Blueprint Genetics

Sample report as of June 14, 2022. Regional differences may apply. For complete and up-to-date test methodology description, please see your report in Nucleus online portal. Accreditation and certification information available at ***blueprintgenetics.com/certifications***

My Retina Tracker Program Panel Plus

REFERRING HEALTHCARE PROFESSIONAL

NAME **HOSPITAL**

PATIENT

NAME **DOB** **AGE** **GENDER** **ORDER ID**

Male

PRIMARY SAMPLE TYPE **SAMPLE COLLECTION DATE** **CUSTOMER SAMPLE ID**

SUMMARY OF RESULTS

PRIMARY FINDINGS

The patient is hemizygous for *RPGR* c.2817_2818del, p.(Glu940Argfs*138), which is pathogenic.

PRIMARY FINDINGS: SEQUENCE ALTERATIONS

GENE	TRANSCRIPT	NOMENCLATURE	GENOTYPE	CONSEQUENCE	INHERITANCE	CLASSIFICATION
RPGR	NM_001034853.2	c.2817_2818del, p.(Glu940Argfs*138)	HEM	frameshift_variant	X-linked	**Pathogenic**
	ID	**ASSEMBLY**	**POS**	**REF/ALT**		
		GRCh37/hg19	X:38145433	TCC/T		
					PHENOTYPE	
	gnomAD AC/AN	**POLYPHEN**	**SIFT**	**MUTTASTER**	Cone-rod dystrophy, X-linked, 1, Macular degeneration, X-linked atrophic, Retinitis pigmentosa, Retinitis pigmentosa 3	
	0/0	N/A	N/A	N/A		

SEQUENCING PERFORMANCE METRICS

PANEL	GENES	EXONS / REGIONS	BASES	BASES > 20X	MEDIAN COVERAGE	PERCENT > 20X
My Retina Tracker Program Panel Plus	314	4998	989155	986087	217	99.69

PANEL	GENES	EXONS / REGIONS	BASES	BASES > 1000X	MEDIAN COVERAGE	PERCENT > 1000X
Mitochondrial genome	37	-	15358	15358	17182	100

