



HerediGENE

Genekor Medical S.A. | 52, Spaton Ave., 15344, Gerakas, Athens, Greece
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 Scientific Director: George Nasioulas PhD

SAMPLE INFORMATION

Name :	FIRST NAME SURNAME	Date Received :	-
Medical ID :	-	Date of Report :	-
Date of Birth :	-	Req. Physician :	FIRST NAME SURNAME DR.
Location :	-	Barcode :	20XXXXXXEN
Material :	WHOLE PERIPHERAL BLOOD	Sample acceptability :	Pass

HerediGENE: Hereditary Cancer Panel by Next Generation Sequencing

Result

NEGATIVE
NO PATHOGENIC VARIANT IDENTIFIED

Interpretation

This result reduces the likelihood of a genetic predisposition to cancer. However, some mutations in genes of this panel may not be detected by the used methodology. Genes not included in this panel, may also contribute to increased cancer risk. Molecular genetic testing result should always be co-evaluated with the clinical symptoms and family history of the patient.



Electronically Signed by - Georgia Pepe, MSc Molecular Biologist, AMKA:09038403029
 - George Nasioulas, PhD Molecular Biologist, Scientific Director, AMKA:26025301255

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Methodology

Genomic DNA was extracted from the sample under investigation and was analysed by a solution based capture approach using a custom target enrichment panel containing 36 genes involved in hereditary predisposition to cancer, of which 15 genes involved in the homologous recombination (HR) complex (SeqCap EZ Choice, NimbleGen, Roche) (see table). Sequencing was carried out using Illumina technology. Reads were aligned to the reference sequence (GRCh37), and sequence changes were identified and interpreted in the context of a single clinically relevant transcript. All clinically significant observations were confirmed by Sanger Sequencing. All targeted regions were sequenced with $\geq 60x$ depth. Unless otherwise stated, this assay targets all coding regions of the indicated transcripts and 20 base pairs of flanking intronic sequences. For the *HOXB13*, *POLE* and *POLD1* genes, distinct genomic regions have been associated with increased cancer risk. Consequently, the reported regions for the aforementioned genes are: *HOXB13* - rs138213197, *POLE* - Exons 35-48 (NM_006231), *POLD1*- Exons 7-12 (NM_001256849).

The presence of large genomic rearrangements (LGRs), is investigated using the commercial computational algorithm SeqPilot Version 4.4 Build 505 (JSI Medical System). In addition, the computational algorithm panelcn.MOPS (Hum Mutat. 2017, 38:889-897) was also used in the *BRCA1* and *BRCA2* genes. The presence of LGRs is verified by use the MLPA method (Multiplex Ligation-dependent Probe Amplification, MRC Holland; AJHG 67:841-50, 2000).

*Notes:

Every molecular test has an internal 0,5-1% chance of failure. This is due to rare molecular events and factors related to the preparation and analysis of the samples.

The variants reported in *PMS2* gene are detected with coverage $>25\%$. The method used cannot detect low-level mosaicism (with coverage $<25\%$).

The method used achieves 99% sensitivity and specificity for single nucleotide variants and insertions and deletions $<15bp$. Sensitivity to detect genomic rearrangements larger than 15bp but smaller than a full exon may be reduced. Balanced genomic rearrangements cannot be detected.



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Details about non-pathogenic variants

All individuals carry DNA changes (i.e., variants), and most variants do not increase an individual's risk of cancer or other diseases. When identified, variants of uncertain significance (VUS) are reported. Benign variants (Polymorphisms) are not reported and available data indicate that these variants most likely do not cause increased cancer risk. Present evidence does not suggest that non-clinically significant variant findings be used to modify patient medical management beyond what is indicated by the personal and family history and any other clinically significant findings.

