Hereditary Cancer Syndrome Panel: Sequencing and CNV Analysis

Test Code: MM200
Turnaround time: 6 weeks
CPT Codes: 81292 x1, 81295 x1, 81201 x1, 81298 x1, 81321 x1, 81403 x1, 81404 x2, 81405 x3, 81406 x6, 81408 x1, 81163 x1

Condition Description

Approximately 5-10% of all cancers are inherited, meaning that pathogenic variants in a single cancer susceptibility gene can predispose an individual to develop cancer and these pathogenic variants can be passed down in families. The risk for developing cancer can vary dramatically from syndrome to syndrome, from about a 55% risk of developing breast cancer in Peutz-Jeghers syndrome to as high as a 100% risk for colon cancer for familial adenomatous polyposis syndrome. Accurate and timely diagnoses are necessary to provide proper medical surveillance and treatment to affected and at-risk individuals.

Many of the inherited cancers syndromes and cancer susceptibility genes are phenotypically heterogeneous, making molecular testing necessary to confirm a clinical diagnosis. The traditional tiered, single gene approach to genetic testing for inherited cancer syndromes can be costly and time consuming. The Hereditary Cancer Syndrome Panel is designed to detect germline pathogenic variants in individuals with a suspected inherited cancer syndrome. This panel includes sequencing analysis for syndromes such as, Lynch syndrome, Cowden syndrome, Multiple Endocrine Neoplasia syndrome, Birt-Hogg Dube syndrome, and Li-Fraumeni syndrome. Additional syndromes are also tested for by this panel.

Reference:

Genes

AIP, ALK, APC, ATM, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, BUB1B, CDC73, CDH1, CDK4, CDKN1B, CDKN1C, CDKN2A, CHEK2, FH, FLCN, GPC3, MAX, MEN1, MET, MLH1, MRE11, MSH2, MSH6, MUTYH, NBN, NF2, PALB2, PHOX2B, PMS2, POLD1, PRKAR1A, PTEN, RAD50, RAD51C, RAD51D, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, SMARCAB1, STK11, SUFU, TMEF127, TPS3, TSC1, TSC2, VHL, WT1, XPC, XRCC2

Indications

The test is indicated for:
- Individuals with a clinical or suspected diagnosis of an inherited cancer syndrome based on personal or family history of cancer.

Methodology

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Copy Number Analysis: Comparative analysis of the NGS read depth (coverage) of the targeted regions of genes on this panel was performed to detect copy number variants (CNV). The accuracy of the detected variants is highly dependent on the size of the event, the sequence context and the coverage obtained for the targeted region. Due to these variables and limitations a minimum validated CNV size cannot be determined; however, single exon deletions and duplications are expected to be below the detection limit of this analysis.

Detection

Next Generation Sequencing: Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical sensitivity for sequence variant detection is ~99%.

Copy Number Analysis: The sensitivity and specificity of this method for CNV detection is highly dependent on the size of the event, sequence context and depth of coverage for the region involved. The assay is highly sensitive for CNVs of 500 base pairs or larger and those containing at least 3 exons. Smaller (~500 base pairs) CNVs and those that involving only 1 or 2 exons may or may not be detected depending on the sequence context, size of exon(s) involved and depth of coverage.

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:
- Microtainer
Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

**Special Instructions**
This test is for germline mutation analysis. DNA isolated from FFPE tumor samples is not suitable for this test.

**Related Tests**
- Endocrine Cancer: Sequencing Panel and Deletion/Duplication Panels.
- Pheochromocytoma-Paraganglioma: Sequencing and Deletion/Duplication Panels.
- Brain, CNS, and PNS Cancer: Sequencing and Deletion/Duplication Panels.
- High Risk Colorectal Cancer: Sequencing and Deletion/Duplication Panels.
- Renal Cancer: Sequencing and Deletion/Duplication Panels.
- Wilms Tumor: Sequencing and Deletion/Duplication Panels.
- Breast and Ovarian Cancer: Sequencing and Deletion/Duplication Panel.
- Melanoma: Sequencing and Deletion/Duplication Panels.
- Pancreatic Cancer: Sequencing and Deletion/Duplication Panels.
- Gastrointestinal and Colorectal Cancer: Sequencing and Deletion/Duplication Panels.