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MedGenome Labs Ltd
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HLA TYPING REPORT

HLA TYPING REPORT			
Patient information		**Donor information**	
Patient Name	**Ankush Kumar**	Donor name	**Shubham kumar**
Order ID/Sample ID	**906833/8443131**	Order ID/Sample ID	**906833/8443132**
Gender	**Male**	Gender	**Male**
Age / Relationship	**3 Years / Son**	Age / Relationship	**27 Years / Father**
Sample type	**Peripheral Blood in EDTA**	Sample type	**Peripheral Blood in EDTA**
Collection date & time	**09-04-2024 20:50:00**	Collection date & time	**09-04-2024 16:26:00**
Receipt date & time	**10-04-2024 11:12:00**	Receipt date & time	**10-04-2024 11:12:00**
Report date & time	**20-04-2024 12:02:30**		
Clinical indication			
Test Requested	**MGM1348 - HLA Typing High resolution (A*, B*, C*, DRB1*, DQB1*, DPB1*)**		
Requested by	**Dr. Mukesh Dhankar, Kalawati Saran Children's Hospital- Delhi (Delhi)**		

TYPING RESULT						
LOCUS	**HLA-A***	**HLA-B***	**HLA-C***	**HLA-DRB1***	**HLA-DQB1***	**HLA-DPB1***
Ankush Kumar (Patient)						
HLA-CLASS I & II	**A*11:01:01G**	**B*35:01:01G**	**C*04:01:01G**	**DRB1*07:01:01G**	**DQB1*03:03:02G**	**DPB1*02:01:02G**
	A*33:03:01G	**B*52:01:01:01**	**C*12:02:02:01**	**DRB1*14:04:01G**	**DQB1*05:03:01G**	**DPB1*02:01:02G**
Shubham kumar (Donor I) 27 Years/Male- Father of Ankush Kumar(906833/8443132)						
HLA-CLASS I & II	**A*11:01:01G**	**B*52:01:01:01**	**C*01:02:01G**	**DRB1*11:01:01G**	**DQB1*03:01:01G**	**DPB1*02:01:02G**
	A*33:03:01G	**B*55:01:01G**	**C*12:02:02:01**	**DRB1*14:04:01G**	**DQB1*05:03:01G**	**DPB1*03:01:01G**

Comment

G code: G code is a group of alleles that have identical nucleotide sequences in the antigen recognition site. Allele Database Version used in the report is 3.52 & Software version is 2.30.1.29498 Refer Appendix-I for G-Groups and NMDP (National Marrow Donor Program) codes.

Interpretation

The HLA typing of Ankush Kumar (Patient) and Shubham kumar (Potential donor) shows 07/12 allele match (100% match at A* locus, whereas 50% match at B*, C*, DRB1*, DQB1* and DPB1* locus).

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DNA TEST REPORT - MEDGENOME LABS

Full Name / Ref No:	**ANKUSH**	Order ID/Sample ID:	**870359/8375123**
Gender:	Male	Sample Type:	Blood
Date of Birth / Age:	3 years	Date of Sample Collection:	28th February 2024
Referring Clinician:	Dr. Sunil Gomber, Dr Baba Saheb Ambedkar Hospital, New Delhi	Date of Sample Receipt:	29th February 2024
		Date of Order Booking:	29th February 2024
		Date of Report:	3rd April 2024
Test Requested:	**Whole Exome Sequencing (Subsidised test)**		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

Baby *Ankush*, presented with clinical indications of aplastic anemia. He has been evaluated for pathogenic variations.

RESULTS

PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

SNV(s)/INDELS

Gene# (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification$
THPO **(-)** **(ENST00000647395.1)**	Exon 5	c.295C>T **(p.Arg99Trp)**	Homozygous	Congenital amegakaryocytic thrombocytopenia-2 (OMIM#620481)	Autosomal recessive	Pathogenic **(PS4, PS3, PM2, PP3)**

COPY NUMBER VARIANTS CNV(s)

No significant CNVs for the given clinical indications that warrants to be reported was detected.

