CGAT - Hereditary Pan-Cancer v1.0 (07/2025)

Panel Description

This hereditary pan-cancer panel covers 79 genes implicated in hereditary predisposition to cancer. This panel is useful for evaluating hereditary cancer risk for patients with a personal or family history suggestive of a hereditary cancer syndrome, allowing for targeted cancer surveillance based on associated risks as well as allowing for predictive testing, and appropriate screening of at-risk family members. Therapeutic eligibility with certain targeted therapies may also be assessed, for example: eligibility for treatment with poly adenosine diphosphate-ribose polymerase (PARP) inhibitors based on certain gene alterations (eg, BRCA1, BRCA2) in selected tumor types.

Panel Gene Content

AIP	CEBPA	MBD4	PMS2^	SDHB
ALK	CHEK2	MEN1	POLD1	SDHC
APC	CTNNA1	MET	POLE	SDHD
ATM	DDX41	MITF^	POT1	SMAD4
AXIN2	DICER1	MLH1	PRKAR1A	SMARCA4
BAP1	EGFR	MSH2	PTCH1	SMARCB1
BARD1	EPCAM^	MSH3^	PTEN	SMARCE1
BMPR1A	ETV6	MSH6^	RAD51C	STK11
BRCA1	FH	MUTYH	RAD51D	SUFU
BRCA2	FLCN	NBN	RB1	TMEM127
BRIP1	GATA2	NF1	RECQL	TP53
CDC73	GREM1/SCG5^	NF2	RET	TSC1
CDH1	HOXB13	NTHL1	RPS20	TSC2
CDK4	KIT	PALB2	RUNX1	VHL
CDKN1B	LZTR1	PDGFRA	SDHA	WT1
CDKN2A	MAX	PHOX2B^	SDHAF2	

^Note that there are special analytical considerations in specific regions of these genes. See specific considerations below.

Analytical Range & Special Considerations:

- All RefSeq coding exons and up to +/- 30bp of adjacent intronic sequence of the genes listed are covered by at least 20 reads with an expected MQ >15.
- EPCAM: Only copy number alterations affecting the 3' end of EPCAM are relevant to hereditary cancer testing. Therefore, SNVs in EPCAM will not be assessed.
- GREM1: Only duplications affecting the upstream regulatory region of GREM1, including exons 3-6 of SCG5, are analyzed or reported.

- MITF: only SNVs are analyzed (only the c.952G>A p.E318K variant has thus far been associated with cancer risk)
- MSH6: Copy number events affecting MSH6 exon 1 are expected to be detected, but this has not been reliably verified due to lack of positive controls.
- MSH3 and PHOX2B: the polyalanine repeat regions are excluded from analysis.
- PMS2: Due to pseudogene interference, it is not possible to accurately detect variant calls in PMS2 exons 11-15. Therefore, small nucleotide variant calls in these exons, as well as copy number alterations confined to these exons will not be analyzed.