Overview

Test Description

This panel evaluates 78 genes associated with hereditary cancer conditions that predispose to a variety of solid and hematologic malignancies across many organ systems including: breast, gynecologic (ovarian and uterine), colorectal, pancreatic, prostate, kidney, skin, brain and nervous system, and endocrine glands (adrenal, pituitary, parathyroid, thyroid). Some of these predispositions manifest in childhood, but most are adult-onset.

Genetics Information

This test utilizes next-generation sequencing to detect single nucleotide variants, insertions and deletions up to 20 bp, and copy number variants in genes associated with a variety of hereditary conditions predisposing to a variety of cancers including: breast, gynecologic (ovarian and uterine), colorectal, pancreatic, prostate, kidney, skin, brain and nervous system, and endocrine glands (adrenal, pituitary, parathyroid, thyroid).

Indications For Testing

A relevant personal and/or family history suggestive of a hereditary form of cancer.

Clinical Descriptions

This panel includes genes that have an established association with multiple cancer types including breast, colorectal, uterine, ovarian, prostate, kidney, pancreatic, skin, endocrine glands (thyroid, parathyroid, pituitary, adrenal), and nervous system. These genes are primarily associated with adult-onset solid tumors, although some may develop in childhood.

The genes on this panel were specifically selected for their established association with hereditary cancer predisposition. Identification of a pathogenic variant may facilitate increased cancer screening and preventative surgery for early-detection and prevention. Identification of a pathogenic variant also helps identify at-risk family members, who can pursue genetic testing and preventive measures.

The genes on this panel are associated with conditions that have autosomal dominant and/or autosomal recessive inheritance.

Analyzing a wide range of genes in a single test can provide an efficient, cost-effective method of testing for several hereditary cancer conditions. This approach increases the chance of identifying the underlying diagnosis responsible for an individual's or family's cancer predisposition.

Test Details

Genes Tested

AIP, ALK, APC, ATM, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDC73, CDH1, CDK4, CDKN1B, CDKN2A, CEBPA, CHEK2, CTNNA1, DDX41, DICER1, EGFR, EPCAM, ETV6, FH, FLCN, GATA2, GREM1, HOXB13, KIT, LZTR1, MAX, MBD4, MEN1, MET, MITF, MLH1, MSH2, MSH3, MSH6, MUTYH, NF1, NF2, NTHL1, PALB2, PDGFRA, PHOX2B, PMS2, POLD1, POLE, POT1, PRKAR1A, PTCH1, PTEN, RAD51C, RAD51D, RB1, RET, RPS20, RUNX1, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, SMARCB1, SMARCE1, STK11, SUFU, TMEM127, TP53, TSC1, TSC2, VHL, WT1

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 breakpoints. 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 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.

Gene Specific Notes:
APC: analysis includes CNV of promoters 1A and 1B and sequencing of promoter 1B; *BMPR1A:* analysis includes CNV of promoter; *BRCA1:* sequencing analysis extends to CDS +/-20 bp; *BRCA2*: analysis includes detection of c.156_157insAlu and sequencing analysis extends to CDS +/-20 bp; *CDKN2A:* analysis includes sequencing of the p16 (p16INK4a) and p14 (p14ARF) transcripts; *EPCAM:* analysis is limited to CNV of exons 8-9*; GREM1*: analysis is limited to CNV of the promoter; *MLH1:* analysis includes CNV of the promoter; *MSH2:* analysis includes detection of the Boland inversion (inversion of exons 1-7) and detection of NM_000251.3(MSH2):c.942+3A>T; *MSH3:* analysis excludes sequencing of exon 1 repeat region (chr5:80654878-80654946); *PHOX2B:* analysis excludes exon 3, which encompasses the alanine repeat region; *PTCH1:* sensitivity of exon 1 analysis may be reduced; PTEN: analysis includes CNV of the promoter; *SDHA:* analysis excludes CNV; *STK11:* sensitivity of exon 3 analysis may be reduced; *TP53:* analysis includes CNV of the promoter; *TSC1:* sensitivity of exon 21 analysis may be reduced; *VHL:* analysis excludes coverage of the cryptic E1' exon (chr3:10142758-10143009)

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 and reported with interpretive comments detailing their potential or known significance.