TARGET REGION AND GENE LIST

The Blueprint Genetics My Retina Tracker Program Panel Plus Analysis includes sequence analysis and copy number variation analysis of the following genes: *ABCA4*, *ABCC6**, *ABCD1**, *ABHD12*, *ACO2*, *ADAM9*, *ADAMTS18*, *ADGRV1*, *ADIPOR1**, *AGBL5*, *AHI1*, *AIPL1*, *ALMS1**, *AMACR*, *ARHGEF18*, *ARL13B*, *ARL2BP*, *ARL3*, *ARL6*, *ARMC9*, *ARR3*, *ARSG*, *ATF6*, *ATOH7*, *B9D1*, *B9D2*, *BBIP1*, *BBS1*, *BBS10*, *BBS12*, *BBS2*, *BBS4*, *BBS5*, *BBS7*, *BBS9*, *BEST1*, *C1QTNF5*, *C21ORF2*, *C2ORF71*, *C5ORF42*, *C8ORF37*, *CA4*, *CABP4*, *CACNA1F*, *CACNA2D4*, *CAPN5*, *CC2D2A#*, *CDH23*, *CDH3*, *CDHR1*, *CEP104*, *CEP120*, *CEP164*, *CEP19*, *CEP250*, *CEP290**, *CEP41*, *CEP78*, *CEP83*, *CERKL*, *CHM#*, *CIB2*, *CISD2**, *CLN3*, *CLN5*, *CLN6*, *CLN8*, *CLRN1*, *CNGA1#*, *CNGA3*, *CNGB1*, *CNGB3*, *CNNM4*, *COL11A1*, *COL11A2*, *COL18A1*, *COL2A1*, *COL9A1*, *COL9A2*, *COL9A3*, *COQ2*, *CPE*, *CRB1*, *CRX*, *CSPP1*, *CTC1*, *CTNNA1*, *CTNNB1*, *CTSD*, *CWC27*, *CYP4V2*, *DFNB31*, *DHDDS*, *DHX38*, *DNAJC5*, *DRAM2*, *DTHD1*, *DYNC2H1*, *EFEMP1*, *ELOVL4*, *EMC1*, *ESPN**, *EXOSC2*, *EYS**, *FAM161A*, *FDXR*, *FLVCR1*, *FRMD7*, *FZD4*, *GNAT1*, *GNAT2*, *GNB3*, *GNPTG*, *GPR143*, *GPR179*, *GRK1*, *GRM6*, *GUCA1A*, *GUCY2D*, *HARS*, *HGSNAT*, *HK1#*, *HMX1*, *IDH3A*, *IDH3B*, *IFT140*, *IFT172*, *IFT27*, *IFT81#*, *IMPDH1*, *IMPG1*, *IMPG2*, *INPP5E*, *INVS*, *IQCB1*, *ISPD*, *JAG1*, *KCNJ13*, *KCNV2*, *KIAA0556*, *KIAA0586#*, *KIAA0753*, *KIAA1549*, *KIF11*, *KIF7*, *KIZ*, *KLHL7*, *LAMA1*, *LCA5*, *LRAT*, *LRIT3*, *LRP2*, *LRP5**, *LZTFL1*, *MAK*, *MERTK*, *MFN2*, *MFRP*, *MFSD8*, *MKKS*, *MKS1*, *MMACHC*, *MT-ATP6*, *MT-ATP8*, *MT-CO1*, *MT-CO2*, *MT-CO3*, *MT-CYB*, *MT-ND1*, *MT-ND2*, *MT-ND3*, *MT-ND4*, *MT-ND4L*, *MT-ND5*, *MT-ND6*, *MT-RNR1*, *MT-RNR2*, *MT-TA*, *MT-TC*, *MT-TD*, *MT-TE*, *MT-TF*, *MT-TG*, *MT-TH*, *MT-TI*, *MT-TK*, *MT-TL1*, *MT-TL2*, *MT-TM*, *MT-TN*, *MT-TP*, *MT-TQ*, *MT-TR*, *MT-TS1*, *MT-TS2*, *MT-TT*, *MT-TV*, *MT-TW*, *MT-TY*, *MTTP*, *MVK*, *MYO7A*, *NAGLU*, *NDP*, *NEK2#*, *NMNAT1#*, *NPHP1*, *NPHP3*, *NPHP4*, *NR2E3*, *NR2F1*, *NRL*, *NYX*, *OAT*, *OCA2*, *OFD1*, *OPA1*, *OPA3*, *OPN1SW*, *OTX2*, *P3H2*, *PANK2*, *PAX2*, *PCDH15*, *PCYT1A*, *PDE6A*, *PDE6B*, *PDE6C*, *PDE6D*, *PDE6G*, *PDE6H*, *PDSS1#*, *PDSS2*, *PDZD7#*, *PEX1*, *PEX10*, *PEX11B*, *PEX12*, *PEX13*, *PEX14*, *PEX16*, *PEX19*, *PEX2*, *PEX26*, *PEX3*, *PEX5*, *PEX6*, *PEX7*, *PHYH*, *PISD*, *PITPNM3*, *PLA2G5*, *PLK4*, *PNPLA6*, *POC1B*, *POMGNT1*, *PPT1*, *PRCD*, *PRDM13*, *PROM1*, *PRPF3*, *PRPF31*, *PRPF4*, *PRPF6*, *PRPF8*, *PRPH2*, *PRPS1**, *RAB28*, *RAX2*, *RBP3*, *RBP4*, *RCBTB1*, *RD3*, *RDH11*, *RDH12*, *RDH5*, *REEP6*, *RGR*, *RGS9*, *RGS9BP*, *RHO*, *RIMS1*, *RLBP1*, *ROM1*, *RP1*, *RP1L1*, *RP2*, *RPE65*, *RPGR*, *RPGRIP1*, *RPGRIP1L#*, *RS1*, *RTN4IP1*, *SAG*, *SAMD11*, *SCAPER*, *SCLT1#*, *SDCCAG8*, *SEMA4A*, *SGSH*, *SLC24A1*, *SLC25A46*, *SLC45A2*, *SLC7A14*, *SNRNP200*, *SPATA7*, *SPP2*, *SRD5A3**, *TCTN1#*, *TCTN2*, *TCTN3*, *TEAD1*, *TIMM8A**, *TIMP3*, *TMEM107*, *TMEM126A*, *TMEM138*, *TMEM216*, *TMEM231*, *TMEM237*, *TMEM67*, *TOPORS*, *TPP1*, *TRAF3IP1*, *TREX1*, *TRIM32*, *TRPM1*, *TSPAN12*, *TTC21B*, *TTC8*, *TTLL5*, *TTPA*, *TUB*, *TUBB4B*, *TUBGCP4*, *TUBGCP6*, *TULP1*, *TYR**, *TYRP1*, *USH1C*, *USH1G*, *USH2A*, *VCAN*, *VPS13B*, *WDPCP*, *WDR19*, *WFS1*, *YME1L1**, *ZNF408*, *ZNF423* and *ZNF513*. The following exons are not included in the panel as they are not covered with sufficient high quality sequence reads: CC2D2A (NM_020785:7), CHM (NM_001145414:5), CNGA1 (NM_001142564:2), HK1 (NM_001322365:5), IFT81 (NM_031473:12), KIAA0586 (NM_001244189:6, 33), NEK2 (NM_001204182:8), NMNAT1 (NM_001297779:5), PDSS1 (NM_014317:2), PDZD7 (NM_024895:10), RPGRIP1L (NM_015272:23), SCLT1 (NM_001300898:6) and TCTN1 (NM_001173976:2;NM_024549:6).

*Some, or all, of the gene is duplicated in the genome. Read more: https://blueprintgenetics.com/pseudogene/

#The gene has suboptimal coverage when >90% of the gene's target nucleotides are not covered at >20x with a mapping quality score of MQ>20 reads.

The sensitivity to detect variants may be limited in genes marked with an asterisk (*) or number sign (#).

STATEMENT

CLINICAL HISTORY

Patient is a young male with clinical suspicion of retinitis pigmentosa since 2010. Family history: Male relative with retinitis pigmentosa, presenting with significant peripheral vision loss.

CLINICAL REPORT

Sequence analysis using the Blueprint Genetics (BpG) My Retina Tracker Program Panel Plus identified a hemizygous frameshift variant *RPGR* c.2817_2818del, p.(Glu940Argfs*138).

