

***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* |
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**GENOMIC LABORATORY REPORT**

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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 |

**Reason for testing**

Diagnostic testing R211: Inherited polyposis and early onset colorectal cancer. <Patient phenotype / HPO terms>.

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| **Result summary** |
| **Consistent with a genetic diagnosis of *<GENE>*-associated cancer susceptibility (LP)****OR****Genetic diagnosis of *<GENE>*-associated cancer susceptibility (P)** |

**Result**

This individual is heterozygous for a germline <likely> pathogenic *<GENE>* <missense/truncating/splice/copy number> variant (details below). Heterozygous *<GENE>* pathogenicvariants cause <polyposis/cancer susceptibility (OMIM: XXX)>.

**Implications**

Other relatives may have up to a 50% risk of inheriting this variant and genetic predisposition to *<GENE>-*associated cancers.

**Recommended action**

This individual is at increased risk of developing further *<GENE>*-associated cancers/polyps and should be managed appropriately.

We recommend referral to Clinical Genetics, where predictive and diagnostic testing for this variant in their relatives can be arranged.

Date issued: <AUTHORISEDDATE> Authoriser: Clinical Scientist

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**TECHNICAL INFORMATION**

**Variant details**

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| --- | --- | --- | --- | --- |
| Gene | Zygosity | HGVS description | Location: GRCh37 (hg19) | \*Classification |
| *<GENE>* | Heterozygous  | NM\_xxx: c.xxxT>G p.(Xxx) | ChrXX(GRCh37):g.xxxxxxA>C | Likely pathogenic |

**Test methodology**

1. Genes screened in the panel: *APC, BMPR1A, EPCAM, GREM1, MLH1, MSH2. MSH6, MUTYH, NTHL1, PMS2, POLD1, POLE, PTEN, RNF43, SMAD4, STK11* (all coding exons & exon-intron boundaries).
2. Methodology including sensitivity CNV detection, Bioinformatics pipeline etc e.g. 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. Limits of detection e.g.NGS technical sensitivity may be reduced for genes with pseudogenes or paralogs, and copy-number variation >xx nucleotides.
5. \*Variant classification – see Appendix 1 overleaf
6. 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, 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**

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| --- | --- | --- | --- | --- |
| Gene | Zygosity | HGVS description | Location: GRCh37 (hg19) | \*Classification |
| *<GENE>* | Heterozygous  | NM\_xxx:c.xxxT>G | 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^ |
| PS3\_strPM2\_modPP4\_modPP3\_sup | LOF on functional assay xxx et al 2018 (PMID: xxx) Not on gnomAD <insert weblink>XXX et al 2003 (PMID:XXX); XXX et al 2016 (PMID:xxx); Revel score >0.7 | 42 |
| 2 |
| 1 |
| Total: 9 |

^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 2024 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 BRCA1/2 gene-specific and consensus specification for Cancer Susceptibility Genes3 (<https://www.cangene-canvaruk.org/canvig-uk>)

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%3A/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/))