

***Trust Logo***

**<GLH region name>**

**NHS Genomic Laboratory Hub**

|  |  |  |
| --- | --- | --- |
| ***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**

Predictive testing. <<Referral reason>>

|  |
| --- |
| **Result summary** |
| **At elevated risk of <*CHEK2/ATM*>-associated cancers** |

**Result**

This individual is heterozygous for the germline familial <likely> pathogenic <*CHEK2/ATM*> truncating/splice variant (details below). Heterozygous <*CHEK2/ATM*> pathogenic variants cause moderate risk1 cancer susceptibility, particularly breast cancer in females (OMIM: xxx).

**Implications**

Each of her offspring would be at 50% risk of inheriting this variant and genetic predisposition to <*CHEK2/ATM*>-associated cancers. Other relatives are also at increased risk.

**Recommended action**

This individual is at increased risk of developing <*CHEK2/ATM*>-associated cancers and should be managed appropriately, based on their personal and family history. We recommend referral to Clinical Genetics where predictive and diagnostic testing for this variant in her relatives can be arranged.

Date issued: <AUTHORISEDDATE> Authoriser: Clinical Scientist

1. Dorling et al 2021 PMID: 33471991

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**TECHNICAL INFORMATION**

**Familial variant details**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene | Zygosity | HGVS description | Location: GRCh37 (hg19) | \*Classification in proband |
| *GENE* | Heterozygous | NM\_xxx c.xxT>C p.(Xxx) | ChrX(GRCh37):g.xxxxxxA>G | <Likely> Pathogenic |

**Test methodology**

1. METHODOLOGY e.g. Genomic DNA Sanger sequencing with direct chromatogram check: >95% sensitivity
2. Only clinically relevant results are shown; full details of methods and results, including benign/likely benign variants and variants of uncertain clinical significance with limited evidence for pathogenicity and are available on request.
3. \*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 (<https://www.cangene-canvaruk.org/canvig-uk>; <http://www.canvaruk.org/>) and ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ATM Version 1.1 Expert Panel Page: <https://www.clinicalgenome.org/affiliation/50039>4

1Richards *et al.* (2015) Genetics in Medicine 17:405-24. (PMID: [25741868](https://pubmed.ncbi.nlm.nih.gov/25741868/))

2 [www.acgs.uk.com/quality/best-practice-guidelines](file:///C:\Users\dnamd\AppData\Local\Microsoft\Windows\INetCache\Content.Outlook\F1S86UOM\www.acgs.uk.com\quality\best-practice-guidelines)

3 Garrett et al (2020) J Med Genet (PMID: [32170000](https://pubmed.ncbi.nlm.nih.gov/32170000/))

4 <https://clinicalgenome.org/site/assets/files/7451/clingen_hbop_acmg_specifications_atm_v1_1.pdf>

**Sample details**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Your lab ref: | 122001180 | |  | |  | |
| Sample ID: | 1234567 | | Sample collected: | | 05 Jun 2020 | |
| Sample type: | DNA from peripheral 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 (hg19) | \*Classification | |
| *GENE* | Heterozygous | | NM\_xxx:c.xxxT>G p.(xxx) | | ChrXX(GRCh37):g.xxxxxxA>C | <Likely> Pathogenic | |
| Gene-Disease Association | | | | Hereditary cancer susceptibility OMIM xxx | | | |
| Inheritance | | | | Autosomal Dominant | | | |
| **Evidence for variant classification using ACMG/AMP guidelines\***: | | | | | | | Evidence points^ |
| PVS1\_vstr  Pxx | | LOF truncating variant  xxx | | | | | x  x |
| Total: xx |

^Evidence point ranges: VUS: 0-5 (10-90% posterior probability pathogenicity); Likely pathogenic: 6-9 (90-99% posterior probability); Pathogenic: >10 (>99% posterior probability). Points awarded per evidence weighting: sup (supporting) = 1, mod (moderate) = 2, str (strong) = 4, vstr (very strong) = 8 (Tavtigian et al 2020 PMID: [32720330](https://pubmed.ncbi.nlm.nih.gov/32720330/); Garrett et al 2020 PMID: [33208383](https://pubmed.ncbi.nlm.nih.gov/33208383/); [ACGS 2020 variant guidelines](http://www.acgs.uk.com/quality/best-practice-guidelines)

\*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 *CHEK2* gene specific and consensus specification for Cancer Susceptibility Genes3 (<https://www.cangene-canvaruk.org/canvig-uk>; <http://www.canvaruk.org/>) and ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ATM Version 1.1 Expert Panel Page: <https://www.clinicalgenome.org/affiliation/50039>4

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4 <https://clinicalgenome.org/site/assets/files/7451/clingen_hbop_acmg_specifications_atm_v1_1.pdf>