Test results

Multi-Cancer Panel

everything genetic

Patient name	Example	Sample collection date	01/02/2023
Date of birth	03/03/1993	Sample accession date	03/02/2023
Sex at birth	Female	Report date	17/02/2023
Requesting physician	Dr James Mackay	BSPS lab number	23D001
Sample type	Saliva	Everything Genetic barcode	12345678910

Test performed

Everything Genetic Multi-Cancer Panel

Reason for testing

Cancer - Family history (specify below)

Family history of breast cancer

Result: Variant(s) of Unknown Significance (VUS) identified

Gene	Variant	Zygosity	Variant classification
ATM	c.8872_6_8672-2del	Heterozygous	Unknown Significance

About this test

This test evaluates genes for genetic changes that are associated with oncological diseases. Genetic testing, when combined with family history and other medical results, can provide valuable information to clarify an individual's risk of specific cancers, which may be accompanied by potential actionable steps, or it may support a clinical diagnosis and assist with the development of a personalised treatment and management plan.

Clinical interpretation

In the table above, we list variants related to disorders without an apparent overlap with the described phenotype of the patient and/or variants with a zygosity inconsistent with the expected mode of inheritance. As examples, a variant of unknown significance (VUS) in a gene with only partial clinical overlap, or a single heterozygous pathogenic variant in a gene with a recessive phenotype which has a clinical overlap, may be reported here. These variants are mentioned in this report due to the potential contribution to the phenotype of the patient and may help close possible diagnostic gaps. For variants that may be considered clinically relevant, clinical re-evaluation and/or further testing (e.g., familial segregation analysis) could clarify their contribution to patient's phenotype.

CENTOGENE variant classification (based on AMCG recommendations)

Class 1 – Pathogenic

Class 2 – Likely pathogenic

Class 3 – Variant of unknown significance (VUS)

Class 4 – Likely benign

Class 5 – Benign

Additionally, other types of clinically relevant variants can be identified (e.g., risk factors, modifiers).

Next steps

This test did not identify any pathogenic variants but includes at least one result that is not completely understood at this time. Please note that the classification of variants may change over time as a result of new variant interpretation guidelines and/or new information. If a variant of unknown significance is reclassified, Everything Genetic will update this report with the new interpretation and provide notification.

This result should be discussed with a healthcare provider to learn more about this result and the appropriate next steps for further evaluation. Clinical follow up may still be warranted. This result should be interpreted within the context of family history and clinical findings.

Genes analysed

This table represents a complete list of the genes analysed for this individual:

ABRAXAS1	CDK4	HOXB13	MUTYH	PTEN	SDHD
APC	CDKN2A	KIT	NBN	RAD50	SMAD4
ATM	CHEK2	MC1R	NF1	RAD51C	SMARCA4
AXIN2	DICER1	MEN1	NTHL1	RAD51D	STK11
BAP1	DIS3L2	MET	PALB2	RECQL	TGFBR2
BARD1	EPCAM	MITF	PMS1	RET	TP53
BLM	FANCC	MLH1	PMS2	RNF43	TSC1
BMPR1A	FH	MLH3	POLD1	RPS20	TSC2
BRCA1	FLCN	MRE11	POLE	SDHA	VHL
BRCA2	GALNT12	MSH2	POT1	SDHAF2	WT1
BRIP1	HNF1A	MSH3	PRSS1	SDHB	XRCC2
CDH1	HNF1B	MSH6	PTCH1	SDHC	XRCC3

Method

Genomic DNA is enzymatically fragmented and regions of interest are enriched using DNA capture probes. The final indexed libraries are sequenced on an Illumina platform. The coding regions of the panel genes, 10 bp of flanking intronic sequences, and known pathogenic/likely pathogenic variants within these genes included in the enrichment design (coding and non-coding), are targeted for analysis. Data analysis, including alignment to the hg19 human reference genome (Genome Reference Consortium GRCh37), variant calling, and annotation is performed using CentoCloud, a Software as a Service platform that is able to collate information from internal and external reference databases to identify, prioritise and classify genetic variants associated with oncological diseases as to their pathogenicity using ACMG guidelines.

Variants of unknown significance (VUS) will be reported unless the described phenotype(s) is already explained by a detected pathogenic or likely pathogenic variant(s) or the detected VUSs are not related to the described phenotype(s).

The Copy Number Variation (CNV) detection software has a sensitivity of more than 95% for all homozygous/hemizygous deletions, as well as heterozygous deletions/duplications and homozygous/hemizygous duplications spanning at least three consecutive exons.

Limitations

The genetic results are interpreted in the context of the provided clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the provided genetic data or patient information is inaccurate and/or incomplete. If the obtained genetic results are not compatible with the clinical findings, additional testing should be considered.

More complex genetic events such as inversions, translocations, and repeat expansions, are not analysed in this test. In addition, due to technology limitations, certain regions may be poorly covered, or not covered at all. In these regions and others encompassing repetitive, high homology (such as pseudogene homology), and GC-rich sequences, relevant variants can be missed.

The Copy Number Variation (CNV) detection software has a sensitivity of more than 95% for all homozygous/hemizygous deletions, as well as heterozygous deletions/duplications and homozygous/hemizygous duplications spanning at least three consecutive exons. Sensitivity of more than 90% for CNV calling is expected including for single exon. The CNV detection sensitivity is decreased for repetitive and homologous regions, such as pseudogenes. Heterozygous CNVs spanning less than three exons cannot reliably be detected. In cases with low quality DNA, CNV analysis may not be possible to perform.

Potential aberrant splicing is assessed with splice prediction tools. Intronic variants that are beyond 10 nucleotides from exon-intron boundaries are not considered for aberrant splicing analysis, with the exception of known pathogenic splicing variants evidenced by external sources.

Disclaimer

Full exon coverage of all genes is not available and therefore some variants may not be detected.

As with all complex technical analyses, there are potential sources of error, including certain genetic variants in primer annealing sites, inhibitory contaminants in the genomic DNA extracted from the patient sample, technical issues, lower than expected coverage of certain amplicons due to the genomic sequence, changes to the classification of variants, changes to the database used for the annotation of variants, and recent clinical research. This assay should not be used for diagnosis in isolation, but rather used in conjunction with a medical diagnosis, family history and treatment plan provided by a qualified clinician. The assay was performed by Berkshire and Surrey Pathology Services (BSPS) and is currently part of an Extension to Scope application to UKAS under ISO15189:2012 standards.

The data analysis is performed and validated by CENTOGENE GmbH; the requested genetic testing itself is based on the highest and most current scientific and analytical standards. However, in very few cases genetic tests may show an incorrect result, e.g., because of the quality of the material provided or where a test fails for unforeseeable or unknown reasons that cannot be influenced by the test provider in advance.

This report has been reviewed and approved by:

Nadine Collins, Consultant Clinical Scientist

Date: 17/02/2023

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Berkshire and Surrey Pathology Services is accredited by UKAS to BS EN ISO15189:2012.

Signed on behalf of Everything Genetic Ltd

Dr James Mackay, MA, MD, FRCP, FRCPE
Medical Director

Date: 17/02/2023

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