

***Trust Logo***

**<GLH region name>**

**NHS Genomic Laboratory Hub**

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| --- | --- | --- |
| ***Head of Department****Name* |  | *Local Genetics Service**Local Trust**Address**Address**Post Code**Web site address* |
| General Enquiries: *telephone contact*Email: *generic email address* |
|  |

**GENOMIC LABORATORY REPORT**

|  |  |  |
| --- | --- | --- |
| Dr xxx | **Patient Name:** | **Jane DOE** |
| Consultant  | Gender: | Female |
| <<Hospital address>> | Date of Birth: | 14 Jan 1968 |
| NHS No: | 123 456 7890 |
| Hospital No: | NK |
| Your ref: | GC12345 |

**Reason for testing**

Diagnostic testing. <<Referral reason>>. Patient phenotype / HPO terms

|  |
| --- |
| **Result summary** |
| **Consistent with a genetic diagnosis of *BRCA1*-related cancer susceptibility****or****Genetic diagnosis of *BRCA1*-related cancer susceptibility** |

**Result**

This individual is heterozygous for a likely pathogenic *BRCA1* missense variant (details below). Heterozygous *BRCA1* pathogenicvariants cause cancer susceptibility (OMIM: 604370 and 614320).

**Implications**

Each of her offspring would be at 50% risk of inheriting this variant and disorder. Other relatives, particularly females are at increased risk of this disorder.

**Recommended action**

This individual is at increased risk of developing further *BRCA1*-associated tumours and should be monitored appropriately.

*<INSERT ANY APPROPRIATE TREATMENT IMPLICATIONS>*

We recommend involvement of Clinical Genetics where predictive and diagnostic testing for this variant in her relatives can be arranged.

Date issued: <AUTHORISEDDATE> Authoriser: Clinical Scientist

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**TECHNICAL INFORMATION**

**Variant details**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene | Zygosity | HGVS description | Location: GRCh37 (hg37) | \*Classification |
| *BRCA1* | Heterozygous  | NM\_007294.3 c.xxT>C p.(Xxx) | Chr17(GRCh37):g.xxxxxxA>G | Likely pathogenic |

**Test methodology**

1. Genes screened in the panel: *BRCA1* - NM\_007294.3; *BRCA2* - NM\_000059.3; *PALB2* – NM\_024675.3
2. Enrichment method: Agilent SureSelect Custom Design and sequenced on the Illumina platform with a sensitivity of at least 95%.The target region of those selected transcripts is covered to a minimum read depth of 30x.
3. Screening for large deletions and duplications is performed using comparative depth of coverage of NGS data. Deletions/duplications are confirmed by Multiplex Ligation-Dependent Probe Amplification (MRC-Holland).
4. \*Variant classification – see Appendix 1 overleaf
5. Only relevant results are shown; full details of methods and results, including benign/likely benign variants and variants of uncertain clinical significance, are stored on file and are available on request.

**Sample details**

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| --- | --- | --- | --- |
| Your lab ref: | 122001180 |  |  |
| Sample ID | 1234567 | Sample collected: | 05 Jun 2020 |
| Sample type | DNA from peripheral blood | Sample received | 05 Jun 2020 |

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| --- | --- | --- |
| Dr xxx | **Patient Name:** | **Jane DOE** |
| Consultant  | Gender: | Female |
| <<Hospital address>> | Date of Birth: | 14 Jan 1968 |
| NHS No: | 123 456 7890 |
| Hospital No: | NK |
| Your ref: | GC12345 |

**Appendix 1: Variant classification**

**Variant details**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene | Zygosity | HGVS description | Location: GRCh37 (hg37) | \*Classification |
| *BRCA1* | Heterozygous  | NM\_007294.3 c.xxT>C p.(Xxx) | Chr17(GRCh37):g.xxxxxxxA>G | Likely pathogenic |

|  |  |
| --- | --- |
| Gene-Disease Association | Hereditary cancer susceptibility OMIM 604370 and 614320 |
| Inheritance | Autosomal Dominant  |
| **Evidence for variant classification using ACMG/AMP guidelines**:  |
| PM2 | Not in gnomAD [[add](https://gnomad.broadinstitute.org/region/17-41215361-41215401?dataset=gnomad_r2_1) weblink] |
| PS3 | Loss of Function by Findlay et al 2018 assay (PMID: 30209399; <https://sge.gs.washington.edu/BRCA1/>) |
| PS4\_mod | Xxxx et al 2013 (PMID: xxx) and Xxxx et al 2019 (PMID: xxx) |
| PP3 | Revel score xxx |

\*Variant classification according to the American College of Medical Genetics and Genomics (ACMG)1 and Association for Clinical Genomic Science (ACGS) 2020 guidelines2 and Cancer Variant Interpretation Group-UK consensus specification for Cancer Susceptibility Genes3 ([http://www.canvaruk.org](http://www.canvaruk.org/)/)

1Richards *et al.* (2015) Genetics in Medicine 17:405-24. (PMID 25741868)

2www.acgs.uk.com/quality/best-practice-guidelines

3 Garrett et al (2020) J Med Genet (PMID: 32170000)