Blueprint Genetics

Sample report as of Feb 1st, 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***

Primary Immunodeficiency Panel Plus

REFERRING HEALTHCARE PROFESSIONAL

NAME	HOSPITAL

PATIENT

NAME	DOB	AGE	GENDER	ORDER ID
		0		

PRIMARY SAMPLE TYPE	SAMPLE COLLECTION DATE	CUSTOMER SAMPLE ID

SUMMARY OF RESULTS

PRIMARY FINDINGS

The patient is homozygous for *RMRP* c.-13_-6dup, which is likely pathogenic.

PRIMARY FINDINGS: SEQUENCE ALTERATIONS

GENE	TRANSCRIPT	NOMENCLATURE	GENOTYPE	CONSEQUENCE	INHERITANCE	CLASSIFICATION
RMRP	NR_003051.3	n.-13_-6dup	HOM	upstream_gene_variant	AR	**Likely pathogenic**

ID	ASSEMBLY	POS	REF/ALT
	GRCh37/hg19	9:35658020	C/CCTCAGCTT

gnomAD AC/AN	POLYPHEN	SIFT	MUTTASTER	PHENOTYPE
0/0	N/A	N/A	N/A	Anauxetic dysplasia, Cartilage-hair hypoplasia, Metaphyseal dysplasia without hypotrichosis

SEQUENCING PERFORMANCE METRICS

PANEL	GENES	EXONS / REGIONS	BASES	BASES > 20X	MEDIAN COVERAGE	PERCENT > 20X
Primary Immunodeficiency Panel	336	4607	893274	891909	201	99.85

TARGET REGION AND GENE LIST

The Blueprint Genetics Primary Immunodeficiency Panel Plus Analysis includes sequence analysis and copy number variation analysis of the following genes: *ACD, ACP5, ACTB*, ADA, ADAM17, ADAR, AICDA, AIRE, AK2, ALPI, AP3B1, AP3D1, ARHGEF1, ARPC1B, ATM, ATP6AP1, B2M, BACH2, BCL10, BCL11B, BLM, BLNK, BTK, C17ORF62, C1QA, C1QB, C1QC, C1S, C2*, C3, C5#, C6, C7, C8A, C8B, C9, CARD11, CARD14, CARD9, CASP10, CASP8, CCBE1, CD19, CD247, CD27, CD3D, CD3E, CD3G, CD4, CD40, CD40LG, CD46*, CD55#, CD59, CD70, CD79A, CD79B, CD81, CD8A, CDC42*, CDCA7, CDK9, CEBPE, CECR1, CFB, CFD, CFH*, CFI,*