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**	H01125-3 (Helix)
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		

- *(AIP)* Familial isolated pituitary adenoma
- *(ALK)* ALK-related neuroblastic tumor susceptibility
- *(APC)* Attenuated FAP
- *(APC)* Familial adenomatous polyposis
- *(APC)* Gastric adenocarcinoma and proximal polyposis of the stomach
- *(ATM)* ATM-related cancer susceptibility
- *(AXIN2)* Oligodontia-cancer predisposition syndrome
- *(BAP1)* BAP1 tumor predisposition syndrome
- *(BARD1)* BARD1-related cancer susceptibility
- *(BLM)* Bloom syndrome
- *(BMPR1A and SMAD4)* Juvenile polyposis syndrome
- *(BRCA1 and BRCA2)* Hereditary breast and ovarian cancer syndrome
- *(BRIP1)* BRIP1-related cancer susceptibility
- *(CDC73)* CDC73-related conditions
- *(CDH1 and CTNNA1)* Hereditary diffuse gastric cancer syndrome
- *(CDK4)* Cutaneous melanoma predisposition
- *(CDKN1B)* Multiple endocrine neoplasia type 4
- *(CDKN2A)* Melanoma-neural system tumors syndrome
- *(CDKN2A)* Melanoma-pancreatic cancer syndrome
- *(CEBPA)* Acute myeloid leukemia
- *(CHEK2)* CHEK2-related cancer susceptibility
- *(DDX41)* DDX41-related hematologic malignancy predisposition syndrome
- *(DICER1)* DICER1 pleuropulmonary blastoma tumor predisposition syndrome
- *(EGFR)* Hereditary predisposition to lung cancer
- *(FH)* Hereditary leiomyomatosis and renal cell cancer
- *(FLCN)* Birt-Hogg-Dube syndrome
- *(GREM1)* Hereditary mixed polyposis syndrome
- *(HOXB13)* Hereditary predisposition to prostate cancer
- *(KIT)* Gastrointestinal stromal tumors predisposition
- *(LZTR1)* LZTR1-related schwannomatosis
- *(MAX, SDHA, SDHAF2, SDHB, SDHC, SDHD and TMEM127)* Hereditary paraganglioma-pheochromocytoma syndrome
- *(MBD4)* MBD4-associated neoplasia syndrome
- *(MBD4)* Uveal melanoma predisposition
- *(MEN1)* Multiple endocrine neoplasia type 1
- *(MET)* Hereditary papillary renal cell carcinoma
- *(MITF)* Hereditary predisposition to melanoma
- *(MLH1, MSH2, MSH6, PMS2 and EPCAM)* Constitutional mismatch repair deficiency
- *(MLH1, MSH2, MSH6, PMS2 and EPCAM)* Lynch syndrome
- *(MSH3)* MSH3-associated polyposis
- *(MUTYH)* MUTYH-associated polyposis
- *(NF1)* Neurofibromatosis
- *(NF2)* NF2-related schwannomatosis
- *(NTHL1)* NTHL1-associated polyposis
- *(PALB2)* PALB2-related cancer susceptibility
- *(PDGFRA)* GIST-plus syndrome
- *(POLD1 and POLE)* Polymerase proofreading associated polyposis
- *(POT1)* POT1 tumor predisposition syndrome
- *(PRKAR1A)* Carney complex
- *(PTCH1 and SUFU)* Gorlin syndrome, also known as basal cell nevus syndrome
- *(PTEN)* PTEN hamartoma tumor syndrome
- *(RAD51C)* RAD51C-related cancer susceptibility
- *(RAD51D)* RAD51D-related cancer susceptibility
- *(RB1)* Hereditary retinoblastoma
- *(RET)* Multiple endocrine neoplasia type 2
- *(SMARCA4 and SMARCB1)* Rhabdoid tumor predisposition syndrome
- *(SMARCB1)* SMARCB1-related schwannomatosis
- *(SMARCE1)* Familial meningioma
- *(STK11)* Peutz-Jeghers syndrome
- *(TP53)* Li-Fraumeni syndrome
- *(TSC1 and TSC2)* Tuberous sclerosis complex
- *(VHL)* Von Hippel-Lindau syndrome

In addition, one or more of the genes on this panel are associated with other conditions for which a predisposition to, or carrier status of, may be identified:

