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Order no.: 62504745
Order received: 27 Aug. 2018
Sample type: blood, EDTA
Sample collection date: 21 Aug. 2018
Report date: 05 Oct. 2018
Report type: Final Report

Patient no.: **1318206**, First Name: **Bani**, Last Name: **Jain**
DOB: **23 Dec. 1992**, Sex: **female**, Your ref.: **MH003152162**

Additional report recipient(s): Dr. Sunil K. Tadepalli, Centogene India PVT. LTD., Management, 107, Wegmans Business Park, Know ledge Park - III, 201308 Surajpar-Kasna Road, Greater Noida, India

Test(s) requested: Clinical Exome Sequencing (CentoDX™)

CLINICAL INFORMATION

Abdominal pain, Abnormal ovarian morphology, Abnormality of neutrophils, Abnormality of the abdominal wall, Abnormality of the lymph nodes, Carcinoma, Cervical lymphadenopathy, Eosinophilia, Intestinal lymphoid nodular hyperplasia, Lymphadenopathy, Mucinous neoplasm, Ovarian cyst, Ovarian papillary adenocarcinoma, Papillary thyroid carcinoma, Squamous Papilloma, Thyroid carcinoma
*: Clinical information indicated above follows HPO nomenclature.

Please note that the quality of the interpretation of patient´s genetic data can be negatively influenced by missing clinical information.

NEGATIVE RESULT

INTERPRETATION

No clinically relevant variant related to the described phenotype has been detected.

RECOMMENDATIONS

- genetic and oncologist counselling

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RESULT SUMMARY

The entire dataset was evaluated for variants clinically relevant to the described phenotype. We did not detect any variant which could be indicative of the genetic diagnosis of your patient. In addition, no pathogenic or likely pathogenic variants were detected that would be insufficient for a genetic diagnosis, but would have led us to recommend further testing (e.g. heterozygous variants in genes related to autosomal recessive disorders). Furthermore, genes related to diseases having substantial overlap with the phenotype of the patient (listed below) were re-evaluated. Again, no clinically relevant variants were identified. Note that pathogenic variants cannot be completely excluded since not all exons were fully covered due to limitations of the method. For these genes, an overall coverage of 99.00% was achieved (>20x), with 1505 missing base pairs (coding region including +/- 2bp).
Please be advised that clinical exome sequencing for diagnostic purposes does not guarantee full coverage for all genes and detection of large deletions/duplications.
Specifically analyzed genes:
Ovarian cancer panel, targeted: BARD1, BRCA1, BRCA2, BRIP1, EPCAM, MLH1, MRE11A, MSH2, MSH6, NBN, PMS1, PMS2, RAD50, RAD51C, RAD51D, STK11, TP53
CentoCancer® panel: APC, ATM, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, FH, FLCN, HNF1A, HNF1B, HOXB13, MC1R, MEN1, MET, MITF, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NTHL1, PALB2, PMS1, PMS2, POLD1, POLE, POT1, PRSS1, PTCH1, PTEN, RAD50, RAD51C, RAD51D, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, TSC1, TSC2, VHL, WT1, XRCC2, XRCC3

INCIDENTAL FINDINGS

Incidental findings which we list according to the ACMG guidelines are not provided here due to the lack of consent.

ANALYSIS STATISTICS FOR THE OFFERED GENES

AVERAGE COVERAGE (X)	% TARGET BP COVERED					
	0X	≥ 1X	≥ 5X	≥ 10X	≥ 20X	≥ 50X
154.19	0.36	99.64	99.38	99.16	98.50	92.01

METHODS

Genomic DNA is enzymatically fragmented and regions of interest are selectively enriched using capture probes targeted against coding regions of ~6700 genes with known clinical significance. Libraries are generated with Illumina compatible adaptors and sequenced on an Illumina platform.
Evaluation is focused on coding exons along with flanking +/-10 intronic bases within the captured region. Due to limitations of the method, the target region is not covered 100%. Raw sequence data analysis, including base calling, demultiplexing, alignment to the hg19 human reference genome (Genome Reference Consortium GRCh37) and variant calling is performed using validated in-house software. Relevant variants reported in HGMD®, in ClinVar or in CentoMD® as well as all variants with minor allele frequency (MAF) of less than 1% in gnomAD database are considered. All pertinent inheritance patterns are considered. In addition, provided family history and clinical information are used to evaluate eventually identified variants. All identified variants are evaluated with respect to their pathogenicity and causality, and these are categorized in classes 1 - 5. All variants related to the phenotype of the patient, except benign or likely benign variants, are reported. Any relevant variant(s) identified by NGS is(are) Sanger sequenced to exclude NGS artefacts. In case, Sanger confirmation for the reported variant is still ongoing, we will only contact you if the results are inconsistent.

LIMITATIONS

Test results are interpreted in the context of clinical findings, family history and other laboratory data. Only variations in genes potentially related to the proband's medical condition are reported. Rare polymorphisms may lead to false negative or positive results. Misinterpretation of results may occur if the information provided is inaccurate or incomplete. If results obtained do not match the clinical findings, additional testing should be considered.
Specific genetic events like copy number variants, translocations and repeat expansions may not be reliably detected with targeted Clinical Exome Sequencing. In addition, due to limitations in technology, certain regions may either not be covered or may be poorly covered, where variants cannot be confidently detected.

ADDITIONAL INFORMATION

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This test was developed and its performance validated by CENTOGENE AG. The US Food and Drug Administration (FDA) has determined that clearance or approval of this method is not necessary and thus neither have been obtained. This test has been developed for clinical purposes. All test results are reviewed, interpreted and reported by our scientific and medical experts.

In line with ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing (Genetics in Medicine, 2016), we report incidental findings, i.e. pathogenic variants (class 1) and likely pathogenic variants (class 2) only in the recommended genes for the recommended phenotypes.

To also exclude mistaken identity in your clinic, several guidelines recommend testing a second sample that is independently obtained from the proband. Please note that any further analysis will result in additional costs.

The classification of variants can change over the time. Please feel free to contact CENTOGENE (customer.support@centogene.com) in the future to determine if there have been any changes in classification of any reported variants.

DISCLAIMER

Any preparation and processing of a sample from patient material provided to CENTOGENE by a physician, clinical institute or a laboratory (by a "Partner") and the requested genetic and/or biochemical testing itself is based on the highest and most current scientific and analytical standards. However, in very few cases genetic or biochemical tests may not show the correct result, e.g. because of the quality of the material provided by a Partner to CENTOGENE or in cases where any test provided by CENTOGENE fails for unforeseeable or unknown reasons that cannot be influenced by CENTOGENE in advance. In such cases, CENTOGENE shall not be responsible and/or liable for the incomplete, potentially misleading or even wrong result of any testing if such issue could not be recognized by CENTOGENE in advance.

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