***RPGR* c.2817_2818del, p.(Glu940Argfs*138)**

This variant is absent in gnomAD, a large reference population database (n>120,000 exomes and >15,000 genomes), which aims to exclude individuals with severe pediatric disease. This variant occurs in the ORF15 exon of *RPGR* and is predicted to generate a frameshift leading to a stretch of 137 abnormal amino acids, eventually resulting in a premature stop codon at position 138 in the new reading frame. This is likely to lead to a loss of normal protein function, both through premature truncation and alteration of the biochemical properties of the C-terminus of RPGR. To the best of our knowledge, this variant has not been described in the medical literature or reported in disease-related variation databases such as ClinVar or HGMD. However, we have previously observed this variant in hemizygous state in 2 patients with *RPGR*-related disease (BpG, unpublished observation). Loss of RPGR function is a well-established cause of disease, and a number of truncating variants in *RPGR*, including many downstream of *RPGR* c.2817_2818del, p.(Glu940Argfs*138), have been reported in patients with X-linked retinitis pigmentosa (HGMD).

RPGR

RPGR (OMIM *312610) encodes a protein with a series of 6 N-terminal repeats comprising RCC1-like domain (RLD), characteristic of the highly conserved guanine nucleotide exchange factors. This protein localizes to the outer segment of rod photoreceptors and is essential for their viability. Pathogenic variants in *RPGR* are mainly associated with X-linked retinitis pigmentosa (XLRP, OMIM #300029). Over 70% of the patients with XLRP are explained by variants in *RPGR*. However, *RPGR* variants have also been described in patients with other retinal dystrophies including cone-rod dystrophy, atrophic macular degeneration, and syndromic retinal dystrophy with ciliary dyskinesia and hearing loss, which has been associated with variants *RPGR* c.572_619+9del57 affecting in exon 6 (PMID: 16055928) and *RPGR* c.789_790del, p.(Thr265Leufs*17) in exon 8 in 2 families (PMID: 12920075), respectively. XLRP accounts for 10–20% of families with RP and is the most severe form of RP. In XLRP, affected males are symptomatic from early childhood and most patients are blind by the end of their third decade. Female carriers show a broad spectrum of fundus appearances, ranging from normal to extensive retinal degeneration. Typically, retinal disease in females with XLRP is less severe than that seen in males. In a study by Rozet *et al.*, age at disease onset in affected females was delayed compared to affected males with similar truncating variants (20–40 years vs 10–20 years; PMID: 11950860).

Variants in *RPGR* account for over 70% of the patients with XLRP. The ORF15 exon of *RPGR* has been identified as a mutational hotspot. ORF15 encodes 567 amino acids and has a repetitive domain with high glutamic acid and glycine content (PMID: 10932196, 12657579). The shorter RPGR isoform which includes ORF15 (exon 15) is encoded by exons 1–15 and part of intron 15 (1152 amino acids, transcript ID NM_001034853). The other major isoform of *RPGR* has 815 amino acids and is encoded by exons 1–19 (NM_000328). Both isoforms share exons 1–15 (residues 1–635). Disease-causing variants have been identified in exons 1–15 or in ORF15, while no disease-causing variants have been reported in exons 16–19 (PMID: 17195164).

Currently, HGMD lists 267 different disease-causing *RPGR* variants in NM_000328.3 and 304 in NM_001034853.2 (which includes exon ORF15) (HGMD Professional 2021.4). The majority of the variants are nonsense and frameshift variants leading to loss of function. The disease-causing missense variants are located within the RCC1-like domain (amino acids 54-367, exons 3-10; PMID: 28863407). There is notable inter-and intrafamilial phenotypic variability in XLRP caused by *RPGR* variants. In particular,

patients with variants in exons 1–14 have been shown to demonstrate smaller visual fields than patients with variants in the ORF15 exon (PMID: 14564670). Truncating variants in the C-terminal part of the ORF15 exon in *RPGR* have been associated with XL cone-rod dystrophy, c.2965G>T, p.Glu989*, c.3197_3198delAG, p.(Glu1066Glyfs*12), c.3300_3301delTA, p.(His1100Glnfs*10), and c.3388_3389delTT, p.(Leu1130Lysfs*13), (HGMD; PMID: 23150612, 22264887). It has been concluded that variants located in exons 1–14 and the 5′ end of ORF15 cause retinitis pigmentosa, and variants at the 3′ end of ORF15 cause cone-rod dystrophy (PMID: 32047640).

Mutation nomenclature is based on GenBank accession NM_001034853.2 (*RPGR*) with nucleotide one being the first nucleotide of the translation initiation codon ATG.

CONCLUSION

RPGR c.2817_2818del, p.(Glu940Argfs*138) is classified as pathogenic, based on currently available evidence supporting its disease-causing role. Disease caused by *RPGR* variants is inherited in an X-linked recessive manner; males hemizygous for a disease-causing variant in *RPGR* are affected, whereas heterozygous females show a broad spectrum of fundus appearances, ranging from normal to extensive retinal degeneration. If she is available, we recommend testing of the patient's mother. If she is a carrier, each of her offspring is at 50% risk of inheriting the variant. Any daughters of the patient will inherit the variant. Genetic counseling and family member testing are recommended.

CONFIRMATION

RPGR c.2817_2818del, p.(Glu940Argfs*138) has been confirmed with Sanger sequencing.

