Blueprint Genetics

Sample report as of June 14th, 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

Comprehensive Muscular Dystrophy / Myopathy Panel Plus

REFERRING HEALTHCARE PROFESSIONAL

NAME **HOSPITAL**

PATIENT

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

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

SUMMARY OF RESULTS

PRIMARY FINDINGS

The patient is hemizygous for a duplication *DMD* c.(93+1_94-1)_(649+1_650-1)dup, which encompasses exons 3-7 of *DMD*. This alteration is classified as pathogenic.

PRIMARY FINDINGS: COPY NUMBER ABERRATIONS

GENE	EVENT	COPY NUMBER	GENOTYPE	IMPACT	LINKS	CLASSIFICATION
DMD	COPY NUMBER GAIN	2	HEM	DMD:Partial gene	UCSC	**Pathogenic**
	OMIM	**PHENOTYPE** Becker muscular dystrophy, Dilated cardiomyopathy (DCM), Duchenne muscular dystrophy			**COMMENT** -	

SEQUENCING PERFORMANCE METRICS

PANEL	GENES	EXONS / REGIONS	BASES	BASES > 20X	MEDIAN COVERAGE	PERCENT > 20X
Comprehensive Muscular Dystrophy / Myopathy Panel	124	2923	605315	604541	197	99.87

PANEL	GENES	EXONS / REGIONS	BASES	BASES > 1000X	MEDIAN COVERAGE	PERCENT > 1000X
Mitochondrial genome	37	-	15358	15358	7226	100

TARGET REGION AND GENE LIST

The Blueprint Genetics Comprehensive Muscular Dystrophy / Myopathy Panel Plus Analysis includes sequence analysis and copy number variation analysis of the following genes: *ACAD9, ACADVL, ACTA1, ADCK3, ANO5, ATP2A1, B3GALNT2#, B4GAT1, BAG3, BICD2, BIN1, CAPN3, CASQ1, CAV3, CFL2, CHKB, CNTN1, COL12A1, COL4A1, COL4A2, COL6A1, COL6A2, COL6A3, COQ2, CRYAB, DAG1, DES, DGUOK, DMD, DNAJB6, DPM3, DYSF, EMD, FDX1L, FHL1*, FKRP, FKTN,* FLAD1, *FLNC*,*

GAA, GBE1, GMPPB, GOLGA2, GYG1, HNRNPDL, INPP5K, ISCU, ISPD, ITGA7, KBTBD13, KLHL40, KLHL41, LAMA2, LAMP2, LARGE, LDB3, LIMS2, LMNA, LMOD3, MAP3K20, MEGF10, MICU1, MME, MSTO1#, 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, MTM1, MYH7, MYO18B, MYOT, NEB#, PABPN1, PGK1, PHKA1, PHKB, PLEC, PNPLA2, POGLUT1, POLG, POLG2, POMGNT1, POMGNT2, POMK, POMT1, POMT2, PYGM, PYROXD1*, RBCK1, RRM2B, RYR1, SCN4A, SELENON#, SEPT9, SGCA, SGCB, SGCD, SGCG, SIL1, SLC22A5, SLC25A20, SMCHD1, SMN1#*, SMN2#*, SPEG, SPTBN4, STAC3, SUCLA2, SUCLG1, SYNE1, TANGO2, TCAP, TIA1, TMEM126B, TMEM43, TNNT1, TNPO3, TOR1AIP1, TPM2, TPM3*, TRAPPC11, TRIM32, TSFM#, TTN*, TYMP, VMA21* and VPS13A.* The following exons are not included in the panel as they are not covered with sufficient high quality sequence reads: B3GALNT2 (NM_001277155:2), SELENON (NM_020451:3) and TSFM (NM_001172696:5).

*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 21-year-old adult with raised CK, query myopathy, and relatively high functioning autism. Thigh muscles relatively small compared to leg and foot muscles. CK was checked due to mildly elevated ALT/AST which persisted on and off isotretinoin. Suspicion of asymptomatic hyperCKaemia vs. chronic myopathy.

CLINICAL REPORT

Del/Dup (CNV) analysis using the Blueprint Genetics (BpG) Comprehensive Muscular Dystrophy / Myopathy Panel identified a heterozygous duplication *DMD* c.(93+1_94-1)_(649+1_650-1)dup, encompassing exons 3-7 of *DMD*.

