Henry Ford Health System
CENTER FOR PRECISION DIAGNOSTICS

Known Familial Variant for *BRCA2*

BRCA2									

Indication

This is a targeted mutation analysis for detection of a known familial variant in *BRCA2* gene, BReast CAncer gene 2 that codes for protein that helps repair DNA damage. Germline defects in the *BRCA2* are diagnostic for the autosomal dominant hereditary breast and ovarian cancer (HBOC) syndrome (OMIM ID: 604370). Inherited mutations in *BRCA2* are associated with increased lifetime risk for breast cancer (up to 84%), ovarian cancer (up to 27%), male breast cancer (6%), prostate cancer (up to 20%), pancreatic cancer (2-7%), and melanoma. Identifying individuals with mutation in *BRCA2* can allow informed clinical management that can significantly decrease cancer risks and improve overall survival rates. Some of the current management options for individuals with deleterious *BRCA2* variant include increased frequency and younger age of initiating mammograms and breast MRI, risk-reducing surgery options for breast and ovarian cancer in females, other cancer monitoring and prophylactic treatment options, availability of targeted therapy for cancer treatment (e.g. PARP inhibitors for *BRCA2*-mutant tumors), and identification of at-risk family members. Updated clinical management guidelines for individuals with *BRCA2*-associated HBOC syndrome can be found at www.NCCN.org.

Testing requirements

This test is designed to detect a known pathogenic mutation in *BRCA2* that was previously identified in another member of the family (blood relative). Details about the known familial variant in *BRCA2* have to be provided to our laboratory for analysis. This information should include either a copy of previous sequencing report (preferred) or *BRCA2* variant information that includes transcript change (e.g., c.5303_5304delTT), protein change (e.g., p. p.Leu1768fs*5) and/or genomic locus corresponding to the known variant (e.g., chr 13: 32913795-32913796). Orders that are missing this information will not be processed.

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) assay.

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
81217, G0452

References

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King, MC, et al. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. Science. 2003; 302(5645):643-6.

Antoniou, A, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case Series unselected for family history: a combined analysis of 22 studies. Am. J. Hum. Genet. 2003; 72(5):1117-30.

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Ship Specimens to:

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