MAYO CLINIC LABORATORIES

Targeted Genes and Methodology Details for Hereditary Expanded Cancer Gene Panel

The following applies to XCP / Hereditary Expanded Cancer Panel. Testing is performed to evaluate for the presence of variants in coding regions and extending to +/- 10 base pairs of adjacent intronic sequence on either side of the coding exons of the genes analyzed. In addition, the analysis will cover select noncoding variants. Next-generation sequencing, multiplex ligation-dependent probe amplification (MLPA), and/or a polymerase chain reaction-based quantitative method is performed to test for the presence of copy number variants (CNV) in the genes analyzed. Polymerase chain reaction and gel electrophoresis is performed to test for the presence of the 10 megabase (Mb) inversion of coding exons 1–7 of the *MSH2* gene. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

This list is current from December 2024 to the present. This document is intended to highlight additional evaluations for variants of high clinical interest as well as technical limitations. However, this document does not comprehensively reflect all genomic regions covered by this test. For questions regarding transcripts, genes or regions covered, contact the laboratory at 800-533-1710.

Genomic Build: GRCh37 (hg19) unless otherwise specified

Gene	Reference Transcript	Additional Evaluations	Technical Limitations
AIP	NM_003977.4	-	-
ALK	NM_004304.5	-	-
APC	NM_000038.6	Promoter 1A: c.-172 to c.-19 (variants between c.-565 to c.-173 may be detected) Promoter 1B: c.-30632 to c.-30046	-
ATM	NM_000051.3	-	-
AXIN2	NM_004655.4	-	-
BAP1	NM_004656.4	-	-
BARD1	NM_000465.4	-	-
BLM	NM_000057.4	-	-
BMPR1A	NM_004329.2	-	-
BRCA1	NM_007294.4	+/- 20 base pairs of adjacent intronic sequence on either side of the coding exons	-
BRCA2	NM_000059.3	+/- 20 base pairs of adjacent intronic sequence on either side of the coding exons	-
BRIP1	NM_032043.3	-	-
BUB1B	NM_001211.5	-	-
CDC73	NM_024529.4	-	-
CDH1	NM_004360.5	-	-
CDK4	NM_000075.4	-	-
CDKN1B	NM_004064.4	-	-
CDKN2A	NM_000077.4	-	-
CHEK2	NM_007194.4	-	-
CTNNA1	NM_001903.5	-	-
DICER1	NM_177438.2	-	-
DIS3L2	NM_152383.4	-	Sequence variants and CNV in exon 19 may not be detected or reported
EGFR	NM_005228.5	-	-
ELP1	NM_003640.5	-	-
EPCAM	NM_002354.3	-	Analysis for sequence variants will not be performed

Targeted Genes and Methodology Details for Hereditary Cancer Custom Gene Panel (continued)

Gene	Reference Transcript	Additional Evaluations	Technical Limitations
EXT1	NM_000127.2	-	-
EXT2	NM_207122.1	-	-
FANCA	NM_000135.4	-	-
FH	NM_000143.3	-	-
FLCN	NM_144997.7	CNV in noncoding exons 1–3	-
GPC3	NM_004484.4	-	-
GREM1	NM_013372.7	-	Analyzed for CNV duplication of upstream enhancer region only; analyses for sequence variants and additional CNV will not be performed
HOXB13	NM_006361.5	-	-
KIT	NM_000222.2	-	-
LZTR1	NM_006767.4	-	-
MAX	NM_002382.5	-	-
MC1R	NM_002386.3	-	-
MEN1	NM_130799.2	-	-
MET	NM_001127500.3	-	-
MITF	NM_000248.3	-	Analyzed only for the presence of c.952G>A p.E318K (rs149617956); analysis for other sequence variants and CNV will not be performed
MLH1	NM_000249.3	c.-27C>A (rs587779001) c.454-13A>G (rs267607749) c.1990-16_1990-2del (rs267607881)	-
MLH3	NM_001040108.1	-	CNV in exon 5 will not be detected or reported
MSH2	NM_000251.3	10 Mb inversion of exons 1-7	-
MSH3	NM_002439.5	-	-
MSH6	NM_000179.2	-	-
MUTYH	NM_001128425.1	c.504+19_504+31del (rs781222233)	-
NBN	NM_002485.4	-	CNV in exon 16 will not be detected or reported
NF1	NM_000267.3	-	Analysis for sequence variants beyond coding exons +/- 10 base pairs of adjacent intronic sequence will not be performed
NF2	NM_000268.3	-	-
NTHL1	NM_002528.7	-	-
PALB2	NM_024675.4	-	-
PDGFRA	NM_006206.6	-	CNV in exons 17 and 19 will not be detected or reported
PHOX2B	NM_003924.4	-	-
PMS2	NM_000535.7	-	-

Targeted Genes and Methodology Details for Hereditary Cancer Custom Gene Panel (continued)

Gene	Reference Transcript	Additional Evaluations	Technical Limitations
POLD1	NM_002691.4	-	-
POLE	NM_006231.4	-	-
POT1	NM_015450.3	-	CNV in exon 5 will not be detected or reported
PRKAR1A	NM_002734.4	-	-
PTCH1	NM_000264.5	-	-
PTEN	NM_000314.8	Promoter: c.-1302 to c.-589	-
RAD51B	NM_133509.4	-	-
RAD51C	NM_058216.3	-	-
RAD51D	NM_002878.3	-	-
RB1	NM_000321.2	c.-240 to c.-1	-
RECQL4	NM_004260.3	-	-
REST	NM_005612.5	-	-
RET	NM_020975.6	-	-
RNF43	NM_017763.5	-	-
SDHA	NM_004168.4	-	-
SDHAF2	NM_017841.2	-	-
SDHB	NM_003000.3	-	-
SDHC	NM_003001.3	-	-
SDHD	NM_003002.4	-	-
SMAD4	NM_005359.6	-	-
SMARCA4	NM_001128849.2	-	CNV in exon 27 will not be detected or reported
SMARCB1	NM_003073.5	-	-
SMARCE1	NM_003079.5	-	CNV in exon 2 will not be detected or reported
STK11	NM_000455.5	-	-
SUFU	NM_016169.3	-	-
TMEM127	NM_017849.3	-	-
TP53	NM_000546.5	-	-
TRIP13	NM_004237.4	-	-
TSC1	NM_000368.5	-	-
TSC2	NM_000548.5	-	-
VHL	NM_000551.3	-	-
WRN	NM_000553.6	-	-
WT1	NM_024426.6	-	-

Effective Date	Version	Synopsis of Test Change
June 2023	V2	Updated format (additional columns: Additional Evaluations and Technical Limitations)
December 2024	V3	*FLCN*: Added CNV detection of noncoding exons 1–3