DMD c.(93+1_94-1)_(649+1_650-1)dup

This duplication is estimated to cover the genomic region X:32827549-33032786 and is approximately 205237 base pairs (approximately 205 Kb) in size. However, the exact breakpoints of the duplication cannot be determined using the present method, and therefore its exact size and genomic position are unknown. Although we cannot determine whether this duplication is in tandem in this patient, it has been suggested that at least 83% of duplications are in tandem (PMID 25640679). Based on these data, this out-of-frame duplication is considered likely to be in tandem, and is therefore predicted to disrupt the reading frame leading to protein truncation or nonsense-mediated mRNA decay. The duplication is also predicted to be out of frame by TREAT-NMD DMD Global Database and the reading frame checker of LOVD. Thus, in line with current ACMG variant classification guidelines (PMID 30192042), this duplication is classified as a loss of function variant. There are no individuals with this duplication listed in the Genome Aggregation Database control cohorts (gnomAD SVs v2.1). A duplication of exons 3-7 has been reported in 44 male in the TREAT-NMD DMD Global Database. This duplication has also been published in several individuals with *DMD*-related disease (PMID: 33644936, 22894145, 16917894, 15655674, 27206868, 22510846).

DMD

DMD (MIM *300377) encodes dystrophin, a large muscle protein that is mutated in Duchenne (DMD; MIM #310200) and Becker muscular dystrophy (BDM; MIM #300376) (GeneReviews: Dystrophinopathies NBK1119). DMD begins in early childhood, usually before age 5, and is characterized by progressive skeletal and respiratory muscle weakness, calf hypertrophy and high serum CK values. Other typical features include dilated cardiomyopathy (present in 90% of individuals with DMD/BMD), ankle contractures and scoliosis. The patients become wheelchair dependent between 9-13 years without

steroid therapy, and death occurs typically between 15-25 years of age because of respiratory or cardiac failure. Cardiac involvement is the cause of death in only 20% of individuals with DMD and 50% of those with BMD (PMID: 20627570). Due to respiratory support life expectancy in DMD is prolonged from 6 years up to 25 years in some patients. BMD shows much milder phenotype with a disease onset over 7 years, and wheelchair dependency between ages 16-80 years. BMD is caused by in-frame deletions or duplications of one or several exons or by splice-site and missense mutations. These mutations lead to the production of various amounts of internally truncated, lengthened, or slightly modified dystrophin molecules. This results in a broad spectrum of clinical severity, ranging from a complete absence of symptoms, through mild disease, to severe clinical conditions similar to DMD (PMID: 2491009, 8437017, 8543940).

DMD mutations may also lead to so-called DMD-associated dilated cardiomyopathy (DCM, MIM #302045), which typically presents at the age of 20-40 years in males, and later in life in females. These patients usually have no clinical evidence of skeletal muscle disease; the disease may be classified as "subclinical" BMD. Rapid progression to death in several years has been reported in males and slower progression over a decade or more in females (PMID: 9170393). The inheritance pattern in these progressive neuromuscular diseases is X-linked recessive and they affect mainly males. Most heterozygous female carriers of DMD mutations are asymptomatic; however, between 2.5 and 7.8% of these carriers are manifesting carriers who develop symptoms ranging from mild muscle weakness to a rapidly progressive DMD-like muscular dystrophy. (PMID: 4854942, 2766561, 17259292, 20630757). Females heterozygous for a DMD pathogenic variant are at increased risk for developing dilated cardiomyopathy.

The TREAT-NMD DMD Global Database currently contains 7,150 DMD mutations: 5,685 large mutations (80% of all mutations)(4,897 (86%) deletions of a single exon or larger and 788 (14%) duplications of a single exon or larger) and 1,443 small mutations (20% of all mutations) (726 nonsense, 355 deletions smaller than one exon and 132 duplications smaller than one exon, 199 splice site variants and 31 missense mutations) (PMID: 25604253). Approximately 24-33% of all DMD mutations occur de novo (PMID: 8111545, 19367636). Of the 571 nonsense, frameshift and consensus splice site DMD variants in ClinVar, 565 are classified as pathogenic/likely pathogenic. From the phenotype perspective, DMD and BDM related mutations are more commonly (98.4% and 92%, respectively) radical (truncations, gross del/dup, ins/dels/indels) than those found in DMD-associated DCM (85%).