CFP, CFTR, CHD7, CIITA, CLCN7, CLPB, COG6, COLEC11, COPA, CORO13A#, CR2, CSF2RA#*, CSF2RB, CSF3R, CTC1, CTLA4, CTPS1, CTSC, CXCR4, CYBA, CYBB, CYP27A1, DBR1, DCLRE1C*, DDX58, DGAT1, DGKE, DIAPH1, DKC1, DNAJC21, DNASE1L3, DNASE2, DNMT3B, DOCK2, DOCK8, DSG1, EFL1*, ELANE, EPG5, ERCC6L2, EXTL3, FADD, FANCA, FAS, FASLG, FAT4, FCGR3A*, FCHO1, FERMT3, FOXN1, FOXP3, G6PC, G6PC3, G6PD, GATA2, GFI1, GINS1, GUCY2C, HAVCR2, HAX1, HELLS, HMOX1, HYOU1, ICOS, IFIH1, IFNAR2, IFNGR1, IFNGR2, IGLL1*, IKBKB, IKZF1, IL10, IL10RA, IL10RB, IL12B, IL12RB1#, IL17RA, IL17RC, IL1RN, IL21, IL21R, IL23R, IL2RA, IL2RB, IL2RG, IL36RN, IL6R, IL6ST*, IL7, IL7R, IRAK4, IRF2BP2, IRF4, IRF7, IRF8, ISG15, ITGB2, ITK, JAGN1, JAK1, JAK3, KRAS*, LAMTOR2, LAT, LCK, LIG1, LIG4, LPIN2, LRBA, LYST, MAGT1, MALT1, MAP3K14, MASP1, MEFV, MKL1, MOGS, MRE11A, MSN*, MTHFD1, MVK, MYD88, MYO5A, NBN, NCF1#*, NCF2, NCF4, NCSTN, NFE2L2, NFKB1, NFKB2, NFKBIA, NHEJ1, NHP2, NLRC4, NLRP1, NLRP12, NLRP3, NOD2, NOP10, NRAS, NSMCE3, OBFC1, OFD1, ORAI1, OTULIN, PARN*, PEPD, PGM3, PIGA*, PIK3CD*, PIK3R1, PLCG2, PMS2*, PNP, POLA1, POLD1, POLE, POLE2, POMP, PRF1, PRG4, PRKCD, PRKDC, PSENEN, PSMB4, PSMB8, PSTPIP1, PTPRC, RAB27A, RAC2, RAG1, RAG2, RANBP2*, RASGRP1, RBCK1, RECQL4, RELA*, RELB, RFX5, RFXANK, RFXAP, RHOH, RIPK1, RLTPR, RMRP, RNASEH2A, RNASEH2B, RNASEH2C, RNF168, RNF31, RNU4ATAC, RORC, RPSA, RTEL1, SAMD9, SAMD9L, SAMHD1, SBDS*, SEC61A1, SERPING1, SH2D1A, SLC29A3, SLC35C1, SLC37A4, SLC39A7, SLC46A1, SLC7A7, SMARCAL1, SMARCD2, SP110, SPINK5, SPPL2A, SRP54, SRP72*, STAT1, STAT2, STAT3, STAT5B*, STIM1, STK4, STX11, STXBP2, TAP1, TAP2, TAPBP, TAZ, TBX1, TCF3, TCN2, TERC, TERT, TFRC, TGFB1, THBD, TINF2, TLR3, TMC6, TMC8, TMEM173, TNFAIP3, TNFRSF13B, TNFRSF1A#, TNFRSF4, TNFRSF9, TRAF3IP2, TREX1, TRNT1, TTC37, TTC7A, TYK2, UBA1, UNC119, UNC13D, UNC93B1*, UNG, USB1, USP18#*, VPS13B, VPS45#, WAS, WDR1, WIPF1, WRAP53, XIAP*, ZAP70, ZBTB24 and ZNF341*.* The following exons are not included in the panel as they are not covered with sufficient high quality sequence reads: C5 (NM_001317164:21), CD55 (NM_001114752:10;NM_001300903:10), CORO1A (NM_007074:11), CSF2RA (NM_001161530:9), IL12RB1 (NM_153701:10), NCF1 (NM_000265:1,5,8,9,11), TNFRSF1A (NM_001346092:6), USP18 (NM_017414:11) and VPS45 (NM_001279353:13). This panel targets protein coding exons, exon-intron boundaries (± 20 bps) and selected non-coding, deep intronic variants (listed in the SUMMARY OF THE TEST section). This panel should be used to detect single nucleotide variants and small insertions deletions (INDELs) and copy number variations defined as single exon or larger deletions and duplications. This panel should not be used for the detection of repeat expansion disorders or diseases caused by mitochondrial DNA (mtDNA) mutations. The test does not detect balanced translocations or complex rearrangements, and it may not detect low-level mosaicism.

*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 an infant with recurrent infections and failure to thrive.

CLINICAL REPORT

Sequence analysis using the Blueprint Genetics (BpG) Primary Immunodeficiency Panel identified a homozygous upstream gene variant *RMRP* c.-13_-6dup.

RMRP c.-13_-6dup

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. The variant is located in the promoter region of the *RMRP* gene and duplicates 8 nucleotides long sequence AAGCTGAG (-13_-6 relative to transcription initiation site, NR_003051.3). This duplication reside in the region between the TATA box and the transciption initiation site. The variant *RMRP* c.-13_-6dup has previously been reported in a compound heterozygous state together with a pathogenic variant n.71A>G (also known as n.70A>G) in one Mexican family with patients affected with cartilage-hair hypoplasia (PMID: 12107819). The variant has been detected by other laboratories in the context of clinical testing and submitted to ClinVar (ID: 633394). HGMD Professional 2021.4 lists around 30 different small duplications/ insertions in non-coding region suggesting that this is one the disease causing mechanisms for *RMRP.*

