

***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:** | **John DOE** |
| Consultant  | Gender: | Male |
| <<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 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**

As this individual is male, his risk of developing <*CHEK2/ATM>*-associated cancers remains low.Each of his offspring would be at 50% risk of inheriting this variant and disorder. His descendants and other relatives are at increased risk of developing <*CHEK2/ATM*>-associated cancers.

**Recommended action**

We recommend referral to Clinical Genetics where specific cancer risk figures for males can be discussed, and predictive or diagnostic testing for this variant in his 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 (hg37) | \*Classification in proband |
| *<GENE>* | Heterozygous | NM\_xxx c.xxT>C p.(Xxx) | ChrXX(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 very limited evidence for pathogenicity 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) 2[www.acgs.uk.com/quality/best-practice-guidelines](file:///%5C%5C3PA0-DATA-SERVER%5CDATA%5CSCH%5CGEN%5CDNA%5CSHARED%5CDNA%5CHereditary%20cancers%5CService%20Management%5CHC%20report%20examples%5CCanVIG%20report%20templates%202020%5Cwww.acgs.uk.com%5Cquality%5Cbest-practice-guidelines)

3 Garrett et al (2020) J Med Genet (PMID: 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:** | **John DOE** |
| Consultant  | Gender: | Male |
| <<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\***:  | Exponent (Bayesian) score^ |
| PVS1\_vstrPxxx | LOF truncating variantxxx | xx |
| 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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2 [www.acgs.uk.com/quality/best-practice-guidelines](file:///C%3A%5CUsers%5Cdnamd%5CAppData%5CLocal%5CMicrosoft%5CWindows%5CINetCache%5CContent.Outlook%5CF1S86UOM%5Cwww.acgs.uk.com%5Cquality%5Cbest-practice-guidelines)

3 Garrett et al (2020) J Med Genet (PMID: [32170000](https://pubmed.ncbi.nlm.nih.gov/32170000/)); <https://www.cangene-canvaruk.org/canvig-uk>

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