STEP	DATE
Order date	
Sample received	
Sample in analysis	
Reported	

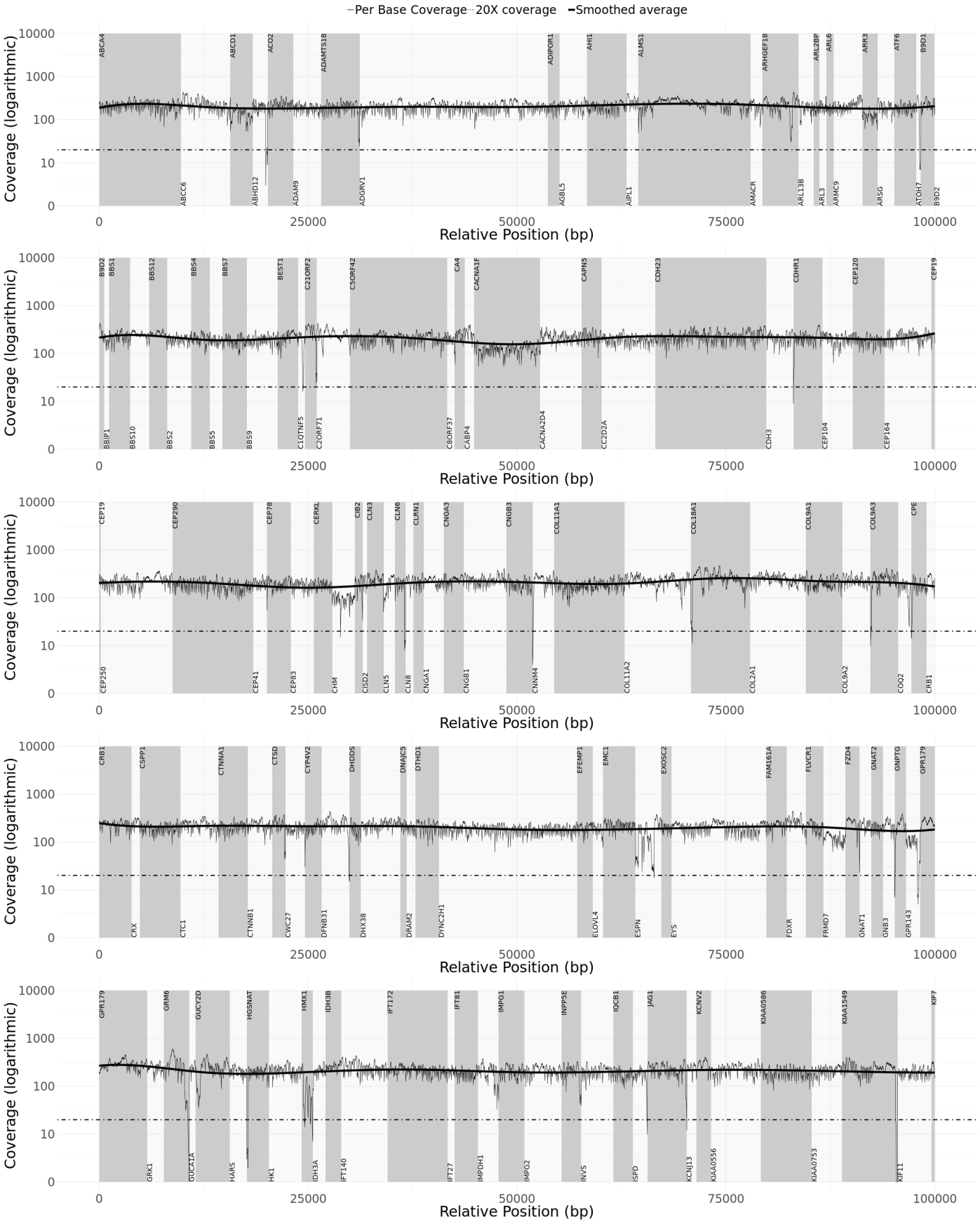
(This statement has been prepared by our geneticists and physicians, who have together evaluated the sequencing results.)