RMRP

The *RMRP* (MIM *157660) gene encodes the RNA component of mitochondrial RNA processing endoribonuclease, which cleaves mitochondrial RNA at a priming site of mitochondrial DNA replication. This RNA also interacts with the telomerase reverse transcriptase catalytic subunit to form a distinct ribonucleoprotein complex that has RNA-dependent RNA polymerase activity and produces double-stranded RNAs that can be processed into small interfering RNA. Mutations in the untranslated *RMRP* gene are associated with a spectrum of disorders that share similar phenotypic characteristics including cartilage-hair hypoplasia (CHH; MIM #250250), Metaphyseal dysplasia without hypotrichosis (MDWH; MIM #250460), and anauxetic dysplasia (AD; MIM #607095). CHH-AD spectrum disorders are characterized by severe disproportionate short stature, which is usually recognized in the newborn, and occasionally prenatally because of the short extremities (GeneReviews NBK84550). Other findings include joint hypermobility and often fine silky hair, immunodeficiency, anemia, impaired spermatogenesis, gastrointestinal dysfunction, and increased risk for malignancy, particularly lymphoma. Hematological, immunological, gastroenterological, pulmonary, and often orthopedic consultations are needed for the assessment of the above-mentioned common CHH-associated clinical features. Hypoplastic anemia affects almost 80% of patients during early childhood, and Hirschsprung disease is present in 7-8 % of the patients. Administration of live vaccines is not recommended if signs of abnormal immunological function or SCID are present. Anauxetic dysplasia (AD) is the most severe phenotype with the most pronounced skeletal phenotype. However, it is very rare. The clinical manifestations of the CHH-AD spectrum disorders are variable, even within the same family. Quite recently, compound heterozygosity for n.71A>G and a 10-nucleotide duplication at position -13 (TACTCTGTGA) was shown to associate with a very mild growth failure and skeletal phenotype (PMID: 28094436). The CHH-AD spectrum is inherited in an autosomal recessive manner. Mutations in *RMRP* have been shown to explain 21/27 (78%) of CHH in ethnically diverse patients (PMID 16838329). Altogether, 102 pathogenic *RMRP* variants have been described (the Leiden Open Variant Database RMRP). According to the database, CHH-AD spectrum disorders are rare in the general population with only a few hundred families

reported. *RMRP* mutations are thought to be of three distinct types. The first category consists of mutations affecting the promoter region: insertions or duplications between 6 and 30 nucleotides long residing in the region between the TATA box and the transcription initiation site and interfering with the transcription of *RMRP*. The second category consists of small changes of conserved nucleotides in the transcript: single nucleotide substitutions and other changes involving at most two nucleotides. These reside in highly conserved residues of the transcribed sequence. The third category includes insertions and duplications in the 5' end of the transcript. A founder variant in *RMRP* (n.71A>G) has been observed in 100% of Old Order Amish, 92% in Finnish, 48% in non-Finnish, and 38% in ethnically heterogeneous CHH patient populations (PMIDs 12107819, 12888988, 19150606, and 16838329). Prevalence in the Amish population has been reported at 1-2/1000 and in Finland 1/23,000.

Mutation nomenclature is based on GenBank accession NR_003051.3 (*RMRP*) with nucleotide one being the first nucleotide of the translation initiation codon ATG.

CONCLUSION

RMRP c.-13_-6dup is classified as likely pathogenic, based on the established association between the gene and the patient's phenotype, the variant's rarity in control populations, identification of the variant in one family with the same phenotype. Disease caused by *RMRP* variants is inherited in an autosomal recessive manner. The patient is homozygous for the variant, which is consistent with autosomal recessive inheritance. If the patient's parents are each confirmed to be carriers of this variant, any siblings of the patient will have a 25% chance of being homozygous for the variant and thus affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being an unaffected non-carrier. Genetic counseling and family member testing are recommended.

