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BRCA1 & BRCA2 Gene panel by NGS- Germline Study

Clinical Indication:

k/c/o Ca Breast

Result

NEGATIVE

(No clinically relevant variant identified)

Key Findings:

Gene & Transcript	Variant	Exon	Coverage / VAF	Zygosity	Clinical Significance
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*Genetic test results are reported based on the recommendations of American College of Medical Genetics

Gene Summary:

BRCA1: This gene encodes a 190 kD nuclear phosphoprotein that plays a role in maintaining genomic stability, and it also acts as a tumor suppressor. The BRCA1 gene contains 22 exons spanning about 110 kb of DNA. The encoded protein combines with other tumor suppressors, DNA damage sensors, and signal transducers to form a large multi-subunit protein complex known as the BRCA1-associated genome surveillance complex (BASC). This gene product associates with RNA polymerase II, and through the C-terminal domain, also interacts with histone deacetylase complexes. This protein thus plays a role in transcription, DNA repair of double-stranded breaks, and recombination. Mutations in this gene are responsible for approximately 40% of inherited breast cancers and more than 80% of inherited breast and ovarian cancers. Alternative splicing plays a role in modulating the subcellular localization and physiological function of this gene. Many alternatively spliced transcript variants some of which are disease-associated mutations, have been described for this gene, but the full-length natures of only some of these variants has been described. A related pseudogene, which is also located on chromosome 17, has been identified.

BRCA2: Inherited mutations in BRCA1 and this gene, BRCA2, confer increased lifetime risk of developing breast or ovarian cancer. Both BRCA1 and BRCA2 are involved in maintenance of genome stability, specifically the homologous recombination pathway for double-strand DNA repair. The largest exon in both genes is exon 11, which harbors the most important and frequent mutations in breast cancer patients. The BRCA2 gene was found on chromosome 13q12.3 in human. The BRCA2 protein contains several copies of a 70 aa motif called the BRC motif, and these motifs mediate binding to the RAD51 recombinase which functions in DNA repair. BRCA2 is considered a tumor suppressor gene, as tumors with BRCA2 mutations generally exhibit loss of heterozygosity (LOH) of the wild-type allele.

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Test Description:

BRCA1 (BReast CAncer gene 1) and BRCA2 (BReast CAncer gene 2) are genes that produce proteins that help repai damaged DNA. Everyone has two copies of each of these genes—one copy inherited from each parent. BRCA1 and BRCA2 are tumor suppressor genes. When they have certain changes, called pathogenic variants (or mutations), cancer can develop People who inherit pathogenic variants in one of these genes have increased risks of several cancers—most notably breast and ovarian cancer, but also several additional types of cancer. People who have inherited a pathogenic variant in BRCA1 and BRCA2 also tend to develop cancer at younger ages than people who do not have such a variant.

This tests uses Next Generation Sequencing, targeted sequencing approach that is restricted to the proteincoding regions of selected genes under investigation. BRCA1 and BRCA2 Panel contains primer pairs that target the coding regions of the tumor suppressor genes BRCA1 and BRCA2, which have been implicated in hereditary breast and ovarian cancers. This panel utilizes 167 amplicons to analyze the coding region of both BRCA1 and BRCA2 genes.

Recommendations:

We recommend confirming the presence of variants by Sanger Sequencing.

BRCA1 & BRCA2 MLPA study is recommended to analyse deletion/duplications in the sample.

The results should be interpreted in the context of the patient's medical evaluation. Correlation of the genetic findings with the clinical condition of the patient is required to arrive at accurate diagnosis, prognosis or for therapeutic decisions.

The classification of variants of unknown significance (VUS) can change over time. For questions about this report, or for assistance please contact the Laboratory.

Test Methodology:

BRCA1 & BRCA2 Panel on Next Generation Sequencing is a targeted sequencing approach that is restricted to the protein- coding regions of selected genes under investigation. BRCA1 and BRCA2 Panel contains primer pairs that target the coding regions of the tumor suppressor genes BRCA1 and BRCA2, which have been implicated in breast and ovarian cancers. This panel utilizes 167 amplicons to analyze the coding region of both BRCA1 and BRCA2 genes.

DNA isolated from Peripheral Blood or Buccal Swab is used for NGS Library preparation.

The libraries were sequenced to mean depth: >150x on next generation sequencing platform.

The raw read sequences obtained from NGS are processed to remove adapters and filter poor quality reads.

Clinically relevant germline mutations were identified and annotated using published variants in literature and a set of diseases databases.

Clinically relevant mutations are annotated using published variants in literatures and a set of diseases databases - ClinVar, OMIM HGMD. The effect of non-synonymous variant is calculated using multiple prediction algorithms such as PolyPhen, SIFT, Mutation Taster2.

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Disclaimer:

This test is limited to BRCA1 & BRCA2 genes analysis only, It should be noted that this test does not sequence all bases in a humar genome, not all variants have been identified or interpreted, and this report is limited only to variants with evidence for causing o contributing to disease/clinical details.

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.

References:

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If Values are marked with * , they are critical values.

***** End Of Report *****