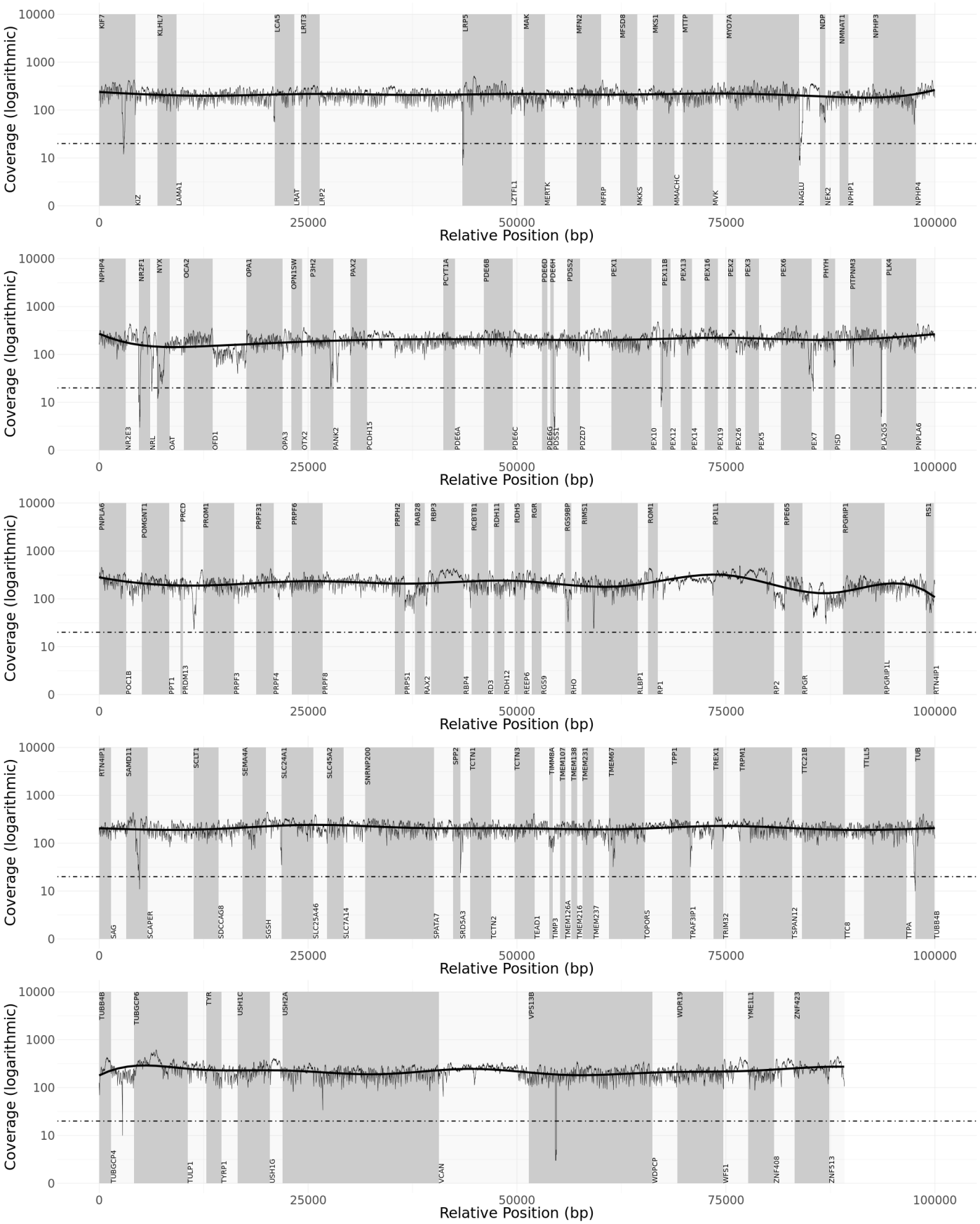
Signature

Name

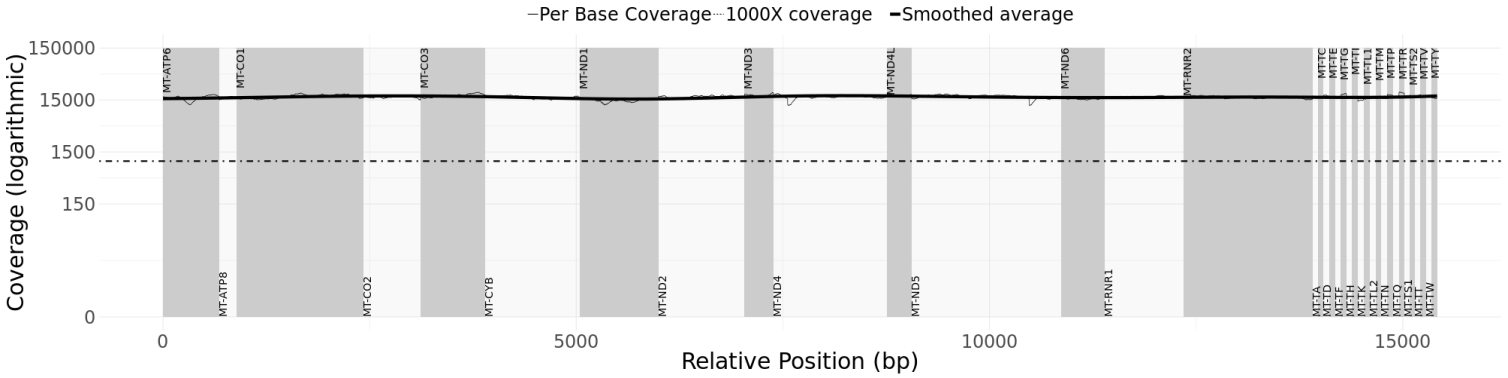
Title

Readability of the coverage plot may be hindered by faxing. A high quality coverage plot can be found with the full report on nucleus.blueprintgenetics.com.





Readability of the coverage plot may be hindered by faxing. A high quality coverage plot can be found with the full report on nucleus.blueprintgenetics.com.