STEP	DATE
Order date	
Sample received	
Sample in analysis	
Reported	

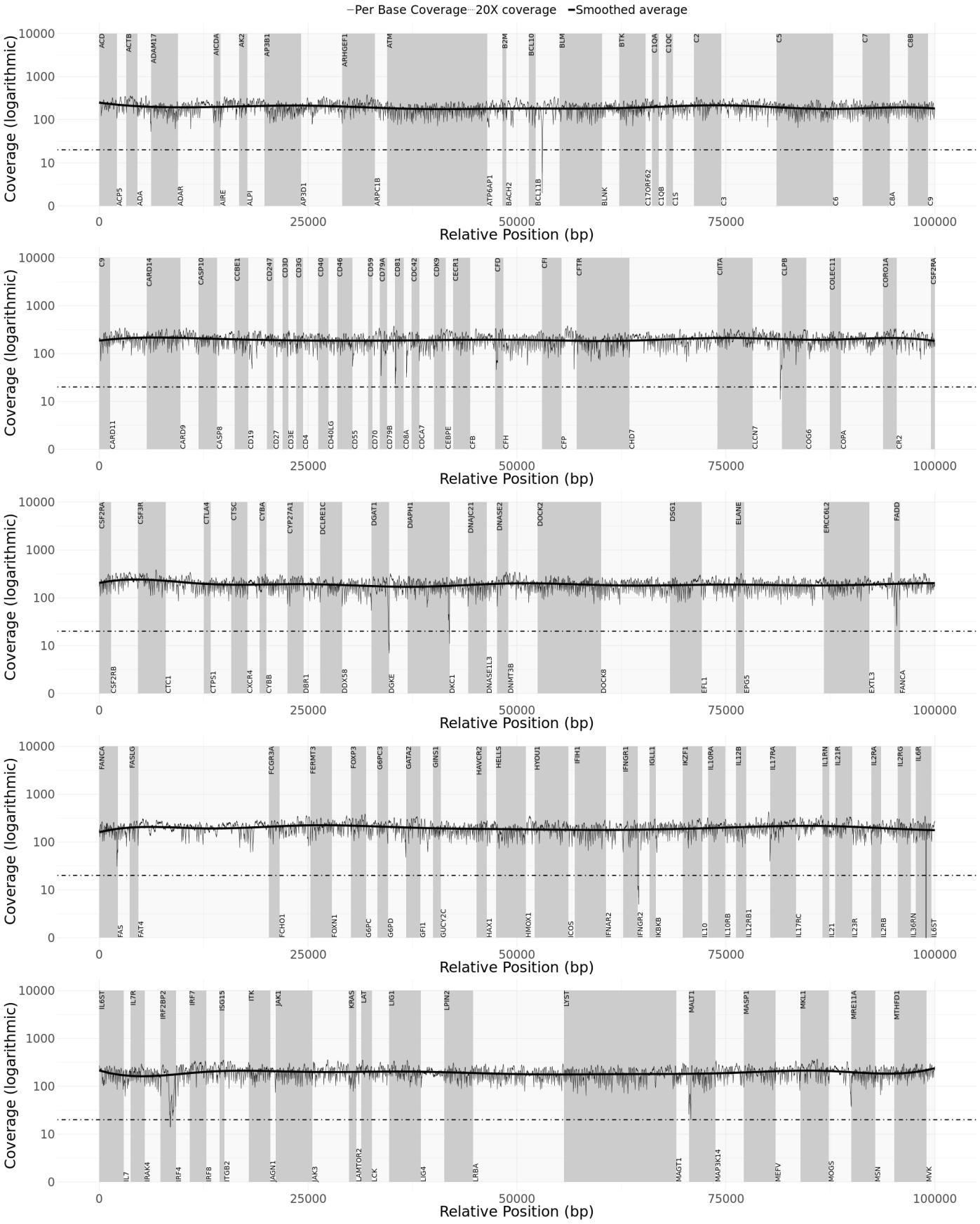
(This statement has been prepared by our geneticists and physicians, who have together evaluated the sequencing results.)