VARIANT INTERPRETATION AND CLINICAL CORRELATION

Variant description: A homozygous missense variant in exon 5 of the ***THPO*** gene **(chr3:g.184373516G>A; Depth: 211x)** that results in the amino acid substitution of Tryptophan for Arginine at codon 99 **(p.Arg99Trp; ENST00000647395.1)** was detected (Table). The observed variant has previously been reported in patients affected with Heritable thrombocytopenia and experimental studies have shown that this missense change affects THPO function [PMID: 32150607]. The variant has been classified as pathogenic by ClinVar database. The variant has not been reported in the 1000 genomes, gnomAD (v3.1), gnomdAD (v2.1) and topmed databases and has a minor allele frequency of 0.007% in our internal database. The *in-silico* predictions# of the variant are damaging by PolyPhen-2 (HumDiv), SIFT and LRT. The reference codon is conserved across species.

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OMIM phenotype: Congenital amegakaryocytic thrombocytopenia-2 (OMIM#620481) is caused by homozygous or compound heterozygous mutation in the *THPO* gene (OMIM*600044). This disorder is characterized by thrombocytopenia with progression to pancytopenia, aplastic anemia, and bone marrow failure. Serum THPO is decreased or inappropriately normal, and bone marrow is hypocellular with decreased or absent megakaryocytes. Most patients present in infancy or early childhood and have a severe disease course, whereas some have later onset and milder symptoms. Bone marrow transplant is ineffective because the defect is extrinsic to hematopoietic cells [PMID: 18842627].

Based on the above evidence[$], ***this THPO variation is classified as a pathogenic variant and has to be carefully correlated with the clinical symptoms.***

The significance/classification of the variant(s) may change based on the genetic testing in parents and other family members.

ADDITIONAL INFORMATION

- No other SNV(s)/INDELS or CNV(s) that warrants to be reported were detected. All the genes covered in this assay have been screened for the given clinical indications. To view the coverage of all genes Click here. NGS test methodology details of this assay are given in the appendix.
- [$]Genetic test results are reported based on the recommendations of American College of Medical Genetics and Genomics (ACMG) [PMID: 25741868, 31690835, 32906214].
- With regard to ACMG recommendations for reporting of incidental findings in whole exome and genome sequencing (PMID: 35802134; ACMG SF v3.1), we report significant pathogenic and/ or likely pathogenic variants in the recommended genes for the recommended phenotypes, only if informed consent is given by the patient.
- Please write an email to genetic.counseling@medgenome.com in case you need assistance for genetic counselling. For any further technical queries please write an email to techsupport@medgenome.com

RECOMMENDATIONS

- Sequencing the variant(s) in the parents and the other affected and unaffected members of the family is recommended to confirm the significance.
- Genetic counselling is advised for interpretation on the consequences of the variant(s).
- If results obtained do not match the clinical findings, additional testing should be considered as per referring clinician's recommendations.
- The sensitivity of NGS assay to detect copy number variants (CNV) is 70-75%. We recommend discussing alternative testing methodology options with MedGenome Tech Support (techsupport@medgenome.com) as required. In case clinician is suspecting CNV as an important genetic etiology, alternate tests like microarray/ MLPA or qPCR may be considered after discussing with the MedGenome TechSupport team.

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Senior Molecular Pathologist & Clinical Head

APPENDIX

TEST METHODOLOGY

Targeted gene sequencing: Selective capture and sequencing of the protein coding regions and clinically relevant in the genome is performed. Variants identified in the exonic regions and splice-site are generally actionable compared to variants that occur in non-coding regions. Targeted sequencing represents a cost-effective approach to detect variants present in multiple/large genes in an individual.