Per Base Coverage
1000X coverage
Smoothed average
Coverage (logarithmic)
150000
15000
1500
150
0
MT-ATP6
MT-CO1
MT-CO3
MT-ND1
MT-ND3
MT-ND4L
MT-ND6
MT-RNR2
MT-TC
MT-TE
MT-TG
MT-TI
MT-TL1
MT-TM
MT-TP
MT-TR
MT-TS2
MT-TV
MT-TY
MT-ATP8
MT-CO2
MT-CYB
MT-ND2
MT-ND4
MT-ND5
MT-RNR1
MT-TA
MT-TD
MT-TF
MT-TH
MT-TK
MT-TL2
MT-TN
MT-TQ
MT-TS1
MT-TT
MT-TW
0
5000
10000
15000
Relative Position (bp)

APPENDIX 5: SUMMARY OF THE TEST

PLUS ANALYSIS

Laboratory process: When required, the total genomic DNA was extracted from the biological sample using bead-based method. DNA quality and quantity were assessed using electrophoretic methods at Blueprint Genetics, Inc. After assessment of DNA quality, qualified genomic DNA sample was randomly fragmented using non-contact, isothermal sonochemistry processing. Sequencing library was prepared by ligating sequencing adapters to both ends of DNA fragments. Sequencing libraries were size-selected with bead-based method to ensure optimal template size and amplified by polymerase chain reaction (PCR). Regions of interest (exons and intronic targets) were targeted using hybridization-based target capture method. The quality of the completed sequencing library was controlled by ensuring the correct template size and quantity and to eliminate the presence of leftover primers and adapter-adapter dimers. Ready sequencing libraries that passed the quality control were sequenced using the Illumina's sequencing-by-synthesis method using paired-end sequencing (150 by 150 bases). Primary data analysis converting images into base calls and associated quality scores was carried out by the sequencing instrument using Illumina's proprietary software, generating CBCL files as the final output.These steps were performed at Quest Diagnostics Nichols Institute.

Bioinformatics and quality control: Base called raw sequencing data was transformed into FASTQ format using Illumina's software (bcl2fastq). Sequence reads of each sample were mapped to the human reference genome (GRCh37/hg19). Burrows-Wheeler Aligner (BWA-MEM) software was used for read alignment. Duplicate read marking, local realignment around indels, base quality score recalibration and variant calling were performed using GATK algorithms (Sentieon) for nDNA. Variant data for was annotated using a collection of tools (VcfAnno and VEP) with a variety of public variant databases including but not limited to gnomAD, ClinVar and HGMD. The median sequencing depth and coverage across the target regions for the tested sample were calculated based on MQ0 aligned reads. The sequencing run included in-process reference sample(s) for quality control, which passed our thresholds for sensitivity and specificity. The patient's sample was subjected to thorough quality control measures including assessments for contamination and sample mix-up. Copy number variations (CNVs), defined as single exon or larger deletions or duplications (Del/Dups), were detected from the sequence analysis data using a proprietary bioinformatics pipeline. The difference between observed and expected sequencing depth at the targeted genomic regions was calculated and regions were divided into segments with variable DNA copy number. The expected sequencing depth was obtained by using other samples processed in the same sequence analysis as a guiding reference. The sequence data was adjusted to account for the effects of varying guanine and cytosine content. Bioinformatics and quality control processes were performed by Blueprint Genetics.

Interpretation: The clinical interpretation team assessed the pathogenicity of the identified variants by evaluating the information in the patient requisition, reviewing the relevant scientific literature and manually inspecting the sequencing data if needed. All available evidence of the identified variants was compared to classification criteria. Reporting was carried out using HGNC-approved gene nomenclature and mutation nomenclature following the HGVS guidelines. Likely benign and benign variants were not reported. The interpretation was performed at Blueprint Genetics.

Variant classification: Our variant classification follows the Blueprint Genetics Variant Classification Schemes modified from the ACMG guideline 2015. Minor modifications were made to increase reproducibility of the variant classification and improve the clinical validity of the report. The classification and interpretation of the variant(s) identified reflect the current state of Blueprint Genetics' understanding at the time of this report. Variant classification and interpretation are subject to professional judgment, and may change for a variety of reasons, including but not limited to, updates in classification guidelines and availability of additional scientific and clinical information. This test result should be used in conjunction with the health care provider's clinical evaluation. Inquiry regarding potential changes to the classification of the variant is strongly recommended prior to making any future clinical decision. For questions regarding variant classification updates, please contact us at support@blueprintgenetics.com

Databases: The pathogenicity potential of the identified variants were assessed by considering the predicted consequence of the change, the degree of evolutionary conservation as well as the number of reference population databases and mutation databases such as, but not limited to, the gnomAD, ClinVar, HGMD Professional and Alamut Visual. In addition, the clinical relevance of any identified CNVs was evaluated by reviewing the relevant literature and databases such as Database of Genomic

Variants and DECIPHER. For interpretation of mtDNA variants specific databases including e.g. Mitomap, HmtVar and 1000G were used.

Confirmation of sequence alterations: Sequence variants classified as pathogenic, likely pathogenic and variants of uncertain significance (VUS) were confirmed using bi-directional Sanger sequencing when they did not meet our stringent NGS quality metrics for a true positive call. In addition, prenatal case with diagnostic findings were confirmed.The confirmation of sequence alterations was performed at Blueprint Genetics, Inc.

Confirmation of copy number variants: CNVs (Deletions/Duplications) were confirmed using a digital PCR assay if they covered less than 10 exons (heterozygous), less than 3 exons (homo/hemizygous) or were not confirmed at least three times previously at our laboratory. Furthermore, CNVs of any size were not confirmed when the breakpoints of the call could be determined.The confirmation of copy number variants was performed at Blueprint Genetics, Inc.