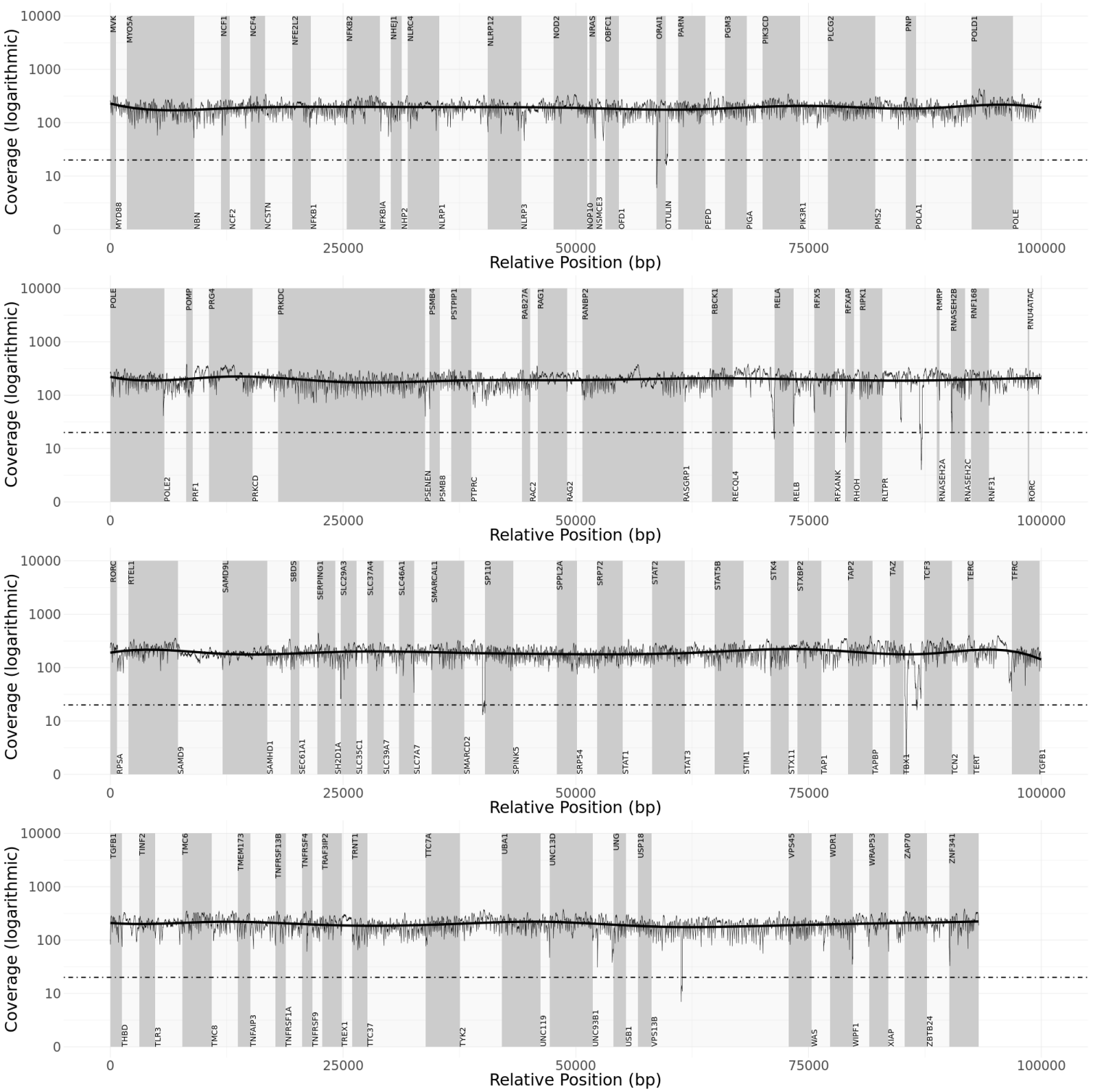
Signature

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.

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100
10
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MYO5A
NBN
NCF1
NCF2
NCF4
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NFKB1
NFKB2
NFKBIA
NHEJ1
NHP2
NLRC4
NLRP1
NLRP12
NLRP3
NOD2
NOP10
NBAS
NSMCE3
OBFC1
OFD1
ORAI1
OTULIN
PARN
PEPD
PGM3
PIGA
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PIK3R1
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PMS2
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75000
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Coverage (logarithmic)
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PRG4
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PRKDC
PSENEN
PSMB4
PSMB8
PSTPIP1
PTPRC
RAB27A
RAC2
RAG1
RAG2
RANBP2
RASGRP1
RBCK1
RECQL4
RELA
RELB
RFX5
RFXANK
RFXAP
RHOH
RIPK1
RLTPR
RMRP
RNASEH2A
RNASEH2B
RNASEH2C
RNF168
RNF31
RNU4ATAC
RORC
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50000
75000
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Relative Position (bp)
Coverage (logarithmic)
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1000
100
10
0
RORC
RPSA
RTEL1
SAMD9
SAMD9L
SAMHD1
SBDS
SEC61A1
SERPING1
SH2D1A
SLC29A3
SLC35C1
SLC37A4
SLC39A7
SLC46A1
SLC7A7
SMARCAL1
SMARCD2
SP110
SPINK5
SPPL2A
SRP54
SRP72
STAT1
STAT2
STAT3
STAT5B
STIM1
STK4
STX11
STXBP2
TAP1
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TBX1
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TCN2
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TERT
TFRC
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25000
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75000
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Relative Position (bp)
Coverage (logarithmic)
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1000
100
10
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THBD
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TLR3
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TMC8
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TNFRSF13B
TNFRSF1A
TNFRSF4
TNFRSF9
TRAF3IP2
TREX1
TRNT1
TTC37
TTC7A
TYK2
UBA1
UNC119
UNC13D
UNC93B1
UNG
USB1
USP18
VPS13B
VPS45
WAS
WDR1
WIPF1
WRAP53
XIAP
ZAP70
ZBTB24
ZNF341
0
25000
50000
75000
100000
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. 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 Blueprint Genetics.
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.