Human genome contains multiple gene promoters and alternatively spliced DMD isoforms (Gene description in the UMD-DMD database). Expression of the full-length dystrophins is controlled individually by three promoters located in the 5'-end region of the gene that is active in neurons (the Brain or Cortical promoter, isoform Dp427c encoded by NM_000109.3), in muscle and glial cells (the M promoter, isoform Dp427m encoded by NM_004006.2), and in Purkinje cells in the brain (the P promoter, isoform Dp427p NM_004009.3). Each of the 14-kb mRNA transcribed from these promoters consists of a unique first exon and a common set of 78 exons. Four amino-terminally truncated forms of dystrophin are transcribed from internal tissue-specific promoters located further downstream. Each of these promoters uses a unique first exon that splices into exons 30, 45, 56, and 63, respectively, to generate smaller proteins. Thus N-terminal DMD mutation does not have an effect on the immunostaining of C-terminal protein.

Mutation nomenclature is based on GenBank accession NM_004006.2 (DMD) with nucleotide one being the first nucleotide of the translation initiation codon ATG.

CONCLUSION

DMD c.(93+1_94-1)_(649+1_650-1)dup, affecting exons 3-7, is classified as pathogenic, based on currently available evidence supporting its disease-causing role. Disease caused by DMD variants is inherited in an X-linked dominant manner. Thus, family member testing is recommended. If the patient's mother is heterozygous for this variant, she has a 50% chance of transmitting the variant to offspring. If the patient's father is hemizygous for the variant, he will transmit the variant to all daughters but not to sons. Offspring who inherit the variant will be affected. DMD-related disease may be caused by a de novo variant. Genetic counseling is recommended.

CONFIRMATION

Duplication *DMD* c.(93+1_94-1)_(649+1_650-1)dup has been confirmed by digital PCR.

| 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:
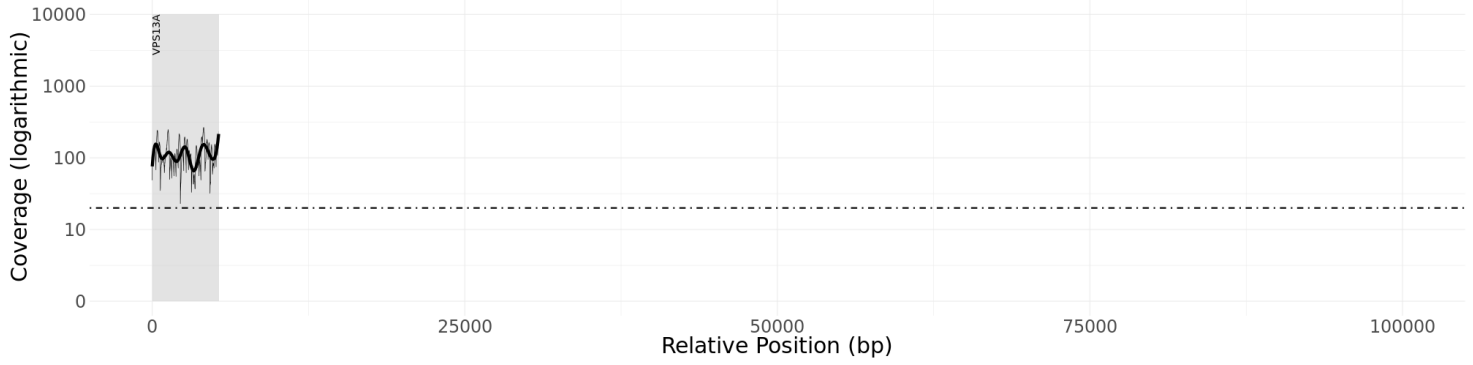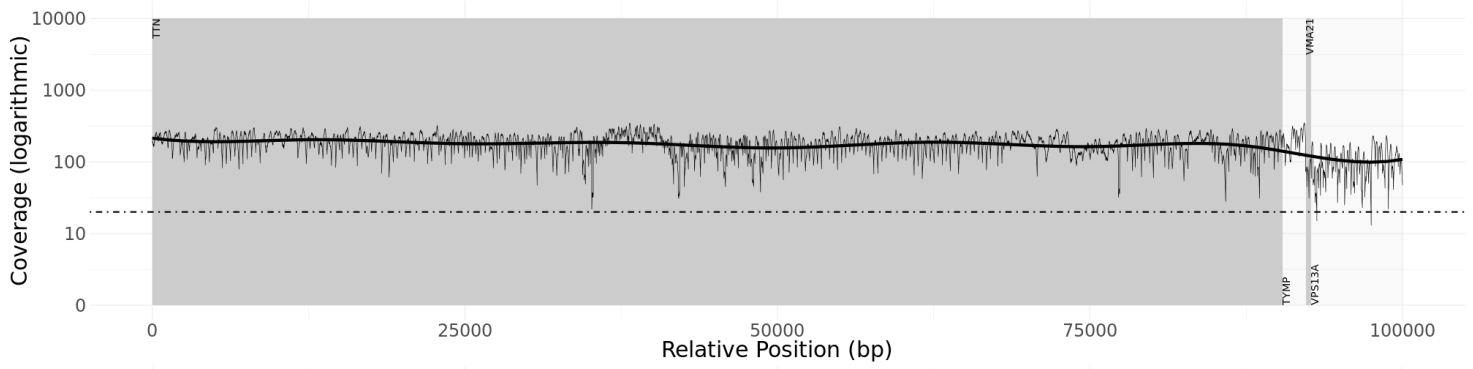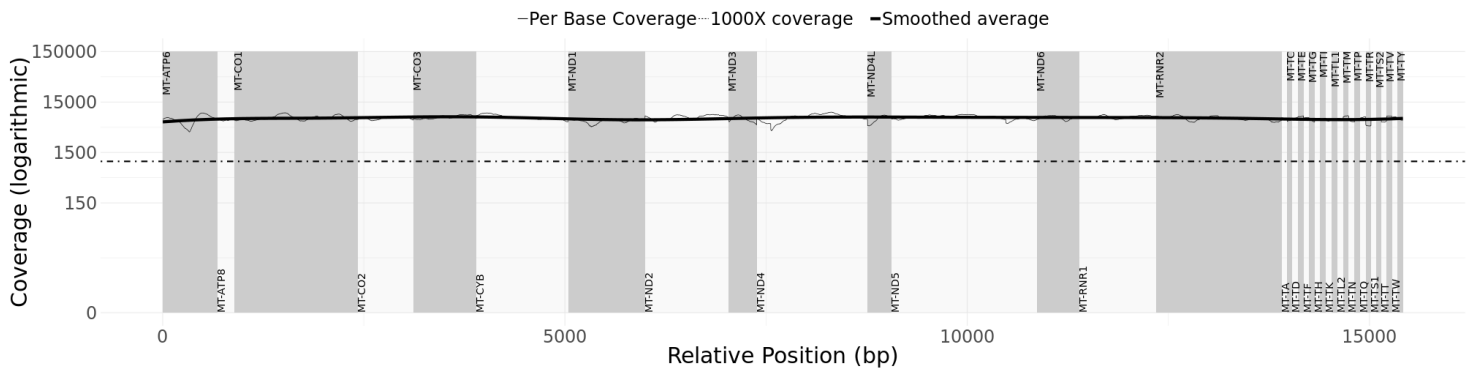
Signature