DNA extracted from blood was used to perform targeted gene capture using a custom capture kit. The libraries were sequenced to mean depth of >80-100X on Illumina sequencing platform. We follow the GATK best practices framework for identification of germline variants in the sample using Sentieon [Sentieon]. The sequences obtained are aligned to human reference genome (GRCh38) using BWA aligner [Sentieon, PMID:20080505] and analyzed using Sentieon for removing duplicates, recalibration and re-alignment of indels [Sentieon]. Sentieon haplotype caller is then used to identify variants in the sample. The germline variants identified in the sample is deeply annotated using VariMAT pipeline. Gene annotation of the variants is performed using VEP program [PMID: 20562413] against the Ensembl release 104 human gene model [PMID: 34791404]. In addition to SNVs and small Indels, copy number variants (CNVs) are detected from targeted sequence data using the ExomeDepth method [PMID: 22942019]. This algorithm detects CNVs based on comparison of the read-depths in the sample of interest with the matched aggregate reference dataset.

Clinically relevant mutations in both coding and non-coding regions are annotated using published variants in literature and a set of diseases databases : ClinVar, OMIM, HGMD, LOVD, DECIPHER (population CNV) and SwissVar [PMID: 26582918, 18842627, 28349240, 21520333, 19344873, 20106818]. Common variants are filtered based on allele frequency in 1000Genome Phase 3, gnomAD (v3.1 & 2.1.1), dbSNP (GCF_000001405.38), 1000 Japanese Genome, TOPMed (Freeze_8), Genome Asia, and our internal Indian population database (MedVarDb v4.0) [PMID: 26432245, 32461613, 11125122, 26292667, 33568819, 31802016]. Non-synonymous variants effect is calculated using multiple algorithms such as PolyPhen-2, SIFT, MutationTaster2 and LRT. Clinically significant variants are used for interpretation and reporting.

Average sequencing depth (x)	Average on-target sequencing depth (x)	Percentage target base pairs covered		
		0x	≥5x	≥20x
391	145.03	0.29	99.53	99.09

Total data generated (Gb)	14.34
Total reads aligned (%)	99.99
Reads that passed alignment (%)	90.28
Data ≥Q30 (%)	98.72

$The classification of the variants is done based on American College of Medical Genetics as described below [PMID: 25741868].

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Variant	A change in a gene. This could be disease causing (pathogenic) or not disease causing (benign).
Pathogenic	A disease causing variant in a gene which can explain the patient's symptoms has been detected. This usually means that a suspected disorder for which testing had been requested has been confirmed.
Likely Pathogenic	A variant which is very likely to contribute to the development of disease however, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion of pathogenicity.
Variant of Uncertain Significance	A variant has been detected, but it is difficult to classify it as either pathogenic (disease causing) or benign (non-disease causing) based on current available scientific evidence. Further testing of the patient or family members as recommended by your clinician may be needed. It is probable that their significance can be assessed only with time, subject to availability of scientific evidence.

#The transcript used for clinical reporting generally represents the canonical transcript (MANE Select), which is usually the longest coding transcript with strong/multiple supporting evidence. However, clinically relevant variants annotated in alternate complete coding transcripts could also be reported.

Variants annotated on incomplete and nonsense mediated decay transcripts will not be reported.

#The *in-silico* predictions are based on Variant Effect Predictor (v104), [SIFT version - 5.2.2; PolyPhen - 2.2.2; LRT version (November, 2009); CADD (v1.6); Splice AI; dbNSFPv4.2] and MutationTaster2 predictions are based on NCBI/Ensembl 66 build (GRCh38 genomic coordinates are converted to hg19 using UCSC LiftOver and mapped to MT2).

Diseases databases used for annotation includes ClinVar (updated on 17042023), OMIM (updated on 01092023), HGMD (v2023.1), LOVD (Nov-18), DECIPHER (population CNV) and SwissVar.

