**High Risk Breast Cancer: Sequencing and Deletion/Duplication Panel**

**Test Code:** MM201  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81323 x1, 81321 x1, 81404 x1, 81405 x1, 81406 x1, 81162 x1

### Condition Description

Most cases of breast cancer are sporadic with no family history of the cancer; but, 5-10% of cases are understood to be due to a hereditary predisposition. Nearly 1 in 8 women (12%) will develop breast cancer in their lifetime (SEER). The clinical features suggestive of a hereditary cancer predisposition involve: diagnosis at a young age (< 50), multiple primary cancers in a single individual, diagnosis of a cancer type that is not common in the general population (such as male breast cancer, ovarian cancer, or pancreatic cancer), and several relatives affected with related cancers over multiple generations.

The EGL Genetics High Risk Breast Cancer Panel includes genes involved in hereditary cancer predisposition syndromes, including hereditary breast and ovarian cancer syndrome (BRCA1 and BRCA2), hereditary diffuse gastric cancer syndrome (CDH1), Li-Fraumeni syndrome (TP53 and PTEN), hamartoma tumor syndrome (PTEN), and Peutz-Jeghers syndrome (STK11).

It is estimated that 20-25% of familial breast cancer risk can be ascribed to mutations in the BRCA1 or BRCA2 genes (van der Groep 2011). The contribution of mutations in the CDH1, PTEN, STK11, and TP53 genes to familial breast cancer risk is considerably lower than the contribution of BRCA1 and BRCA2 mutations.

### References:


### Genes

BRCA1, BRCA2, CDH1, PALB2, PTEN, STK11, TP53

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of high risk breast 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.

**Deletion/Duplication Analysis:** DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that cover the entire genomic region.

### 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. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient’s clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

**Deletion/Duplication Analysis:** Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient’s clinical and/or biochemical phenotype.

### Specimen Requirements

Submit only 1 of the following specimen types

**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.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
15µg
Isolation using the Perkin Elmer™Chemagen™ 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.

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

Related Tests
- BRCA1/BRCA2 Gene Sequencing and Deletion/Duplication Panel
- BRCA1/BRCA2 Gene Sequencing Panel
- BRCA1/BRCA2 Deletion/Duplication Panel
- Hereditary Cancer Syndrome: Sequencing Panel