Analytic validation: The detection performance of this panel is expected to be in the same range as our high-quality, clinical grade NGS sequencing assay used to generate the panel data (nuclear DNA: sensitivity for SNVs 99.89%, indels 1-50 bps 99.2%, one-exon deletion 100% and five exons CNV 98.7%, and specificity >99.9% for most variant types). It does not detect very low level mosaicism as a variant with minor allele fraction of 14.6% can be detected in 90% of the cases. Detection performance for mtDNA variants (analytic and clinical validation): sensitivity for SNVs and INDELs 100.0% (10-100% heteroplasmy level), 94.7% (5-10% heteroplasmy level), 87.3% (<5% heteroplasmy level) and for gross deletions 100.0%. Specificity is >99.9% for all.

Test restrictions: A normal result does not rule out the diagnosis of a genetic disorder since some DNA abnormalities may be undetectable by the applied technology. Test results should always be interpreted in the context of clinical findings, family history, and other relevant data. Inaccurate, or incomplete information may lead to misinterpretation of the results.

Technical limitations: This test does not detect the following: complex inversions, gene conversions, balanced translocations, repeat expansion disorders unless specifically mentioned, non-coding variants deeper than ±20 base pairs from exon-intron boundary unless otherwise indicated (please see the list of non-coding variants covered by the test). Additionally, this test may not reliably detect the following: low level mosaicism, stretches of mononucleotide repeats, indels larger than 50bp, single exon deletions or duplications, and variants within pseudogene regions/duplicated segments. The sensitivity of this test may be reduced if DNA is extracted by a laboratory other than Blueprint Genetics. Laboratory error is also possible. Please see the Analytic validation above.

This test was developed and its analytical performance characteristics have been determined by Blueprint Genetics, Inc. It has not been cleared or approved by the US Food and Drug Administration.

PERFORMING SITES:

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- BLUEPRINT GENETICS OY, KEILARANTA 16 A-B, 02150 ESPOO, FINLAND Laboratory Director: JUHA KOSKENVUO, MD, PhD, CLIA: 99D2092375

REVIEWING DIRECTOR:

JENNIFER SCHLEIT, PHD, FACMG, Laboratory Director

NON-CODING VARIANTS COVERED BY THE PANEL:

NM_022787.3(*NMNAT1*):c.-70A>T
NM_022787.3(*NMNAT1*):c.-69C>T
NM_022787.3(*NMNAT1*):c.-57+7T>G
NM_024887.3(*DHDDS*):c.441-24A>G
NM_000310.3(*PPT1*):c.*526_*529delATCA

NM_000310.3(*PPT1*):c.125-15T>G
NM_000329.2(*RPE65*):c.246-11A>G
NM_000350.2(*ABCA4*):c.6730-19G>A
NM_000350.2(*ABCA4*):c.6148-471C>T
NM_000350.2(*ABCA4*):c.5197–557G>T
NM_000350.2(*ABCA4*):c.5196+1137G>A
NM_000350.2(*ABCA4*):c.5196+1137G>T
NM_000350.2(*ABCA4*):c.5196+1056A>G
NM_000350.2(*ABCA4*):c.4539+2065C>G
NM_000350.2(*ABCA4*):c.4539+2064C>T
NM_000350.2(*ABCA4*):c.4539+2028C>T
NM_000350.2(*ABCA4*):c.4539+2001G>A
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NM_080629.2(*COL11A1*):c.3744+437T>G
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NM_080629.2(*COL11A1*):c.781-450T>G
NM_005272.3(*GNAT2*):c.461+24G>A
NM_206933.2(*USH2A*):c.14583-20C>G
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NM_206933.2(*USH2A*):c.-259G>T
NM_001142763.1(*PCDH15*):c.-29+1G>C
NM_033500.2(*HK1*):c.-390-3838G>C
NM_033500.2(*HK1*):c.-390-3818G>C
NM_033500.2(*HK1*):c.27+14901A>G
NM_006204.3(*PDE6C*):c.481-12T>A
NM_000391.3(*TPP1*):c.887-18A>G
NM_001139443.1(*BEST1*):c.-29+1G>T