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.

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.

Regulation and accreditations: This test was developed and its performance characteristics determined by Blueprint Genetics (see Analytic validation). It has not been cleared or approved by the US Food and Drug Administration. This analysis has been performed in a CLIA-certified laboratory (#99D2092375), accredited by the College of American Pathologists (CAP #9257331) and by FINAS Finnish Accreditation Service, (laboratory no. T292), accreditation requirement SFS-EN ISO 15189:2013. All the tests are under the scope of the ISO 15189 accreditation (excluding mtDNA testing).

PERFORMING SITE:

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

NON-CODING VARIANTS COVERED BY THE PANEL:

NM_000491.3(*C1QB*):c.-17-2A>C
NM_014017.3(*LAMTOR2*):c.*23C>A
NM_000639.1(*FASLG*):c.-261T>C
NM_002389.4(*CD46*):c.286+27delT
NM_018344.5(*SLC29A3*):c.*413G>A
NM_000043.4(*FAS*):c.506-16A>G
NM_000536.3(*RAG2*):c.-28G>C
NM_000062.2(*SERPING1*):c.-163C>T
NM_000062.2(*SERPING1*):c.-161A>G
NM_000062.2(*SERPING1*):c.-100C>G
NM_000062.2(*SERPING1*):c.-22-2A>C/G
NM_000062.2(*SERPING1*):c.-22-2A>C
NM_000062.2(*SERPING1*):c.-22-2A>G

NM_000062.2(*SERPING1*):c.-22-1G>A
NM_000062.2(*SERPING1*):c.686-12A>G
NM_000062.2(*SERPING1*):c.890-14C>G
NM_000062.2(*SERPING1*):c.1250-13G>A
NM_001814.4(*CTSC*):c.-55C>A
NM_000051.3(*ATM*):c.-174A>G
NM_000051.3(*ATM*):c.-31+595G>A
NM_000051.3(*ATM*):c.-30-1G>T
NM_000051.3(*ATM*):c.2639-384A>G
NM_000051.3(*ATM*):c.2839-579_2839-576delAAGT
NM_000051.3(*ATM*):c.3403-12T>A
NM_000051.3(*ATM*):c.3994-159A>G
NM_000051.3(*ATM*):c.4612-12A>G
NM_000051.3(*ATM*):c.5763-1050A>G
NM_000051.3(*ATM*):c.8418+681A>G
NM_016123.3(*IRAK4*):c.1188+520A>G
NM_000431.2(*MVK*):c.769-7dupT
NM_006231.2(*POLE*):c.1686+32C>G
NM_015932.5(*POMP*):c.-95delC
NM_020751.2(*COG6*):c.1167-24A>G
NM_024570.3(*RNASEH2B*):c.65-13G>A
NM_024570.3(*RNASEH2B*):c.511-13G>A
NM_000270.3(*PNP*):c.286-18G>A
NM_001287.5(*CLCN7*):c.916+57A>T
NM_001287.5(*CLCN7*):c.739-18G>A
NM_000243.2(*MEFV*):c.-12C>G
NM_000243.2(*MEFV*):c.-382C>G
NM_001134477.2(*PARN*):c.-165+2C>T
NM_000101.3(*CYBA*):c.288-15C>G
NM_000135.3(*FANCA*):c.4261-19_4261-12delACCTGCTC
NM_000135.2(*FANCA*):c.3239+82T>G
NM_000135.2(*FANCA*):c.2982-192A>G
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NM_000135.2(*FANCA*):c.2504+134A>G
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NM_000135.2(*FANCA*):c.893+920C>A
NM_000151.3(*G6PC*):c.446+39G>A
NM_000151.3(*G6PC*):c.446+42G>A
NM_003647.2(*DGKE*):c.888+40A>G
NM_199242.2(*UNC13D*):c.2831-13G>A
NM_199242.2(*UNC13D*):c.2448-13G>A
NM_199242.2(*UNC13D*):c.118-307G>A
NM_199242.2(*UNC13D*):c.118-308C>T
NM_006949.3(*STXBP2*):c.326-23_326-16delGCCCCACT
NM_000215.3(*JAK3*):c.2680+89G>A
NM_000215.3(*JAK3*):c.1915-11G>A
NM_003721.3(*RFXANK*):c.188-11C>T
NM_172341.2(*PSENEN*):c.-192_-190delAGA
NM_020458.2(*TTC7A*):c.1510+105T>A
NM_001079.3(*ZAP70*):c.838-80G>A