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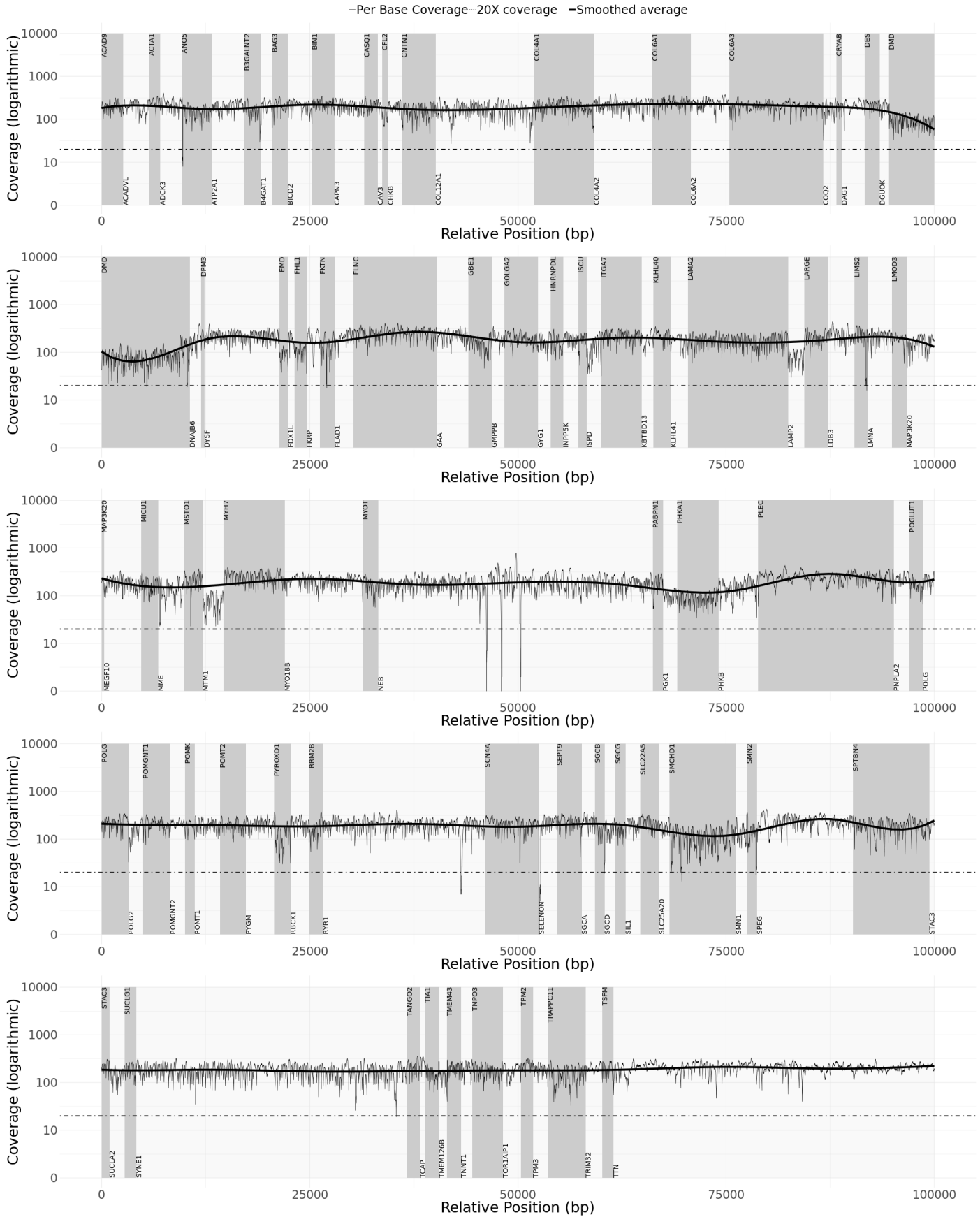
Readability of the coverage plot may be hindered by faxing. A high quality coverage plot can be found with the full report on nucleus.blueprintgenetics.com.

