BRCA1 and BRCA2 Full Gene Sequence Analysis and Common Deletion/Duplication Variants

Testing includes full gene sequencing of exons and 25 base pairs of introns of BRCA 1 and 2 and the common deletions of BRCA1 (exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb). Sequencing does not include the promoter, enhancers or splicing modulators in intronic regions. Deletion duplication analysis is limited to the commonly reported variants; refer to full deletion/duplication testing.

Indication: This testing is indicated for individuals that meet the criteria for Hereditary Breast and Ovarian Cancer listed in the National Comprehensive Cancer Network (NCCN) guidelines. For assistance with interpreting guidelines, please contact Henry Ford Precision Genomic Diagnostics, or refer to genetic counseling for evaluation. Testing on minors is not indicated.

BRCA1 and BRCA2 are genes that code for proteins that help repair DNA damage. Inherited mutations in BRCA 1 or 2, in combination with additional acquired mutations, can result in increased risk for developing cancer. Specific mutations in BRCA1 and BRCA2 increase the risk of breast and ovarian cancers, and have been associated with increased risk of several additional types of cancer. BRCA1 and BRCA2 mutations account for about 20 to 25 percent of hereditary breast cancers and about 5 to 10 percent of all breast cancers. In addition, BRCA1 and BRCA2 account for about 15 percent of ovarian cancers overall. Breast and ovarian cancers associated with BRCA1 and BRCA2 mutations tend to develop at younger ages than their nonhereditary counterparts.

Testing method: Next Generation Sequencing (NGS) for whole gene analysis of single base pair (point) mutations and small (<25bp) deletions and duplications. The TruSight Cancer Sequencing Panel targets 94 genes suspected to play a role in predisposing to cancer, including genes associated with both common (eg, breast, colorectal) and rare cancers. In addition, the panel includes 284 SNPs suspected to be associated with cancer through genome-wide association studies (GWAS). Content selection was based on expert curation of the scientific literature and other high- quality resources. The assay provides coverage of exonic and noncoding DNA in exon- flanking regions, on average 50 bp.

Multiplex ligation-dependent probe amplification (MLPA) PCR assay is used to evaluate common copy number variations (BRCA1 (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb). Testing does not detect mutations in promoters, enhancers, and spice site modulators that are not included in exon sequencing. Testing does not include deletions and duplications not specified as common.

Turnaround time: 7-10 business days

Sample Requirements: 3 ml peripheral blood in EDTA (lavender) top tube

Specimen stability: Ambient - 72 hours; Refrigerated - 1 week

CPT codes: 81211

References:

1. Campeau PM, Foulkes WD, Tischkowitz MD. Hereditary breast cancer: New genetic developments, new therapeutic avenues. Human Genetics 2008; 124(1):31-42

2. Pal T, Permuth-Wey J, Betts JA, et al. BRCA1 and BRCA2 mutations account for a large proportion of ovarian carcinoma cases. Cancer 2005; 104(12):2807-2816

3. Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. Journal of Clinical Oncology 2007; 25(11):1329-1333

4. Tai YC, Domcheck S, Parmigiani G, Chen S. Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. Journal of the National Cancer Institute 2007; 99(23):1811-1814

5. Levy-Lahad E, Friedman E. Cancer risks among BRCA1 and BRCA2 mutation carriers. British Journal of Cancer 2007; 96(1):11-15

6. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology - Genetic/Familial high-risk assessment: Breast and Ovarian. Version 2.2015, NCCN.org

7. Hampel H, Bennett RL, Buchanan A, et al. 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. Genetics in Medicine, advanced online publication 13 November 2014

8. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genetics in Medicine, advanced online publication 5 March 2015

9. 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