towards classification. Variants of uncertain significance are not reported unless specifically requested.

Reclassification

Helix reviews variant classifications annually when they arise in routine processes and upon request from providers. The timing of re-review depends on clinical risk. Providers can request a variant re-review by contacting Helix Customer Support. If a classification by Helix is updated, Helix identifies affected past patients and issues revised reports. Updated results are communicated to providers prior to results being uploaded to the EHR, and patients are notified through the EHR patient portal.

Variant Evaluation

Variant classification is performed using the guidelines set forth by the American College of Medical Genetics and Genomics and the Association for Molecular Pathology, with modifications as suggested by domain specific Expert Panels of the Clinical genome Resource (ClinGen) when available. Variant pathogenicity is categorized as benign, likely benign, variant of uncertain significance (VUS), likely pathogenic, or pathogenic.

Laboratory Details

Turnaround Time - Standard	Typically 6 to 21 days	**Turnaround Time - Requery (SOQO®)**	Typically ≤ 5 days
Available in NY State	Yes	**Procedure Code**	H00824-6 (Helix)

Laboratory Details

Test Classification	This test was developed, and its performance characteristics determined, by Helix, Inc. in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.
Regulatory Information	• CLIA Complexity: High • Test Classification: Non-Waived/ Laboratory Developed Test
CLIA Category	Chemistry / Routine Chemistry
Performing Laboratory Information	• CLIA Laboratory Number: 05D2117342 • Laboratory Hours of Operation: Monday-Saturday (7AM-10:30PM PST) • Address: 10170 Sorrento Valley Road, Suite 100, San Diego, CA 92121 • Helix Customer Service: (844) 211-2070 • Email: support@helix.com

The following applies to the Helix Family Variant Testing. Testing is performed to evaluate for the presence of variants in coding regions and extending to +/- 10 base pairs of adjacent intronic sequences on either side of the coding exons of the genes analyzed. In addition, the analysis will cover select non-coding variants, as listed below. Next-generation sequencing is performed to test for the presence of small variants and copy number variants in the genes analyzed. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

This list is current from April 2026 to the present. This document is intended to highlight additional evaluations for variants of high clinical interest as well as technical limitations. For questions regarding genes, reference transcripts, or specific regions covered, contact Helix Customer Service at (844) 211-2070.

Genomic Build: GRCh38

Gene	Transcript	Special Gene Notes
ABCA1	NM_005502.4	Analysis for exon 40 will not be performed
ABCC9	NM_020297.4	–
ABCD1	NM_000033.4	–
ABCG5	NM_022436.3	–
ABCG8	NM_022437.3	–
ACAD9	NM_014049.5	–
ACADVL	NM_000018.4	–
ACTA2	NM_001613.4	–
ACTC1	NM_005159.5	–
ACTN2	NM_001103.4	–
ACVRL1	NM_000020.3	–
ADAMTS10	NM_030957.4	–
AGL	NM_000642.3	Chr1: 99916398 (c.4260-12A>G)
AIP	NM_003977.4	–
ALK	NM_004304.5	–
ALMS1	NM_001378454.1	–
ALPK3	NM_020778.5	Sensitivity in *ALPK3* exon1 may be reduced
ANGPTL3	NM_014495.4	–
ANK2	NM_001148.6	–
APC	NM_000038.6	Includes CNV detection of Promoters 1A and 1B and sequencing of Promoter 1B
APOA1	NM_000039.3	–