Genes Analyzed

Gene	Reference sequence	Gene	Reference sequence
APC	NM_000038	MSH2*	NM_000251
ATM	NM_000051	MSH6*	NM_000179
BARD1	NM_000465	MUTYH*	NM_001128425
BMPR1A	NM_004329	NBN	NM_002485
BRCA1*	NM_007294	NF1	NM_000267
BRCA2*	NM_000059	PALB2*	NM_024675
BRIP1	NM_032043	PMS2	NM_000535
CDH1	NM_004360	POLD1 (Exons 7-12)	NM_001256849
CDK4	NM_000075	POLE (Exons 35-48)	NM_006231
CDKN2A (p14ARF, p16INK4a)	NM_000077	PTEN	NM_000314
CHEK2*	NM_007194	RAD50*	NM_005732
EPCAM*	NM_002354	RAD51C*	NM_058216
FANCA	NM_000135	RAD51D*	NM_002878
FANCM	NM_020937	RET	NM_020975
HOXB13:c.251G>A p.(G84E)	NM_006361	SMAD4	NM_005359
MEN1	NM_000244	STK11	NM_000455
MLH1*	NM_000249	TP53*	NM_000546
MRE11A	NM_005591	VHL	NM_000551

Genes of the homologous recombination (HR) complex are labelled **blue**

* Unless otherwise noted analysis of large rearrangement was performed on the following genes:

BRCA1, BRCA2, CHEK2, EPCAM (Εξώνια 8, 9), MLH1, MSH2, MSH6, MUTYH, PALB2, RAD50 (Exons 1, 2, 4, 10, 14, 21, 23 and 25), RAD51C, RAD51D, and TP53.



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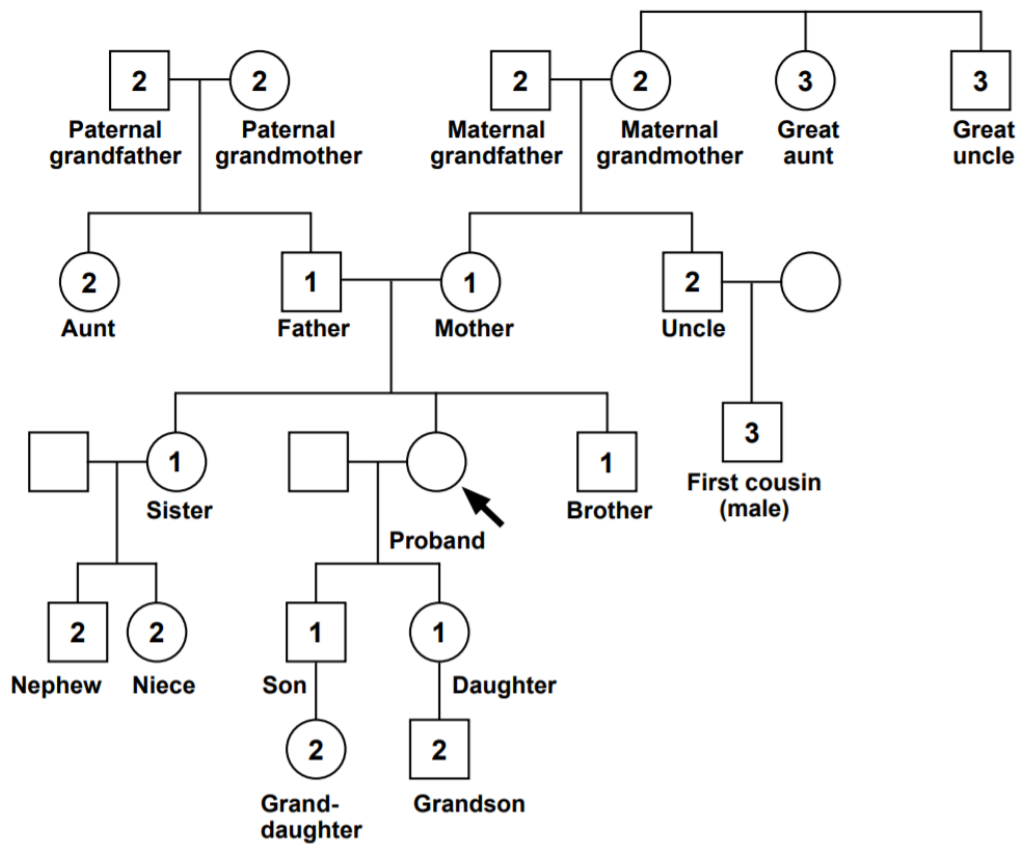


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Family tree



Note: The information shown on the family tree has been provided by the patient and not by medical records.



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