**Clinical Details:**

**FAMILIAL CANCER PANEL REPORT**

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| --- | --- |
| **Test Description:**  The BRCA1 & BRCA2 assay targets the familial cancer-related genes: *BRCA1, BRCA2.* | **RESULT SUMMARY:** |
|  |

**Test Result:**

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| --- | --- | --- | --- | --- | --- |
| Gene | EXON | REFERENCE | Nucleotide VARIANT | Protein Change | Classification |
| BRCA2 | ex11/27 | NM\_000059.3 | c.2339C>G | NP\_000050.2:p.(Ser780\*) | C5: Pathogenic |

**Clinical Interpretation**

***BRCA2*:** BRCA2 encodes Breast And Ovarian Cancer Susceptibility Protein 2. Inherited mutations in BRCA2 (or the related BRCA1) 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 heterozygous variant c.2339C>G was detected in exon 11 of the BRCA2 gene. This variant results in a premature stop codon, p.(Ser780\*), leading to a truncated BRCA2 protein with predicted loss of BRCA2 protein function. This variant is recorded multiple times in ClinVar as pathogenic (ENIGMA), and has been reported in individuals with breast and/or ovarian cancer (Konstantopoulou et al, Clin Genet (2014) 85(1):36-42 and Kwong et al, J Mol Diagn (2016) 18(4):580-94). Based on current knowledge, this is considered a pathogenic (Class 5) variant. This is consistent with a diagnosis of hereditary breast and/or ovarian cancer. This result has diagnostic and clinical management implications for both the patient and other at-risk family members developing disease. First-degree relatives of this patient have a 50% risk of inheriting the abnormal gene and predictive testing is available through the appropriate genetic service.

**Comment:**

For counselling and the assessment of the risk to the patient and other at risk 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 & BRCA2 genes. The variant detected using NGS was confirmed using sanger sequencing.

**MLPA:** Gene dosage was assessed using Multiplex Ligation-Dependent Probe Amplification (MLPA) technology and kits available from MRC-Holland. The specific kits used are BRCA1 (P002D) & BRCA2 (P045C). This analysis detects large rearrangements.

Variants are described according to HGVS nomenclature version 15.11 (<http://varnomen.hgvs.org/>) with minor differences in accordance with Molecular Pathology policy. The policy as it pertains to this report is available by contacting the laboratory. Class 1 and 2 variants (benign and likely benign) are not reported.

**Confirmatory testing on a second independent sample is recommended. (IS THIS RELEVANT? DELETE FOR UV's)**

***Reference Sequence GenBank Accession Number:*** *BRCA1 NM\_007294.3; BRCA2 NM\_000059.3*

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/.

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

**Disclaimer:**

*Peter Mac assumes sample identification, family relationships, and clinical diagnoses are as stated on the request. Our clinical recommendations may be based on evidence from third-party data sources and should be interpreted in the context of all other clinical and laboratory information for this patient.*

Please contact the laboratory on 03 8559 8403 if you wish to discuss this report further.

**Reported by: Lumin Xue 9-Oct-2018 8:54 AM**

**Reported by: Jennifer Nakos 29-Oct-2018 11:17 AM**

**Authorised by:**