GENEVOLVE
Genomics Division

Name	:	**ABCD**	**Age**	:	**00 Years**
Lab No.	:	**000000000**	**Gender**	:	**XYZ**
Ref by	:	**UNKNOWN**	**Reported**	:	**01/12/2023 15:32:44**
Collected	:	**03/11/2023 00:11:00**	**Report Status**	:	**Final**
A/c Status	:	**P**			
Collected at	:	**LPL – SUNSHINE HEALTHCARE LIMITED**	**Processed at**	:	**LPL-NATIONAL REFERENCE LAB National Reference laboratory, Block E, Sector 18, Rohini, New Delhi -110085**

CARRIER SCREENING (420 GENES)

CLINICAL DETAILS

00-years-old male tested for screening purpose.

RESULT SUMMARY

A Hemizygote variant detected in *G6PD* and Pathogenic variant detected in *HBB* gene.

VARIANT TABLE

GENE	GENOMIC LOCATION	VARIANT	TYPE	ZYGOSITY	CONDITION/ PHENOTYPE GROUP	CLASSIFICATION
G6PD	chrX:154535277	(NM_000402.4):c.466A>G; p.Asn156Asp	Missense	Hemizygote	G6PD deficiency, Hemolytic anemia	Conflicting interpretations of pathogenicity
HBB	chr11:5227002	(NM_000518.5):c.20A>T; p.Glu7Val	Missense	Carrier	Thalassemias, beta	Pathogenic

RECOMMENDATIONS

- Genetic counselling is recommended to discuss the implications of this test result for this family. For assistance for genetic counselling, please contact LPL Client services.
- Test results should be interpreted in the context of this individual's clinical history.
- This result is for screening purpose only. The variants detected in this individual are not diagnostic and need to be correlated with clinical / Therapeutic details and other laboratory parameters.
- Confirmatory testing advised SNV/CNV.

CONCLUSION – Gene and disease association

G6PD deficiency, Hemolytic anemia

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a condition in which red blood cells break down when the body is exposed to certain drugs or the stress of infection. It is an X-linked recessive condition. Red blood cell destruction can be triggered by infections, certain foods (such as fava beans), and certain medicines, including: Antimalarial medicines such as quinine, high doses of Aspirin.

Thalassemia, beta

Beta thalassemia is a blood disorder that reduces the production of hemoglobin. Low levels of hemoglobin lead to a lack of oxygen in many parts of the body. Affected individuals also have a shortage of red blood cells (anemia), which can cause pale skin, weakness, fatigue, and more serious complications.

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TEST METHODOLOGY

Ion AmpliSeq targeted sequencing is used to analyze 14,044 amplicons covering the coding regions (CDS) of 420 genes including +/-25 bp flanking intron/exon boundaries, as well as selected intergenic, intronic and homologous regions. Note that the CDS regions were defined either by specific transcript or a combination of multiple transcripts. The targeted regions are sequenced with the aim to achieve a uniformity of ≥93%, aq20 mean read length of >155 basepairs, and coverage of >200X with the reads are aligned to human genome assembly GRCh38 (hg38). Targeted regions assess the potential of >28,530 putative carrier single nucleotide variants (SNVs) and insertion/deletions (indels) from the ClinVar archive of human variation and privately curated non-public variant sources. Variant calling is subject to quality control metrics including low read coverage. Variant calling of indels is limited in regions of homopolymer lengths of greater than eight nucleotides. Variant detection issues are possible in regions with low sequence complexity, large regional copy number changes, large indels, and regions with high homology to other genomic loci. Detection rates will be determined using analytical sensitivity, literature estimates for the disease allele contribution, and population frequency predictions. If variants have not been previously described in the literature, the detection rate might not be reported. Further, detection rates do not take into account the disease-specific rates of de novo mutation.

