Kemenkes
RS Sardjito

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Phone (0274) 587333

Patient Identity

Name	:	Referring Clinician	:
Laboratory Number	:	Sampling Date	:
Gender	:	Testing Date	:
DOB	:	Reporting Date	:
Race	:	Referring Institution	:
Specimen Type	:	Testing Laboratory	:
Sample ID	:		

Table notes
Het: Heterozygous
Hom: Homozygous
VUS: Variant of Uncertain Significance

SIFT range: **Deleterious 0.0** – 1.0 Tolerated
PP2 range: Tolerated 0.0 – **1.0 deleterious**

RESULT INTERPRETATION

CONCLUSION

Variants of clinical significance **were found** in the tested sample using the targeted sequencing approach for the **cardiac rare disease** gene panel. For the tested genes and approach used, please find the explanation below in the Methodology section. Further testing would be required to confirm the findings (Please find the below explanation in the Disclaimers and Limitations section).

RECOMMENDATION

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ADDITIONAL INFORMATION

VALIDATED BY

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METHODOLOGY

The genomic library was prepared using the Native Barcoding Kit 24 V14 (SQK-NBD114.24), loaded onto a PromethION Flow Cell R10.4.1 (FLO-PRO114M) and sequenced using the PromethION2Solo platform. Using a targeted next-generation sequencing approach, we use the nanopore adaptive sampling method by Oxford Nanopore Technologies (ONT), which allows real-time enrichment of target regions. A total of 200 curated genes associated with targeted diseases (i.e. muscular dystrophy and cardiovascular rare diseases) were selected based on literature and database sources. The BED file for targeted sequencing was constructed by defining the genomic coordinates of these 200 genes, including flanking regions to ensure comprehensive coverage. This file was then used to guide the adaptive sampling process, focusing sequencing efforts on the selected regions of interest. The bases were uniquely aligned to the Genome Reference Consortium Human Build 38 (GRCh38). Small variant calling was conducted using the wf-human-variation workflow in EPI2ME, and depth of sequencing was measured using mosdepth with the minimum requirement being 30X. While read alignment statistics were assessed with fastcat. Small variant calling, including single nucleotide variants and small insertions/deletions, was performed with Clair3. Variants were annotated using SnpEff with ClinVar data. Pathogenic and likely pathogenic variants relevant to the patient's phenotype were reported. VUS were included at the discretion of the professional clinical teams. Benign and low-quality variants were filtered out. For secondary findings, we follow ACMG SF v3.2 guidelines. The inclusion of secondary findings is optional and based on patient-informed consent.

DISCLAIMERS AND LIMITATIONS

1. Counselling with a Genetic Counsellor and/or the referring Clinician is required to help comprehend the results and interpretation in this report.
2. The results were interpreted based on the provided specimen, clinical information, family history, and multidisciplinary team discussion. If the information provided is incorrect or insufficient, the test may result in suboptimal data.
3. The variant classification and interpretation derived from the mentioned databases are based on the current available scientific, medical information, and technology. Please see below in the References section for the references and/or database versions used. Consequently, the variant classification and interpretation within this report might change in the future due to advancements within the field.
4. There is a possibility that the genomic region(s) where the disease-causing variant exists was not captured or sequenced with sufficient quality. Additionally, disorders due to GC-rich sequences, mitochondrial variants with low heteroplasmy levels, low-level mosaicism, epigenetic, and large aberrations such as nucleotide repeat expansion or contraction, repetitive homologous region, high-homology region, heterozygous CNVs less than three exons may not be reliably detected and warrants further validations able to capture such aberrations.
5. A case of negative result with no variants of clinical significance detected does not rule out the possibility of the patient having genetic aetiology for the suspected clinical manifestations found.

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REFERENCES

1. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genetics in Medicine. 2015 May;17(5):405–24.
2. Resources and databases versions used:
    - OMIM
    - ClinVar
    - gnomAD
    - dbSNP
    - SIFT
    - PolyPhen2
3.