Requesting Physician: B. Smith
Collected Date: 21-Apr-2019
Date received: 21_Apr-2019
Specimen type: Blood

FAMILIAL BREAST & OVARIAN CANCER GENE SCREEN REPORT

Test requested: BRCA1 & BRCA2 gene screening

Clinical details: Personal history of OVCA diagnosed at age 49

Test result: **AN UNCLASSIFIED GENETIC WAS DETECTED**

BRCA2 NM_000059.3 c.[2473A>G];[=]: p.Asn825Asp in exon 11

Results interpretation:

The heterozygous mutation c.[2473A>G];[=]: p.Asn825Asp was identified in exon 11 of the BRCA2 gene. This variant is not listed on the Breast Information Core (BIC) database. This variant has been reported once on both LOVD 3.0 and ClinVar as of unknown clinical significance but has not to our knowledge been reported further in the literature. Three protein function prediction programs (SIFT, PolyPhen-2 and AGVGD) predict that it is unlikely to affect protein function. Based on current knowledge this is an unclassified variant and predictive testing is NOT available for this mutation.

Please note that common polymorphisms, synonymous changes and intronic variants outside of splice sites have not been reported.

Comment:

For counselling and assessment of the risk to the patient and family members please contact the appropriate genetic service.

Test description:

DNA sequencing analysis: Automated Next-Generation Sequencing of all coding exons and flanking intron junctions of the BRCA1 and BRCA2 genes.

MLPA: Gene dosage was assessed using Multiplex Ligation-Dependent Probe Amplification (MLPA) and kits available from MRC-Holland. The specific kits used were BRCA1 (P002D) and BRCA2 (P045B). This analysis detects large rearrangements.

This analysis does NOT exclude the possibility of other mutations not amenable to our analytical methods being present.

The nomenclature used throughout this report is in accordance with the Human Genome Variation Society (HGVS) guidelines, which can be found at www.hgvs.org.

Reference Sequence GenBank Accession Number: BRCA1 KM_007294.3; BRCA2 NM_000059.3.

In all family DNA studies, the accuracy of the report assumes stated relationships within the kindred, clinical diagnosis and identification of samples to be correct. Data are not available to accurately quantitate the very small but finite errors inherent in the use of molecular biological techniques for diagnosis.

Reported by: A Brown

Authorised by: S Barnes

Requesting Physician: B. Smith
Collected Date: 21-Apr-2019
Date received: 21_Apr-2019
Specimen type: Blood

FAMILIAL BREAST & OVARIAN CANCER GENE SCREEN REPORT

Test requested: BRCA1 & BRCA2 gene screening

Clinical details: Personal history of ovarian cancer diagnosed at age 52

Test result: **AN UNCLASSIFIED GENETIC WAS DETECTED**

BRCA1 NM_007294.3 c.[5207T>C];[=]: p.Val1736Ala in exon 20

Results interpretation:

The genetic variant c.[5207T>C];[=]: p.Val1736Ala was identified in exon 20 of the BRCA1 gene has been previously reported in the Breast Information Core (BIC) database 18 times as an unclassified variant. Of three functional predictive algorithms, SIFT and AGVGD indicate that this variant is likely to affect protein function. However, PolyPhen-2 predicts it to be benign. Lee *et al, Cancer Res* (2010): 70(12):4880-90 found this mutation to have compromised transcriptional activity, which they suggest is likely to result in a strong functional effect. Functional assays by Carvalho *et al, Cancer Res* (2007); 67:(4) found this variant to be deleterious. There are conflicting interpretations regarding the clinical significance of this variant and therefore at this point in time it is an unclassified variant. Segregation analysis in the family may provide further evidence of its pathogenicity.

Please note that common polymorphisms, synonymous changes and intronic variants outside of splice sites have not been reported.

Comment:

For counselling and assessment of the risk to the patient and family members please contact the appropriate genetic service.

Test description:

DNA sequencing analysis: Automated Next-Generation Sequencing of all coding exons and flanking intron junctions of the BRCA1 and BRCA2 genes.

MLPA: Gene dosage was assessed using Multiplex Ligation-Dependent Probe Amplification (MLPA) and kits available from MRC-Holland. The specific kits used were BRCA1 (P002D) and BRCA2 (P045B). This analysis detects large rearrangements.

This analysis does NOT exclude the possibility of other mutations not amenable to our analytical methods being present.

The nomenclature used throughout this report is in accordance with the Human Genome Variation Society (HGVS) guidelines, which can be found at www.hgvs.org.

Reference Sequence GenBank Accession Number: BRCA1 KM_007294.3; BRCA2 NM_000059.3.

In all family DNA studies, the accuracy of the report assumes stated relationships within the kindred, clinical diagnosis and identification of samples to be correct. Data are not available to accurately quantitate the very small but finite errors inherent in the use of molecular biological techniques for diagnosis.

Reported by: A Brown

Authorised by: S Barnes