GENE LIST

AAAS	*ACADS*	*AGL*	*AMH*	*ASNS*	*BBS10*	*BRIP1*	*CEP290*	*CLN8*	*CPT1A*	*CYP11B2*	*DHCR7*	*DPYD*	*ERCC4*
ABCA12	*ACADSB*	*AGPS*	*AMHR2*	*ASPA*	*BBS12*	*BSND*	*CERKL*	*CLRN1*	*CPT2*	*CYP17A1*	*DHDDS*	*DYSF*	*ERCC5*
ABCA4	*ACADVL*	*AGXT*	*AMT*	*ASS1*	*BBS2*	*BTD*	*CFTR*	*CNGA3*	*CRB1*	*CYP19A1*	*DKC1*	*EDA*	*ERCC6*
ABCB11	*ACAT1*	*AIRE*	*AP1S1*	*ATM*	*BBS4*	*BTK*	*CHM*	*CNGB3*	*CTNS*	*CYP1B1*	*DLD*	*EDAR*	*ERCC8*
ABCB4	*ACOX1*	*ALDH3A2*	*AQP2*	*ATP6V1B1*	*BBS9*	*CANT1*	*CHRNE*	*COL11A2*	*CTSC*	*CYP21A2*	*DMD*	*EIF2AK3*	*ESCO2*
ABCC6	*ACSF3*	*ALDH7A1*	*AR*	*ATP7A*	*BCHE*	*CAPN3*	*CHRNG*	*COL4A3*	*CTSD*	*CYP27A1*	*DNAH5*	*EIF2B5*	*ETFA*
ABCC8	*ADA*	*ALDOB*	*ARG1*	*ATP7B*	*BCKDHA*	*CASQ2*	*CIITA*	*COL4A4*	*CTSK*	*CYP27B1*	*DNAI1*	*IKBKAP*	*ETFB*
ABCD1	*ADAMTS2*	*ALG6*	*ARSA*	*ATP8B1*	*BCKDHB*	*CBS*	*CLN3*	*COL4A5*	*CYBA*	*DBT*	*DNAI2*	*EMD*	*ETFDH*
ACAD9	*ADGRG1*	*ALMS1*	*ARSB*	*ATRX*	*BCS1L*	*CC2D1A*	*CLN5*	*COL7A1*	*CYBB*	*DCLRE1C*	*DNAL1*	*ERCC2*	*ETHE1*
ACADM	*AGA*	*ALPL*	*ASL*	*BBS1*	*BLM*	*CDH23*	*CLN6*	*CPS1*	*CYP11B1*	*DDB2*	*DOK7*	*ERCC3*	*EVC*
EVC2	*FANCC*	*GALK1*	*GFM1*	*GLE1*	*GUCY2D*	*HFE*	*HPS3*	*IVD*	*LIFR*	*MCCC2*	*MLYCD*	*MTHFR*	*NDRG1*
EXOSC3	*FANCG*	*GALNS*	*GH1*	*GNE*	*GUSB*	*HFE2*	*HPS4*	*KCNJ11*	*LIPA*	*MCOLN1*	*MMAA*	*MTM1*	*NDUFAF5*
EYS	*FH*	*GALNT3*	*GHRHR*	*GNPTAB*	*HADHA*	*HGD*	*HSD17B3*	*LAMA2*	*LIPH*	*MECP2*	*MMAB*	*MTRR*	*NDUFS4*
F11	*FKRP*	*GALT*	*GJB1*	*GNPTG*	*HADHB*	*HGSNAT*	*HSD17B4*	*LAMA3*	*LOXHD1*	*MED17*	*MMACHC*	*MTTP*	*NDUFS6*
F2	*FKTN*	*GAMT*	*GJB2*	*GNS*	*HAX1*	*HLCS*	*HSD3B2*	*LAMB3*	*LPL*	*MEFV*	*MMADHC*	*MUT*	*NEB*
F8	*G6PC*	*GBA*	*GJB3*	*GORAB*	*HBA1*	*HMGCL*	*HYLS1*	*LAMC2*	*LRPPRC*	*MESP2*	*MOCS1*	*MYO15A*	*NEU1*
F9	*G6PD*	*GBE1*	*GJB6*	*GP1BA*	*HBA2*	*HMOX1*	*IDS*	*LCA5*	*LYST*	*MFSD8*	*MPI*	*MYO7A*	*NLRP7*
FAH	*GAA*	*GCDH*	*GLA*	*GP1BB*	*HBB*	*HOGA1*	*IDUA*	*LDLR*	*MAN2B1*	*MKKS*	*MPL*	*NAGLU*	*NPC1*
FAM161A	*GALC*	*GCH1*	*GLB1*	*GP9*	*HEXA*	*HPD*	*IL2RG*	*LDLRAP1*	*MAT1A*	*MKS1*	*MPV17*	*NAGS*	*NPC2*
FANCA	*GALE*	*GDF5*	*GLDC*	*GRHPR*	*HEXB*	*HPS1*	*ITGB3*	*LHCGR*	*MCCC1*	*MLC1*	*MRE11*	*NBN*	*NPHP1*
NPHS1	*PANK2*	*PEX10*	*PMM2*	*PSAP*	*RLBP1*	*SBDS*	*SLC17A5*	*SLC37A4*	*SMPD1*	*TECPR2*	*TRIM37*	*TYR*	*VRK1*
NPHS2	*PC*	*PEX12*	*PNPO*	*PTS*	*RMRP*	*SEPSECS*	*SLC19A2*	*SLC39A4*	*SRD5A2*	*TFR2*	*TRMU*	*TYRP1*	*VSX2*
NR0B1	*PCCA*	*PEX2*	*POLG*	*PUS1*	*RNASEH2C*	*SERPINA1*	*SLC22A5*	*SLC3A1*	*ST3GAL5*	*TGM1*	*TSEN54*	*UGT1A1*	*VWF*
NR3C2	*PCCB*	*PEX6*	*POMC*	*PYGM*	*RPE65*	*SGCA*	*SLC25A13*	*SLC40A1*	*STAR*	*TH*	*TSFM*	*UNC13D*	*WAS*