NM_001139443.1(*BEST1*):c.-29+5G>A
NM_024649.4(*BBS1*):c.951+58C>T
NM_000260.3(*MYO7A*):c.-48A>G
NM_000260.3(*MYO7A*):c.3109-21G>A
NM_000260.3(*MYO7A*):c.5327-14T>G
NM_000260.3(*MYO7A*):c.5327-11A>G
NM_000260.3(*MYO7A*):c.5857-27_5857-26insTTGAG
NM_000372.4(*TYR*):c.1037-18T>G
NM_001080463.1(*DYNC2H1*):c.2819-14A>G
NM_001080463.1(*DYNC2H1*):c.6478-16G>A
NM_001844.4(*COL2A1*):c.1527+135G>A
NM_002905.3(*RDH5*):c.-33+2dupT
NM_025114.3(*CEP290*):c.6012-12T>A
NM_025114.3(*CEP290*):c.2991+1655A>G
NM_025114.3(*CEP290*):c.1910-11T>G
NM_025114.3(*CEP290*):c.103-18_103-13delGCTTTT
NM_000431.2(*MVK*):c.769-7dupT
NM_020366.3(*RPGRIP1*):c.1468-263G>C
NM_020366.3(*RPGRIP1*):c.1611+27G>A
NM_020366.3(*RPGRIP1*):c.2367+23delG
NM_020366.3(*RPGRIP1*):c.2367+23delG
NM_020366.3(*RPGRIP1*):c.2711-13G>T
NM_000275.2(*OCA2*):c.1117-11T>A
NM_000275.2(*OCA2*):c.1117-17T>C
NM_000275.2(*OCA2*):c.1045-15T>G
NM_000275.2(*OCA2*):c.574-19A>G
NM_017882.2(*CLN6*):c.297+113G>C
NM_033028.4(*BBS4*):c.77-216delA
NM_032520.4(*GNPTG*):c.610-16_609+28del
NM_014714.3(*IFT140*):c.2577+25G>A
NM_001171.5(*ABCC6*):c.4403+11C>G
NM_001171.5(*ABCC6*):c.3506+15G>A
NM_001171.5(*ABCC6*):c.1780-29T>A
NM_001171.5(*ABCC6*):c.1432-22C>A
NM_000086.2(*CLN3*):c.1056+34C>A
NM_000086.2(*CLN3*):c.461-13G>C
NM_001077416.2(*TMEM231*):c.824-11T>C
NM_000180.3(*GUCY2D*):c.-9-137T>C
NM_000199.3(*SGSH*):c.249+27_249+28delGG
NM_015629.3(*PRPF31*):c.1073+20_1073+36delCGGTAGGCATGGGGGTC
NM_015629.3(*PRPF31*):c.1374+654C>G
NM_001298.2(*CNGA3*):c.-37-1G>C
NM_152384.2(*BBS5*):c.619-27T>G
NM_153638.2(*PANK2*):c.*40G>C
NM_000214.2(*JAG1*):c.1349-12T>G
NM_001271441.1(*C21ORF2*):c.1000-23A>T
NM_001195794.1(*CLRN1*):c.254-649T>G
NM_130837.2(*OPA1*):c.449-34dupA
NM_130837.2(*OPA1*):c.2179-40G>C
NM_006005.3(*WFS1*):c.-43G>T
NM_006017.2(*PROM1*):c.2077-521A>G

NM_000253.2(*MTTP*):c.619-5_619-2delTTTA
NM_000253.2(*MTTP*):c.1237-28A>G
NM_004744.3(*LRAT*):c.541-15T>G
chr5:g.33985176-33985176
chr5:g.33985764-33985764
NM_000287.3(*PEX6*):c.2301-15C>G
NM_000287.3(*PEX6*):c.2300+28G>A
NM_001142800.1(*EYS*):c.-448+5G>A
chr6:g.100040906-100040906
chr6:g.100040987-100040987
chr6:g.100041040-100041040
NM_021620.3(*PRDM13*):c.-8128A>C
NM_021620.3(*PRDM13*):c.-8107T>C
NM_000288.3(*PEX7*):c.-45C>T
NM_152419.2(*HGSNAT*):c.821-28_821-10delTTGCTTATGCTTTGTACTT
chr9:g.116037909-116037909
NM_000273.2(*GPR143*):c.885+748G>A
NM_000273.2(*GPR143*):c.659-131T>G
NM_003611.2(*OFD1*):c.935+706A>G
NM_003611.2(*OFD1*):c.1130-22_1130-19delAATT
NM_003611.2(*OFD1*):c.1130-20_1130-16delTTGGT
chrX:g.38128234-38128234
NM_001034853.1(*RPGR*):c.1059+363G>A
NM_000266.3(*NDP*):c.-207-1G>A
NM_000266.3(*NDP*):c.-208+5G>A
NM_000266.3(*NDP*):c.-208+2T>G
NM_000266.3(*NDP*):c.-208+1G>A
NM_000266.3(*NDP*):c.-343A>G
NM_000266.3(*NDP*):c.-391_-380delCTCTCTCTCCCTinsGTCTCTC
NM_000266.3(*NDP*):c.-396_-383delTCCCTCTCTCTCTC
NM_000390.2(*CHM*):c.315-1536A>G
NM_000390.2(*CHM*):c.315-4587T>A
chrX:g.85302626-85302626
chrX:g.85302634-85302634
chrX:g.85302634-85302634
chrX:g.85302644-85302644
NM_004085.3(*TIMM8A*):c.133-23A>C
NM_194277.2(*FRMD7*):c.285-118C>T

GLOSSARY OF USED ABBREVIATIONS:

AD = autosomal dominant
AF = allele fraction (proportion of reads with mutated DNA / all reads)
AR = autosomal recessive
CNV = Copy Number Variation e.g. one exon or multiexon deletion or duplication
gnomAD = genome Aggregation Database (reference population database; >138,600 individuals)
gnomAD AC/AN = allele count/allele number in the genome Aggregation Database (gnomAD)
HEM = hemizygous
HET = heterozygous
HOM = homozygous
ID = rsID in dbSNP

MT = Mitochondria
MutationTaster = *in silico* prediction tools used to evaluate the significance of identified amino acid changes
Nomenclature = HGVS nomenclature for a variant in the nucleotide and the predicted effect of a variant in the protein level
OMIM = Online Mendelian Inheritance in Man®
PolyPhen = *in silico* prediction tool used to evaluate the significance of amino acid changes
POS = genomic position of the variant in the format of chromosome:position
SIFT = *in silico* prediction tool used to evaluate the significance of amino acid changes