- *ATM)* Ataxia-telangiectasia
- *(BRCA1, BRCA2, PALB2, BRIP1 and RAD51C)* Fanconi anemia
- *(CTNNA1)* Butterfly-shaped pigmentary macular dystrophy
- *(ETV6)* Thrombocytopenia 5
- *(FH)* Fumarate hydratase deficiency
- *(KIT)* Mastocytosis
- *(KIT)* Piebaldism
- *(LZTR1)* Noonan syndrome
- *(MET)* Nonsyndromic deafness
- *(PHOX2B)* Congenital central hypoventilation syndrome
- *(PRKAR1A)* Acrodysostosis
- *(RET)* Hirschsprung's disease
- *(SDHA and SDHB)* Mitochondrial complex II deficiency
- *(SMAD4)* Myhre syndrome
- *(SMARCA4, SMARCB1 and SMARCE1)* Coffin-Siris syndrome
- *(SUFU)* Joubert syndrome
- *(VHL)* Familial erythrocytosis type 2
- *(WT1)* Denys-Drash syndrome

The following applies to the Helix Hereditary Comprehensive Cancer Panel Plus. 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 January 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	Additional Evaluations	Technical Limitations
AIP	NM_003977.4	–	–
ALK	NM_004304.5	–	–
APC	NM_000038.6	Includes CNV detection of Promoters 1A and 1B and sequencing of Promoter 1B	–
ATM	NM_000051.4	–	–
AXIN2	NM_004655.4	–	–
BAP1	NM_004656.4	–	–
BARD1	NM_000465.4	–	–
BLM	NM_000057.4	–	–
BMPR1A	NM_004329.3	Includes CNV detection in the promoter	–
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	–	–
CDC73	NM_024529.5	–	–
CDH1	NM_004360.5	–	–
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	–	–

Gene	Transcript	Additional Evaluations	Technical Limitations
CHEK2	NM_007194.4	–	–
CTNNA1	NM_001903.5	–	–
DICER1	NM_177438.3	–	–
DDX41	NM_016222.4	–	–
EGFR	NM_005228.5	–	–
EPCAM	NM_002354.3	–	Results limited to CNV and limited to exons 8 and 9
ETV6	NM_001987.5	–	–
FH	NM_000143.4	–	–
FLCN	NM_144997.7	–	–
GATA2	NM_032638.5; NM_001145661.2	–	–
GREM1	NM_013372.7	–	Results limited to CNV of promoter region
HOXB13	NM_006361.6	–	–
KIT	NM_000222.3	–	–
LZTR1	NM_006767.4	–	–
MAX	NM_002382.5	–	–
MBD4	NM_001276270.2	–	–
MEN1	NM_001370259.2	–	–
MET	NM_000245.4	–	–
MITF	NM_000248.4	–	--
MLH1	NM_000249.4	Includes CNV detection in the promoter	–
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	–	–
MUTYH	NM_001048174.2; NM_001128425.2	–	–
NF1	NM_001042492.3	–	–
NF2	NM_000268.4	–	–
NTHL1	NM_002528.7	–	–
PALB2	NM_024675.4	–	–

Gene	Transcript	Additional Evaluations	Technical Limitations
PDGFRA	NM_006206.6	–	–
PHOX2B	NM_003924.4	–	Excludes exon 3, which encompasses the alanine repeat region
PMS2	NM_000535.7	–	–
POLD1	NM_002691.4	–	–
POLE	NM_006231.4	–	–
POT1	NM_015450.3	–	–
PRKAR1A	NM_002734.5	–	–
PTCH1	NM_000264.5; NM_001083603.3	–	Sensitivity in *PTCH1* exon 1 may be reduced
PTEN	NM_000314.8	Includes CNV detection in the promoter	–
RAD51C	NM_058216.3	–	–
RAD51D	NM_002878.4	–	–
RB1	NM_000321.3	–	–
RET	NM_020975.6	–	–
RPS20	NM_001023.4	–	–
RUNX1	NM_001754.5	–	–
SDHA	NM_004168.4	–	CNVs not reported
SDHAF2	NM_017841.4	–	–
SDHB	NM_003000.3	–	–
SDHC	NM_003001.5	–	–
SDHD	NM_003002.4	–	–
SMAD4	NM_005359.6	–	–
SMARCA4	NM_003072.5; NM_001387283.1	–	–
SMARCB1	NM_003073.5	–	–
SMARCE1	NM_003079.5	–	–
STK11	NM_000455.5	–	Sensitivity in *STK11* exon 3 may be reduced
SUFU	NM_016169.4	–	–
TMEM127	NM_017849.4	–	–
TP53	NM_000546.6	Includes CNV detection in the promoter	–

Gene	Transcript	Additional Evaluations	Technical Limitations
TSC1	NM_000368.5	–	Sensitivity in *TSC1* exon 21 may be reduced
TSC2	NM_000548.5	–	–
WT1	NM_024426.6	–	–
VHL	NM_000551.4	–	Excludes coverage of cryptic exon E1' (chr3:10142758-10143009)