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Web: www.lalpathlabs.com, **CIN:** L74899DL1995PLC065388

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							A13	*2*					
NTRK1	*PCDH15*	*PEX7*	*POMGNT1*	*RAB23*	*RPGRIP1L*	*SGCB*	*SLC25A15*	*SLC4A11*	*STRC*	*TMC1*	*TSHB*	*USH1C*	*WISP3*
OAT	*PDHA1*	*PFKM*	*POR*	*RAG1*	*RS1*	*SGCD*	*SLC25A20*	*SLC6A8*	*SUCLA2*	*TMEM216*	*TSHR*	*USH2A*	*WNT10A*
OCRL	*PDHB*	*PHGDH*	*PPT1*	*RAG2*	*RTEL1*	*SGCG*	*SLC26A2*	*SLC7A7*	*SUMF1*	*TPO*	*TTC37*	*VPS13A*	*WRN*
OPA3	*PEPD*	*PIGN*	*PREPL*	*RAPSN*	*SACS*	*SGSH*	*SLC26A3*	*SLC7A9*	*SURF1*	*TPP1*	*TTN*	*VPS13B*	*XPA*
OTC	*PET100*	*PKHD1*	*PROP1*	*RARS2*	*SAMD9*	*SLC12A3*	*SLC26A4*	*SMARCAL1*	*TAT*	*TREX1*	*TTPA*	*VPS45*	*XPC*
PAH	*PEX1*	*PLA2G6*	*PRPS1*	*RDH12*	*SAMHD1*	*SLC12A6*	*SLC35A3*	*SMN1*	*TCIRG1*	*TRIM32*	*TYMP*	*VPS53*	*ZFYVE26*

VARIANT CLASSIFICATION (BASED ON ACMG RECOMMENDATIONS)

Pathogenic	A genetic variant that causes, increases or contributes to an individual's disease or disorder.
Likely pathogenic	A genetic variant is most likely responsible for causing disease or disorder, but need additional scientific evidence to be certain.
Variant of uncertain significance (VUS)	A variant that has unknown effect in the development of disease or disorder and not be enough scientific evidence to confirm or refute a disease association or the study may be inconsistent.
Likely benign	A variant is not responsible, expected, or probable to major cause disease, but need additional scientific evidence to be certain.
Benign	A variant is not a cause / responsible for a disease or disorder.

VARIANT CALLING

SNV/indels

Variants with evidentiary support for inherited disorders using ClinVar and privately curated non-public variant sources will be reported. In addition, variants predicted to have a negative impact on gene function will be reported using modified variant classifications according to the American College of Medical Genetics and Genomics (ACMG) pathogenic criteria (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4544753/) evaluated as very strong (PVS1), strong (PS1), and benign criterion evaluated as stand-alone (BA1).

When PVS1 criteria are met, the variant will be classified as "predicted to be pathogenic." If PVS1 criteria are not met and PS1 classification is achieved, the variant will be classified as "predicted to be likely pathogenic."

Using database population frequency estimates, when the criterion for BA1 is met and PVS1 and PS1 are not, the variant will be classified as "predicted to be benign."

Finally, if all criteria are not achieved or found true for both PVS1\PS1 and BA1, the variant will be classified as a variant of unknown significance (VOUS).