Gene	Transcript	Special Gene Notes
APOA5	NM_001371904.1	–
APOB	NM_000384.3	–
APOC2	NM_000483.5	–
ATM	NM_000051.4	–
ATP7B	NM_000053.4	–
AXIN2	NM_004655.4	–
BAG3	NM_004281.4	–
BAP1	NM_004656.4	–
BARD1	NM_000465.4	–
BGN	NM_001711.6	–
BLM	NM_000057.4	–
BMP10	NM_014482.3	–
BMPR1A	NM_004329.3	Includes CNV detection in the promoter
BRAF	NM_004333.6; NM_001374258.1	Sensitivity to *BRAF* exon1 may be reduced
BRCA1	NM_007294.4	Sequencing analysis extends to CDS +/-20 bp
BRCA2	NM_000059.4	Includes c.156_157insAlu and Sequencing analysis extends to CDS +/-20 bp
BRIP1	NM_032043.3	–
BTD	NM_001370658.1	–
CACNA1C	NM_000719.7; NM_001167623.2	–
CACNA1D	NM_001128840.3; NM_000720.4	–
CACNA1S	NM_000069.3	Sensitivity to exon 91 may be reduced
CALM1	NM_006888.6	–
CALM2	NM_001743.6	–
CALM3	NM_005184.4	–
CASQ2	NM_001232.4	–
CAV3	NM_033337.3	–
CBS	NM_000071.3	–

Gene	Transcript	Special Gene Notes
CDC73	NM_024529.5	–
CDH1	NM_004360.5	–
CDH2	NM_001792.5	Sensitivity in *CDH2* exon1 may be reduced
CDK4	NM_000075.4	–
CDKN1B	NM_004064.5	–
CDKN2A	NM_000077.5; NM_058195.4	Includes analysis of both the p16 (p16INK4a) and p14 (p14ARF) transcripts
CEBPA	NM_004364.5	–
CETP	NM_000078.3	–
CHEK2	NM_007194.4	–
COL3A1	NM_000090.4	–
COL5A1	NM_000093.5	–
COL5A2	NM_000393.5	–
CPT2	NM_000098.3	–
CREB3L3	NM_032607.3	–
CRYAB	NM_001289808.2	–
CSRP3	NM_003476.5	–
CTNNA1	NM_001903.5	–
CYP27A1	NM_000784.4	–
DDX41	NM_016222.4	–
DES	NM_001927.4	–
DICER1	NM_177438.3	–
DMD	NM_004006.3	ChrX:33174335 (c.31+36947G>A) ChrX:31261663 (c.9225-647A>G) ChrX:31261301 (c.9225-285A>G)
DNAJC19	NM_145261.4	–
DOLK	NM_014908.4	–
DSC2	NM_024422.6	–
DSG2	NM_001943.5	–
DSP	NM_004415.4	–
DTNA	NM_001386795.1	–

Gene	Transcript	Special Gene Notes
EFEMP2	NM_016938.5	–
EGFR	NM_005228.5	Results limited to NM_005228*(EGFR):* c.2369C>T (p.Thr790Met)
ELAC2	NM_018127.7	–
EMD	NM_000117.3	–
ENG	NM_001114753.3	–
EPCAM	NM_002354.3	Results limited to CNV and limited to exons 8 and 9
ETV6	NM_001987.5	–
F2	NM_000506.5	Results limited to c.*97G>A
F5	NM_000130.5	Results limited to c.1601G>A (p.Arg534Gln)
FBN1	NM_000138.5	–
FBN2	NM_001999.4	–
FH	NM_000143.4	–
FHL1	NM_001159699.2; NM_001159702.3	–
FKRP	NM_024301.5	–
FKTN	NM_001079802.2	Chr9:105606576 (c.648-1243G>T)
FLCN	NM_144997.7	–
FLNA	NM_001110556.2	–
FLNC	NM_001458.5	–
FOXE3	NM_012186.3	Analysis begins at chr1:47416567 (GRCh38) and excludes the first quarter of exon 1
GAA	NM_000152.5	Chr17:80104542 (c.-32-13T>G) Chr17:80104552 (c.-32-3C>A) Chr17:80104554 (c.-32-1G>C) Chr17:80108467 (c.1076-22T>G)
GATA2	NM_032638.5; NM_001145661.2	–
GLA	NM_000169.3	ChrX: 101399747 (c.640-801G>A)
GPD1	NM_005276.4	–
GPIHBP1	NM_178172.6	–
GREM1	NM_013372.7	Results limited to CNV of promoter region
HCN4	NM_005477.3	–