NM_001079.3(*ZAP70*):c.1624-11G>A
chr20:g.23030319-23030319
NM_000361.2(*THBD*):c.-302C>A
NM_021067.3(*GINS1*):c.-60A>G
NM_021067.3(*GINS1*):c.-48C>G
NM_006892.3(*DNMT3B*):c.2421-11G>A
NM_000022.2(*ADA*):c.1079-15T>A
NM_000022.2(*ADA*):c.976-34G>A
NM_000628.4(*IL10RB*):c.*52C>T
NM_000211.3(*ITGB2*):c.742-14C>A
NM_000211.3(*ITGB2*):c.500-12T>G
NM_017424.2(*CECR1*):c.1082-1113delA
NM_080647.1(*TBX1*):c.-777C>T
NM_080647.1(*TBX1*):c.-620A>C
NM_000355.3(*TCN2*):c.581-176A>T
NM_000355.3(*TCN2*):c.581-176A>G
NM_182916.2(*TRNT1*):c.609-26T>C
NM_002295.4(*RPSA*):c.-34+5G>C
NM_032638.4(*GATA2*):c.1017+572C>T
NM_032638.4(*GATA2*):c.1017+513_1017+540delGGAGTTTCCTATCCGGACATCTGCAGCC
NM_032638.4(*GATA2*):c.1017+532T>A
NR_001566.1(*TERC*):n.-22C>T
chr3:g.169482906-169482906
NR_001566.1(*TERC*):n.-100C>G
chr3:g.169483086-169483086
NM_198253.2(*TERT*):c.2383-15C>T
NM_198253.2(*TERT*):c.-57A>C
NM_002185.3(*IL7R*):c.379+288G>A
NM_000587.2(*C7*):c.63-23T>A
NM_006846.3(*SPINK5*):c.283-12T>A
NM_006846.3(*SPINK5*):c.1431-12G>A
NM_006846.3(*SPINK5*):c.1820+53G>A
NM_003764.3(*STX11*):c.*85_*86insT
NM_000535.5(*PMS2*):c.1145-31_1145-13delCTGACCCTCTTCTCCGTCC
NM_000535.5(*PMS2*):c.23+21_23+28delTCCGGTGT
NM_000492.3(*CFTR*):c.-495C>T
chr7:g.117119797-117119797
NM_000492.3(*CFTR*):c.-249G>C
NM_000492.3(*CFTR*):c.-165G>A
NM_000492.3(*CFTR*):c.-85C>G
NM_000492.3(*CFTR*):c.-34C>T
NM_000492.3(*CFTR*):c.53+124T>C
NM_000492.3(*CFTR*):c.870-1113_870-1110delGAAT
NM_000492.3(*CFTR*):c.1117-26_1117-25delAT
NM_000492.3(*CFTR*):c.1393-18G>A
NM_000492.3(*CFTR*):c.1585-9412A>G
NM_000492.3(*CFTR*):c.1585-19T>C
NM_000492.3(*CFTR*):c.1679+34G>T
NM_000492.3(*CFTR*):c.1680-886A>G
NM_000492.3(*CFTR*):c.1680-883A>G
NM_000492.3(*CFTR*):c.1680-877G>T