Copy Number Variant (CNV) analysis

A read depth-based copy number analysis is used to analyze the amplicons targeting coding regions of the genes, as well as selected intergenic and intronic regions. CNV deletions will be classified ""predicted to be likely pathogenic"" and duplications are classified as VOUS. The precise breakpoints of large deletions in the target genes and intergenic regions cannot be

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determined, but are estimated from copy number analysis. Copy number calling requires three or more amplicons but algorithmic sensitivity to the single exon-level CNVs can be dependent on the coverage of the neighboring region, amplicon proximity, and the size of the CNV event. Given the algorithmic requirements, a 1 kilobase CNV deletion in the focused CNV genes (30 targets) could potentially be detected in a single coding region segment with the exception of *USH2A* (CDS5); *SLC3A1* (CDS9); *PREPL* (CDS2); *NEB* (CDS74,82-85,91-93,98-101,160); *VPS13A* (CDS74); *FANCC* (CDS11); *ATM* (CDS11,42); *PAH* (CDS1,10); *GALC* (CDS1); *HEXA* (CDS1); *CLN3* (CDS7); *ITGB3* (CDS15); *SAMHD1* (CDS1); *DMD* (CDS1, 8, 18, 26, 66, 83, 85); *GLA* (CDS4) Copy number event and variant analysis will be considered jointly for the genes GJB2 and GJB6, in the case of one parent with GJB2 mutation and one parent with GJB6 deletion mutation a risk state warning is issued. Genes that have closely related pseudogenes, highly related paralogues, or other homology-related issues may be addressed by different analysis methods (see special case gene analysis). Special algorithms are used to detect variants in SMN1, CYP21A2, HBA1/2, GBA.

REPORTING VARIANTS or PRIORITIZATION

Variants are annotated using ClinVar and user-defined databases. Variants are classified according to the standards and guidelines for sequence variant interpretation established by the ACMG. Reported variant classifications are pathogenic and likely pathogenic. Reporting of VOUS is user-determined. Likely benign and benign variants are not reported. It is recommended to include user-defined variant reporting information in the lab comment section of the report.

All results must always be interpreted in the context of familial, ancestral, and disease data.

DISCLAIMER

Any preparation and processing of a sample from patient material provided to GENEVOLVE 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 GENEVOLVE or in cases where any test provided by GENEVOLVE fails for unforeseeable or unknown reasons that cannot be influenced by GENEVOLVE in advance. In such cases, GENEVOLVE 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 GENEVOLVE in advance.

This report provides information about the patient's mutations that may aid the physician’s decision making process, but this test should not be the sole source of information for making decisions on patient care and treatment. These tests should be interpreted in the context of standard clinical, laboratory, and pathological findings. Identification of a mutation in one or more of these genes does not guarantee activity of the drug in a given indication. Insertions and deletions greater than 20bp in size may not be detected by this assay. Mutations in the intronic regions have not been included in this report.

The test should not be used for detection of complex genetic events such as inversions, translocations and for analysis of sequence. In addition, due to technology limitations, certain regions may be either not or poorly covered. In these regions variants cannot be confidently detected. Extremely low coverage calls are expected to be artifacts based on our extensive validations and consequently are not considered during the analysis. Misinterpretation of results may occur if the provided information is inaccurate and/or incomplete. If the obtained genetic results do not concur with the clinical findings, additional testing should be considered.

The information provided in this report was collected from various sources that we believe to be reliable and quality control procedures have been put in place to ensure the information provided is as accurate, comprehensive, and current as possible. The information provided should only be utilized as a guide or aid and the decision to select any therapy option based on the information reported here resides solely with the discretion of the treating physician. Patient care and treatment decisions should only be made by the physician after taking into account all relevant information available including but not limited to the patient’s condition, family history, findings upon examination, results of other diagnostic tests, and the current standards of care. This report should only be used as an aid and the physician should employ clinical judgment in arriving at any decision for patient care or treatment.

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RAW DATA

A table with additional variant filtering details can be provided with the raw data (if requested).

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IMPORTANT INSTRUCTIONS

Test results released pertain to the specimen submitted. All test results are dependent on the quality of the sample received by the Laboratory. Laboratory investigations are only a tool to facilitate in arriving at a diagnosis and should be clinically correlated by the Referring Physician . Report delivery may be delayed due to unforeseen circumstances. Inconvenience is regretted . Certain tests may require further testing at additional cost for derivation of exact value. Kindly submit request within 72 hours post reporting. Test results may show interlaboratory variations . The Courts/Forum at Delhi shall have exclusive jurisdiction in all disputes /claims concerning the test(s) & or results of test(s). Test results are not valid for medico legal purposes. This is computer generated medical diagnostic report that has been validated by Authorized Medical Practitioner /Doctor. The report does not need physical signature.
(#) Sample drawn from outside source.
If Test results are alarming or unexpected, client is advised to contact the Customer Care immediately for possible remedial action.
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