Gene	Transcript	Special Gene Notes
HFE	NM_000410.4	Results limited to c.845G>A (p.Cys282Tyr) and c.187C>G (p.His63Asp)
HNF1A	NM_000545.8	–
HOXB13	NM_006361.6	Results limited to NM_006361.6(*HOXB13*): c.251G>A (p.Gly84Glu)
HRAS	NM_005343.4; NM_176795.5	–
JPH2	NM_020433.5	–
JUP	NM_002230.4	–
KCNE1	NM_000219.6	–
KCNE2	NM_172201.2	–
KCNH2	NM_000238.4	Chr7:150958048-150958065 (c.910_916+11del)
KCNJ2	NM_000891.3	–
KCNQ1	NM_000218.3	Sensitivity in *KCNQ1* exon 1 may be reduced Chr11:2461715 (c.386+16231G>A) Chr11:2585210-2585211 (c.1033-1_1117dup)
KIT	NM_000222.3	–
KRAS	NM_004985.5; NM_033360.4	–
LAMP2	NM_002294.3	–
LCAT	NM_000229.2	–
LDLR	NM_000527.5	–
LDLRAP1	NM_015627.3	–
LIPA	NM_000235.4	–
LIPG	NM_006033.4	–
LMF1	NM_022773.4	–
LMNA	NM_170707.4; NM_005572.4	–
LOX	NM_002317.7	–
LPL	NM_000237.3	–
LRP6	NM_002336.3	–
LZTR1	NM_006767.4	–
MAP2K1	NM_002755.4	–
MAP2K2	NM_030662.4	Sensitivity in *MAP2K2* exon 1 may be reduced

Gene	Transcript	Special Gene Notes
MAX	NM_002382.5	–
MBD4	NM_001276270.2	–
MED12	NM_005120.3	–
MEN1	NM_001370259.2	–
MET	NM_000245.4	–
MFAP5	NM_003480.4	–
MITF	NM_000248.4	Results limited to NM_000248.4(*MITF):* c.952G>A (p.Glu318Lys)
MLH1	NM_000249.4	Includes CNV detection in the promoter
MRAS	NM_001085049.3	–
MSH2	NM_000251.3	Includes detection of the exon 1-7 rearrangement known as the Boland Inversion and of c.942+3A>T
MSH3	NM_002439.5	Excludes known repeat region in *MSH3* exon 1
MSH6	NM_000179.3	–
MTO1	NM_012123.4	–
MTTP	NM_001386140.1	–
MUTYH	NM_001048174.2; NM_001128425.2	–
MYBPC3	NM_000256.3	Chr11:47332275-47332299 (c.3628-41_2628-17del25) Chr11:47347065 (c.906-36G>A) Chr11:47346372 (c.927-2A>G) Chr11:47343281 (c.1224-19G>A) Chr11:47343314 (c.1224-52G>A) Chr11:47343158 (c.1227-13G>A) Chr11:47340403 (c.1927+600C>T)
MYH11	NM_002474.3; NM_001040113.2	–
MYH7	NM_000257.4	–
MYL2	NM_000432.4	–
MYL3	NM_000258.3	–
MYL4	NM_002476.2	–
MYLK	NM_053025.4	–
MYLK3	NM_182493.3	–
MYPN	NM_032578.4	–

Gene	Transcript	Special Gene Notes
NEXN	NM_144573.4	–
NF1	NM_001042492.3	–
NF2	NM_000268.4	–
NKX2-5	NM_004387.4	–
NOTCH1	NM_017617.5	–
NRAS	NM_002524.5	–
NTHL1	NM_002528.7	–
OTC	NM_000531.6	–
PALB2	NM_024675.4	–
PCCA	NM_000282.4	–
PCCB	NM_000532.5	–
PCSK9	NM_174936.4	–
PDGFRA	NM_006206.6	–
PHOX2B	NM_003924.4	Excludes exon 3, which encompasses the alanine repeat region
PKP2	NM_001005242.3	–
PLN	NM_002667.5	–
PLOD1	NM_000302.4	–
PMS2	NM_000535.7	–
PNPLA2	NM_020376.4	–
POLD1	NM_002691.4	CNVs not reported, and sequencing isolated to the exonuclease domain
POLE	NM_006231.4	CNVs not reported, and sequencing isolated to the exonuclease domain
POT1	NM_015450.3	–
PPA2	NM_176869.3	–
PPARG	NM_138711.6	–
PPCS	NM_024664.4	–
PRDM16	NM_022114.4	Analysis for exon 1 will not be performed
PRKAG2	NM_016203.4	Sensitivity in *PRKAG2* exon 5 may be reduced
PRKAR1A	NM_002734.5	–
PRKG1	NM_006258.4	–
PTCH1	NM_000264.5; NM_001083603.3	Sensitivity in *PTCH1* exon 1 may be reduced