NM_000492.3(*CFTR*):c.2908+19G>C
NM_000492.3(*CFTR*):c.2909-15T>G
NM_000492.3(*CFTR*):c.2988+33G>T
NM_000492.3(*CFTR*):c.3140-26A>G
NM_000492.3(*CFTR*):c.3140-16T>A
NM_000492.3(*CFTR*):c.3140-11A>G
NM_000492.3(*CFTR*):c.3469-1304C>G
NM_000492.3(*CFTR*):c.3717+40A>G
NM_000492.3(*CFTR*):c.3718-2477C>T
NM_000492.3(*CFTR*):c.3873+33A>G
NM_000492.3(*CFTR*):c.3874-4522A>G
NM_000492.3(*CFTR*):c.*1233T>A
NM_017780.3(*CHD7*):c.2836-15C>G
NM_017780.3(*CHD7*):c.5051-15T>A
NM_017780.3(*CHD7*):c.5405-18C>A
NM_017780.3(*CHD7*):c.5405-17G>A
NM_017780.3(*CHD7*):c.5405-13G>A
NM_203447.3(*DOCK8*):c.742-18C>G
NM_203447.3(*DOCK8*):c.742-15T>G
NM_203447.3(*DOCK8*):c.1797+61A>C
chr9:g.35658026-35658026
chr9:g.35658026-35658026
chr9:g.35658026-35658026
chr9:g.35658026-35658026
chr9:g.35658027-35658027
chr9:g.35658027-35658027
chr9:g.35658027-35658027
chr9:g.35658027-35658027
chr9:g.35658027-35658027
chr9:g.35658028-35658028
chr9:g.35658028-35658028
chr9:g.35658029-35658029
chr9:g.35658029-35658029
chr9:g.35658032-35658032
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
NM_016937.3(*POLA1*):c.1375-354A>G
NM_000397.3(*CYBB*):c.-69A>C
chrX:g.37639262-37639262
NM_000397.3(*CYBB*):c.-67T>C
NM_000397.3(*CYBB*):c.-65C>T
NM_000397.3(*CYBB*):c.-64C>T
NM_000397.3(*CYBB*):c.46-14_46-11delTTCTinsGAA
NM_000397.3(*CYBB*):c.46-11T>G
NM_000397.3(*CYBB*):c.142-28_142-12delACTCTGCTCCCTTTCCC
NM_000397.3(*CYBB*):c.142-12delCinsACCTCTTCTAG
NM_000397.3(*CYBB*):c.483+978G>T
NM_000397.3(*CYBB*):c.674+1080A>G
NM_000397.3(*CYBB*):c.674+1337T>G
NM_000397.3(*CYBB*):c.675-1157A>G

NM_000397.3(*CYBB*):c.1152-11T>G
NM_000377.2(*WAS*):c.1339-19_1339-11delTGATCCCTGinsATCTGCAGACC
NM_014009.3(*FOXP3*):c.*878A>G
NM_014009.3(*FOXP3*):c.*876A>G
NM_014009.3(*FOXP3*):c.-23+5G>A
NM_014009.3(*FOXP3*):c.-23+2T>G
NM_014009.3(*FOXP3*):c.-23+1G>A
NM_014009.3(*FOXP3*):c.-23+1G>T
NM_000206.2(*IL2RG*):c.*307_*308delAA
NM_000206.2(*IL2RG*):c.*308A>G
NM_000206.2(*IL2RG*):c.270-15A>G
NM_000206.2(*IL2RG*):c.-105C>T
NM_000061.2(*BTK*):c.1567-23A>C/G
NM_000061.2(*BTK*):c.1567-23A>G
NM_000061.2(*BTK*):c.1567-23A>C
NM_000061.2(*BTK*):c.1177+28_1177+29insAGAAAAAAGGT
NM_000061.2(*BTK*):c.895-11C>A
NM_000061.2(*BTK*):c.310-28_310-27delGCinsTG
NM_000061.2(*BTK*):c.240+109C>A
NM_000061.2(*BTK*):c.240+108T>G
NM_000061.2(*BTK*):c.142-205A>G
NM_000061.2(*BTK*):c.141+11C>T
NM_000061.2(*BTK*):c.-31+6T>G
NM_000061.2(*BTK*):c.-31+5G>A/C/T
NM_000061.2(*BTK*):c.-31+5G>A
NM_000061.2(*BTK*):c.-31+5G>T
NM_000061.2(*BTK*):c.-31+5G>C
NM_000061.2(*BTK*):c.-31+1G>A/C
NM_000061.2(*BTK*):c.-31+1G>A
NM_000061.2(*BTK*):c.-31+1G>C
NM_000061.2(*BTK*):c.-31G>A
NM_000061.2(*BTK*):c.-193A>G
NM_002351.4(*SH2D1A*):c.138-17_138-11delAGTTTAT
NM_000074.2(*CD40LG*):c.289-32_289-25delAAAATGAC
NM_000074.2(*CD40LG*):c.289-15T>A
NM_000074.2(*CD40LG*):c.347-915A>T
NR_024048.1(*TAZ*):n.694+4G>A
NM_000116.3(*TAZ*):c.778-63_778-51delCTCCCAGGGCACC
NM_001363.3(*DKC1*):c.-142C>G
NM_001363.3(*DKC1*):c.-141C>G
NM_001363.3(*DKC1*):c.85-15T>C

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.