LIMITATIONS

- Genetic testing is an important part of the diagnostic process. However, genetic tests may not always give a definitive answer. In some cases, testing may not identify a genetic variant even though one exists. This may be due to limitations in current medical knowledge or testing technology. Accurate interpretation of test results may require knowing the true biological relationships in a family. Failing to accurately state the biological relationships in {my/my child's} family may result in incorrect interpretation of results, incorrect diagnoses, and/or inconclusive test results.
- Test results are interpreted in the context of clinical findings, family history and other laboratory data. Only variants 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.
- Specific events like copy number variants, translocations, repeat expansions and chromosomal rearrangements may not be reliably detected with whole exome sequencing. Variants in untranslated region, promoters and intronic variants are not assessed using this method.
- Genetic testing is highly accurate. Rarely, inaccurate results may occur for various reasons. These reasons include, but are not limited to: mislabeled samples, inaccurate reporting of clinical/medical information, rare technical errors or unusual circumstances such as bone marrow transplantation, blood transfusion; or the presence of change(s) in such a small percentage of cells that may not be detectable by the test (mosaicism).
- The variant population allele frequencies and in silico predictions for GRCh38 version of the Human genome is obtained after lifting over the coordinates from hg19 genome build. The existing population allele frequencies (1000Genome,

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Sample No 0007 ANKUSH UZC
Patient ID
Name
Sample Comment

Ward

Position
Doctor
Birth
Nickname

Positive

Diff Morph. Count

WBC	3.34	[10^3/uL]
RBC	2.15	[10^6/uL]
HGB	6.3	[g/dL]
HCT	18.6	[%]
MCV	86.5	[fL]
MCH	29.3	[pg]
MCHC	33.9	[g/dL]
PLT	10 *	[10^3/uL]
RDW-SD	48.4	[fL]
RDW-CV	15.5	[%]
PDW	10.8	[fL]
MPV	9.2	[fL]
P-LCR	19.9	[%]
PCT	0.01	[%]
NRBC	0.01	[10^3/uL]
NEUT	0.24 *	[10^3/uL]
LYMPH	2.91 *	[10^3/uL]
MONO	0.17 *	[10^3/uL]
EO	0.02	[10^3/uL]
BASO	0.00	[10^3/uL]
IG	0.02 *	[10^3/uL]
RET		[%]
IRF		[%]
LFR		[%]
MFR		[%]
HFR		[%]
RET-He		[pg]
IPF		[%]

	0.3	[%]
	7.2	[%]
	87.1	[%]
	5.1	[%]
	0.6	[%]
	0.0	[%]
	0.6	[%]

[10^6/uL]

WBC-BF	[10^3/uL]
RBC-BF	[10^6/uL]
MN	[10^3/uL]
PMN	[10^3/uL]
TC-BF#	[10^3/uL]

[%]
[%]

WBC IP Message
Neutropenia
Blasts/Abn Lympho?
Atypical Lympho?

RBC IP Message
Anemia

PLT IP Messa
Thrombocytop

WDF

RET

RBC

Kindly send peripheral
Evaluation

EMERGENCY LAB
CHILDREN HOSPITAL NEW DELHI

Specimen ID: 15
Patient ID: 7674
First Name: ANKUSH

Test: CD
Gender: M
Last Name: -

Specimen: WB

Run Date/Time: 02/04/2026 09:25 PM
Collection:
Location: U2
Comments: Checked Typical

Date of Birth:
Age:
Sequence #: 11144
Physician:
Kindly Correlate clinically

Test	Result	Flags	Units	Low	High
WBC	4.46	R	x10³/µL	3.71	10.67
LY	36.1	RH	%	18.94	46.71
MO	5.06	R	%	4.88	12.81
NE	5.16	RI	%	40.62	71.65
EO	0.45	RI	%	0.74	6.73
BA	0.15	R	%	0.05	0.48
LY#	3.93	RH	x10³/µL	1.15	3.52
MO#	0.23	R	x10³/µL	0.25	0.99
NE#	2.31	RI	x10³/µL	1.85	6.72

Test	Result	Flags	Units	Low	High
RBC	1.90	L	x10⁶/µL	3.87	5.68
HGB	5.50	L	g/dL	12.00	16.75
HCT	15.9	L	%	35.1	48.7
MCV	83.8		fL	78.4	97.6
MCH	29.1		pg	26.5	33.5
MCHC	34.7		g/dL	32.9	35.4
RDW	15.0		%	12.7	15.6
RDW-SD	43.6		fL	38.9	49.0
PLT	1.8	-R	x10³/µL	150.5	366.8

Messages

Abnormal Diff
Cellular Interference
Suspect Diff