Henry Ford Health System
CENTER FOR PRECISION DIAGNOSTICS

Hereditary Multi-Cancer Risk Assessment Panel (39 genes)

APC	*ATM*	*BMPR1A*	*BRCA1*	*BRCA2*	*BRIP1*	*CDH1*	*CDK4*	*CDKN2A*	*CHEK2*
DICER1	*EPCAM*	*FH*	*KIT*	*MAX*	*MEN1*	*MLH1*	*MSH2*	*MSH6*	*MUTYH*
NBN	*NF1*	*PALB2*	*PMS2*	*PTEN*	*RAD51C*	*RAD51D*	*RET*	*SDHAF2*	*SDHB*
SDHC	*SDHD*	*SMAD4*	*STK11*	*TMEM127*	*TP53*	*TSC1*	*TSC2*	*VHL*	

Indication

This Hereditary Multi-Cancer Risk Assessment Panel is a comprehensive 39-gene analysis that identifies inherited risks for hereditary cancers across several major organ systems including cancers of the breast, ovary, uterus, prostate, and gastrointestinal system (rectum, small bowel, stomach, colon, and pancreas). Inherited genetic mutations in *BRCA1* and *BRCA2* account for about 20 to 25% of hereditary breast cancers and about 5 to 10% of all breast cancers. In addition, mutations in *BRCA1* and *BRCA2* genes cause around 15% of ovarian cancers. This panel also includes genes responsible for very rare hereditary cancer syndromes, such as Lynch syndrome (*MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM*), familial adenomatous polyposis (*APC, MUTYH*), Juvenile polyposis syndrome (*BMPR1A*, *SMAD4*), Li-Fraumeni syndrome (*TP53*), Cowden syndrome (*PTEN*), hereditary diffuse gastric cancer (*CDH1*), Peutz-Jeghers syndrome (*STK11*), neurofibromatosis type I (*NF1*), Tuberous sclerosis complex (*TSC1*, *TSC2*), Von Hippel-Lindau syndrome (*VHL*), multiple endocrine neoplasia (*MEN1*, *RET*), and hereditary paraganglioma-pheochromocytoma syndromes (*MAX*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, *TMEM127*). These syndromes have been associated with increased lifetime risk for multiple cancer types, including breast, ovarian, pancreatic, neuroendocrine, and colorectal cancer, and are also characterized by other clinical features specific for each syndrome. In addition, this panel includes several other genes associated with hereditary predisposition to breast, colorectal, neuroendocrine, renal and/or pancreatic cancer (*ATM*, *BRIP1*, *CHEK2*, *CDK4*, *CDKN2A*, *DICER1*, *FH*, *KIT*, *NBN*, *PALB2*, *RAD51C*, *RAD51D*).

Hereditary cancer syndrome is a genetic predisposition to develop certain types of cancers, often at an early age. Hereditary cancer risk assessment is performed to identify patients and families who may be at risk. Clues that a hereditary cancer syndrome may be present include the following:

- Cancer diagnosed at an unusually young age
- Several different types of cancer in the same person
- Multiple primary tumors
- Several close blood relatives that have the same type of cancer, especially when on the same side of the family
- Unusual presentation of a specific type of cancer
- The presence of birth defects that are known to be associated with inherited cancer syndromes
- Occurrence of certain types of adult cancer in which the probability of harboring a hereditary cancer syndrome is high (i.e. triple negative breast cancer; ovarian, tubal or peritoneal cancer; colorectal cancer or endometrial cancer with DNA mismatch repair deficiency)

Testing method

Next Generation Sequencing (NGS) provides coverage of all coding exons and noncoding DNA in exon-flanking regions (on average 50 bp) enriched using hybrid capture Illumina TruSight Cancer Sequencing Panel. Single base pair (point) mutations, small insertions/deletions (1-25 bp), complex insertions and deletions, or larger deletions and duplication (<100 bp) are detected using a combination of clinically validated computational data analysis methods for sequence variant calling, filtering, and annotation. Gross deletions and duplications at each targeted gene and exon are evaluated through comparative depth of coverage analysis of NGS targeted sequencing data using clinically validated analysis algorithm. All reportable copy number variants are confirmed by independent methodology using gene-specific Multiplex Ligation-dependent Probe Amplification (MLPA) or genome-wide SNP microarray assay. If a pathogenic mutation or deletion is detected in exons 13, 14 or 15 of *PMS2*, confirmatory send out testing will be performed to determine if this variant is located in the *PMS2* gene or pseudogene, *PMS2CL*.

Turnaround time

5-10 business days

Sample requirements

3 ml peripheral blood in EDTA (lavender) top tube
Specimen stability: Ambient - 72 hours; Refrigerated - 1 week

CPT codes

81432, 81433, 81435, 81436, 81437, 81438, G0452

References

Hamplel H, Bennett RL, Buchanan A, Pearlman R, Wiesner GL. A practice guideline from the American College of Medical Genetics and genomics and the National Society of Genetic Counselors: referral indications for cancer predisposition assessment. Genet Med 2015;17:70-87.

Lu KH, Wood ME. Daniels M, Burke C, et al. American Society of Clinical Oncology Expert Statement: collection and use of a cancer family history for oncology providers. J Clin Oncol 2014;32:833-840.

Benafif S, Eeles R. Diagnosis and Management of Hereditary Carcinoids. Recent Results Cancer Res 2016;205:149-168.

Ship Specimens to:

Henry Ford Center for Precision Diagnostics
Henry Ford Hospital
Clinic Building, K6, Core Lab E-655
2799 W. Grand Blvd.
Detroit, MI 48202