

Hereditary Endometrial Cancer Risk Panel (18 genes)

<i>ATM</i>	<i>BRCA1</i>	<i>BRCA2</i>	<i>BRIP1</i>	<i>CDH1</i>	<i>CHEK2</i>	<i>EPCAM</i>	<i>MLH1</i>	<i>MSH2</i>	<i>MSH6</i>
<i>MUTYH</i>	<i>NBN</i>	<i>PALB2</i>	<i>PMS2</i>	<i>PTEN</i>	<i>RAD51C</i>	<i>STK11</i>	<i>TP53</i>		

Indication

This Hereditary Endometrial Cancer Risk Panel is a comprehensive 18-gene analysis that identifies inherited risks for hereditary endometrial (uterine) cancer. Most cases of endometrial cancer are sporadic. However, a small proportion of individuals have hereditary endometrial cancer (approximately 2-5% of cases). The two most common inherited syndromes known to increase a woman's lifetime risk of endometrial cancer are Lynch syndrome caused by inherited mutations in *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM* and Cowden syndrome caused by inherited mutations in *PTEN*. This panel also includes genes responsible for other rare hereditary cancer syndromes, such as Li-Fraumeni syndrome (*TP53*), hereditary breast and ovarian cancer syndrome (*BRCA1*, *BRCA2*), hereditary diffuse gastric cancer (*CDH1*), and Peutz-Jeghers syndrome (*STK11*). These syndromes have been associated with increased lifetime risk for multiple cancer types, including endometrial 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 with breast or ovarian cancer (*ATM*, *BRIP1*, *CHEK2*, *MUTYH*, *NBN*, *PALB2*, *RAD51C*) were also included in this analysis.

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, G0452

References

Hampel 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.

Hereditary breast and ovarian cancer syndrome. ACOG Practice Bulletin No. 103. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2009;113:957-966

Kurian AW. BRCA1 and BRCA2 mutations across race and ethnicity: distribution and clinical implications. *Curr Opin Obstet Gynecol* 2010;22:72-78

Folkins AK, Longacre TA. Hereditary gynaecological malignancies: advances in screening and treatment. *Histopathology* 2013;62:2-30

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