MEDICOVER GENETICS

MOLECULAR GENETIC REPORT
GM19.12345

Lochhamer Street 29, 82152 Martinsried, Germany, Email: info@medicover-genetics.com
Date: 21.12.2019

Report to:

Requesting Physician Name

Address

Contact Information

Order Number	**19 2019 1234**
Born	**01.01.1976**
Sex	M
Date test requested:	21.11.2019
Sample collected:	21.11.2019
Sample / Specimen:	DNA from EDTA blood

Order: Pancreatic cancer panel
Additional Information /patient phenotype: Pancreatic carcinoma, mother of the person seeking advice at the age of 60 years who also suffered from pancreatic carcinoma and deceased

RESULT SUMMARY:

In the analyzed portions of the genes BRCA1, BRCA2, CDKN2A, PALB2, STK11 and TP53 no pathogenic/probably pathogenic variant was detected, as well as no deletion or duplication of a larger gene segment.

Result

The result of the sequencing analysis cannot confirm the suspicion of a hereditary pancreatic carcinoma based on a causative variant in *BRCA1, BRCA2, CDKN2A, PALB2, STK11* or *TP53*. With the sequencing and CNV diagnostics applied here, approximately 97% of the variants currently listed in HGMD® are detected in the genes under investigation. A hereditary predisposition for pancreatic carcinoma based on an alteration in another gene not examined here cannot be excluded. To date, no major gene locus for familial pancreatic carcinoma is known, but there is an increased risk in various hereditary tumor syndromes (Peutz-Jeghers syndrome, familial atypical multiple birthmark and melanoma syndrome, hereditary breast/ovarian carcinoma) and hereditary pancreatitis (Matsubayashi et al. World J Gastroenterol 23:935; Underhill et al. 2016, Clin Ther 38:1600). However, causative variants in the currently known genes are detected in only about 8% of index patients (Schwartz et al. 2019, Clin Genet 96:579).

Recommended action

- Genetic counselling

VARIANT DETAILS: none identified

Gene	HGVS description	Exon	Location on GRCh38	Zygosity
NA	*NA*	*NA*	*NA*	*NA*
OMIM-P	**Consequence**	**Mode of inheritance**	**ACMG/AMP criteria** (Richards et al.; Ellard et al.)	**Classification**
NA	*NA*	*NA*	*NA*	*NA*

TEST METHODOLOGY

Sequencing	Enrichment	SNV and CNV Data analysis	data evaluation	Reference genome
Next Generation Sequencing (Illumina)	Twist Human Core Exome plus RefSeq SpikeIn	Illumina Dragen Bio-IT Platform	VarSeq by GoldenHelix	hg38, NCBI GR38
Quality criteria	**SNV detection sensitivity**	**Classification of variants**	**in silico algorithms**	**Databases**
>30 (precision >99,9%) in min. 75% of bases	99.92 - 99.93 %; confirmation of reported SNV with Sanger sequencing, data analysis with SeqPilot	Richards et al. 2015, Genet Med 17:405; Ellard et al. "ACGS Best Practice Guidelines for Variant Classification 2020“	MaxEntScan, SpliceSiteFinder-like, REVEL	HGMD Professional release, ClinVar, gnomAD

ANALYZED GENES

BRCA1 (NM_007294.3), BRCA2 (NM_000059.3), CDKN2A (NM_000077.4), PALB2 (NM_024675.3), STK11 (NM_000455.4), TP53 (NM_000546.5)

PERCENTAGE OF SEQUENCED BASES WITH COVERAGE >20X

100 %

LIST OF EXONS WITH COVERAGE <20X

-

TECHNICAL LIMITATIONS

mosaics (<20%); indels >21bp; repeat expansions; variants in: homopolymeric regions or regions of high sequence homology, unenriched regions (untranslated regions, introns, promoter and enhancer regions) or enriched but insufficiently covered regions; determination of the phase of multiple variants in one gene; balanced genomic rearrangements

CLASSES OF VARIANTS

Class 5: pathogenic variant – are reported, posterior probability >99 %
Class 4: likely pathogenic variant – are reported, posterior probability >90 %
Class 3: uncertain significance – only be listed in the report if they have potential to be upgraded to class 4, posterior probability >50 %
Class 2: likely benign – not reported, posterior probability <10 %
Class 1: benign – not reported, posterior probability <0,1 %

Report released by

John Doe