

***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** |
| **Inconclusive result – consider further action** |

**Result**

This individual is heterozygous for a germline *BRCA1* missense variant of uncertain significance (details below).

**Implications**

This finding in isolation is insufficient to justify a change in clinical management.

**Recommended action**

To aid variant re-classification, further evidence is required.

We recommend involvement of Clinical Genetics for familial segregation analysis/(RNA studies/etc) if appropriate.

Further evidence may become available about this variant in the future: if new clinical decisions based on this variant are required for this family, please request the laboratory to review this variant.

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(BRCA1):c.xxxT>G | Chr17(GRCh37):g.xxxxxxA>C | Variant of uncertain significance |

**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 | Blood | Sample received | 05 Jun 2020 |

|  |  |  |
| --- | --- | --- |
| 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(BRCA1):c.xxxT>G | | Chr17(GRCh37):g.xxxxxxA>C | Variant of uncertain significance |
| Gene-Disease Association | | | | Hereditary cancer susceptibility OMIM 604370 and 614320 | | |
| Inheritance | | | | Autosomal Dominant | | |
| **Evidence for variant classification using ACMG/AMP guidelines**: | | | | | | |
| PM2 | | Not on gnomad [<weblink>](https://gnomad.broadinstitute.org/variant/17-41249298-A-C) | | | | |
| PS4\_mod | | XXX et al 2003 (PMID:XXX)  XXX et al 2016 (PMID:xxx) | | | | |
| PP3 | | Revel score 0.808. | | | | |
|  | |  | | | | |

\*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)