Diagnostic Laboratories

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Name :		**Visit No. :**	202309236
Patient ID :		**Visit DateTime :**	30/08/2023 00:00
Local Patient No :	**Ref No :** L36834	**Sample Type :**	PB
Physician Name :	ORPHANOS GEORGE	**Collected Date Time :**	30/08/2023 00:00
Physician Email :		**Physician Fax :**	
Hospital/Clinic/Lab	GERMAN ONCOLOGY CENTRE	**Hospital Fax :**	25208006

MOLECULAR CANCER PATHOLOGY AND GENETICS

Test Description	Result	Comments / Reference
12613 - Hereditary Cancer Investigation (NGS+Digital MLPA)		
Reason for Referral	Hereditary cancer predisposition investigation	
D001-Digital MLPA Cancer Panel	PENDING	D001 Digital MLPA cancer Panel 1 includes a total number of 690 probes for the detection of copy number alterations in 30 genes involved in hereditary cancer.
RESULTS SUMMARY	NO PATHOGENIC VARIANTS DETECTED	

REMARKS

CLINICAL INFORMATION
Strong family history of cancer.

TEST RESULTS AND INTERPRETATION

VARIANTS OF CLINICAL SIGNIFICANCE
No clinically relevant variants have been detected in the genes tested.

RECOMMENDATIONS - FURTHER TESTING ADVICE
It is possible that this patient has a pathogenic variant outside of the genetic regions or genes analysed. Clinical exome sequencing or high-resolution CGH array with LOH analysis may be able to determine the presence of pathogenic variants that could contribute to the patient's phenotype.

CAUTION - TEST LIMITATIONS
Results should be interpreted in the context of clinical findings, family history and other laboratory data. All genetic tests have limitations, and a normal result does not rule out the diagnosis of a genetic disorder since some DNA abnormalities may be undetectable by the applied technology. Certain conditions such as segmental overgrowth syndromes may carry a somatic variant is some tissue areas and not in others. In those cases tissue sampling of the affected tissue may be necessary. Although the assay has met the quality criteria of at least 20x coverage of more than 95% of the target sequences, due to limitations of the method, some target regions might not be covered 100%. The assay was designed to detect mutations in the coding region and the exon intron junctions of the genes described above. The possibility of gene deletions, pathogenic variants outside of the coding regions analysed or variants in regulatory or deep intronic regions cannot be excluded. Sample deterioration or polymorphic variations in the patient sample may interfere with mutation detection and could lead to false negative or false positive results. Allele dropouts cannot be excluded.

PANEL INFORMATION
The Hereditary Cancer Panel includes the following genes: APC, ATM, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CDKN2C, CHEK2, EPCAM, FH, FLCN, GREM1, HNF1A, HNF1B, HOXB13, KIT, LZTR1, MAX, MC1R, MEN1, MET, MITF, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NF1, NF2, NTHL1, PALB2, PDGFRA, PMS1, PMS2, POLD1, POLE, POT1, PRSS1, PTCH1, PTCH2, PTEN, RAD50, RAD51C, RAD51D, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCB1, SPRED1, STK11, SUFU, TERT, TMEM127, TP53, TP53BP1, TSC1, TSC2, VHL, WT1, XRCC2, XRCC3

METHOD DESCRIPTION
Total genomic DNA was extracted, DNA quantity and quality was assessed spectrophotometrically and the genomic DNA fragmented followed by DNA library preparation with hybrid capture-based target enrichment followed by sequencing on an Illumina platform. Analysis was performed via Agilent SureCall/VarsomeClinical CE-IVD software with limit of detection of >15%. A proprietary library of sequences from 5,000 individuals from the local population is used to exclude common population variants. The pathogenicity potential of the identified variants is assessed by considering the presence of the variant in the local population and other reference populations, the in silico prediction consequence of the variant, the biochemical properties of the codon change, the degree of evolutionary conservation of the sequence and review of the relevant literature.

(*) The Method is included in the laboratory's scope of accreditation. This is an Electronic Copy

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REMARKS

DIGITAL MLPA

NGS based digital MLPA analysis is utilized to detect CNVs in 30 genes associated with hereditary predisposition to breast, ovarian, colorectal, gastric, prostate, pancreatic, endometrial cancer or melanoma. Target genes included in Digital MLPA: APC, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, GREM1, MITF, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, POLE, PTEN, RAD51C, RAD51D SMAD4, STK11, TP53.

LABORATORY POLICIES

Variants that do not result in an amino acid substitution and common population variants are typically not reported. Likely benign and benign variants are typically not reported. Variants of unknown clinical significance are only reported if found in genes associated with the indication of testing. It is advisable that pathogenic and likely pathogenic variants that establish a molecular diagnosis be confirmed with bidirectional Sanger sequencing in parents and other family members (available upon request). Secondary incidental findings unrelated to the patient's diagnosis are reported according to the ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing unless otherwise instructed by the requesting physician. Bioinformatic reanalysis of the sequencing data and reassessment of the classification of variants of unknown clinical significance is typically not carried out unless requested at least six months after the report date. A reanalysis fee may apply. Results are provided in printed and or electronic form to the requested physician. Results may be forwarded to another physician if requested by the physician in writing. No report will be issued to the patient directly.

Authorised By

Approved Date

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