Gene	Transcript	Special Gene Notes
PTEN	NM_000314.8	Includes CNV detection in the promoter
PTPN11	NM_002834.5	–
RAD51C	NM_058216.3	–
RAD51D	NM_002878.4	–
RAF1	NM_002880.4	–
RB1	NM_000321.3	–
RBM20	NM_001134363.3	–
RET	NM_020975.6	–
RIT1	NM_006912.6	–
RPE65	NM_000329.3	–
RPS20	NM_001023.4	–
RUNX1	NM_001754.5	–
RYR1	NM_000540.3	–
RYR2	NM_001035.3	–
SAR1B	NM_016103.4	Sensitivity in *SAR1B* exon 4 may be reduced
SCN5A	NM_000335.5; NM_001099404.2	–
SDHA	NM_004168.4	CNVs not reported
SDHAF2	NM_017841.4	–
SDHB	NM_003000.3	–
SDHC	NM_003001.5	–
SDHD	NM_003002.4	–
SERPINA1	NM_000295.5, NM_001127701.1	Results limited to c.1096G>A (Z allele), c.863A>T (S allele)
SGCD	NM_000337.6	–
SHOC2	NM_007373.4	–
SKI	NM_003036.4	–
SLC22A5	NM_003060.4	Chr5:132369824 (c.-149G>A) Chr5:132378362 (c.394-16T>A) Chr5:132386973 (c.825-52G>A)
SLC2A10	NM_030777.4	–

Gene	Transcript	Special Gene Notes
SLC4A3	NM_005070.4	–
SMAD2	NM_005901.6	–
SMAD3	NM_005902.4	–
SMAD4	NM_005359.6	–
SMARCA4	NM_003072.5; NM_001387283.1	–
SMARCB1	NM_003073.5	–
SMARCE1	NM_003079.5	–
SOS1	NM_005633.4	–
SOS2	NM_006939.4	Sensitivity in *SOS2* exon 1 may be reduced
STAC3	NM_145064.3	Sensitivity to exon 7 may be reduced
STK11	NM_000455.5	Sensitivity in *STK11* exon 3 may be reduced
SUFU	NM_016169.4	–
SYNE2	NM_182914.3	–
TAFAZZIN	NM_000116.5	–
TBX20	NM_001077653.2	–
TCAP	NM_003673.4	–
TECRL	NM_001010874.5	–
TGFB2	NM_003238.6	–
TGFB3	NM_003239.5	–
TGFBR1	NM_004612.4	Analysis for exon 1 will not be performed
TGFBR2	NM_003242.6	–
TMEM127	NM_017849.4	–
TMEM43	NM_024334.3	–
TMEM70	NM_017866.6	–
TNNC1	NM_003280.3	–
TNNI3	NM_000363.5	–
TNNI3K	NM_015978.3	–
TNNT2	NM_001276345.2	–
TP53	NM_000546.6	Includes CNV detection in the promoter

Gene	Transcript	Special Gene Notes
TPM1	NM_001018005.2	–
TRDN	NM_006073.4	Chr6:123636725 (c.22+29A>G)
TRIM63	NM_032588.4	–
TSC1	NM_000368.5	Sensitivity in *TSC1* exon 21 may be reduced
TSC2	NM_000548.5	–
TTN	NM_001267550.2	Analysis for exons 172 to 197 will not be performed
TTR	NM_000371.4	–
VCL	NM_014000.3	–
VHL	NM_000551.4	Excludes coverage of cryptic exon E1' (chr3:10142758-10143009)
WT1	NM_024426.6	–