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: MD, PhD, CLIA: 99D2092375

NON-CODING VARIANTS COVERED BY THE PANEL:

NM_020451.2(*SELENON*):c.*1107T>C, NM_170707.3(*LMNA*):c.513+45T>G, NM_170707.3(*LMNA*):c.937-11C>G, NM_170707.3(*LMNA*):c.1608+14G>A, NM_170707.3(*LMNA*):c.1609-12T>G, NM_020247.4(*ADCK3*):c.*72dupG, NM_005609.2(*PYGM*):c.661-601G>A, NM_005609.2(*PYGM*):c.425-26A>G, NM_213595.2(*ISCU*):c.418+382G>C, NM_000231.2(*SGCG*):c.-127_-121delACAGTTG, NM_000231.2(*SGCG*):c.-1+1G>T, NM_001845.4(*COL4A1*):c.*35C>A, NM_001845.4(*COL4A1*):c.*32G>A/T, NM_001845.4(*COL4A1*):c.*31G>T, NM_013382.5(*POMT2*):c.1333-14G>A, NM_000070.2(*CAPN3*):c.380-13T>A, NM_000070.2(*CAPN3*):c.1746-20C>T, NM_173089.1(*CAPN3*):c.-188G>C, NM_000070.2(*CAPN3*):c.2184+21G>A, NM_000070.2(*CAPN3*):c.2185-16A>G, NM_000018.3(*ACADVL*):c.-144_-132delCCCAGCATGCCCCinsT, NM_001270447.1(*ACADVL*):c.822-27C>T, NM_001270447.1(*ACADVL*):c.822-11T>G, NM_001270447.1(*ACADVL*):c.1146+15C>T, NM_001270447.1(*ACADVL*):c.1252-15A>G, NM_001270447.1(*ACADVL*):c.1747+23C>T, NM_000023.2(*SGCA*):c.585-31_585-23delTCTGCTGAC, NM_000023.2(*SGCA*):c.585-31_585-24delTCTGCTGA, NM_000023.2(*SGCA*):c.748-12_748-11delCTinsAA, NM_006640.4(*SEPT9*):c.-134G>C, NM_000152.3(*GAA*):c.-32-13T>A, NM_000152.3(*GAA*):c.-32-13T>G, NM_000152.3(*GAA*):c.-32-3C>A/G, NM_000152.3(*GAA*):c.-32-2A>G, NM_000152.3(*GAA*):c.-32-1G>C, NM_000152.3(*GAA*):c.-17C>T, NM_000152.3(*GAA*):c.1076-22T>G, NM_000152.3(*GAA*):c.2190-345A>G, NM_000152.3(*GAA*):c.2647-20T>G, NM_015295.2(*SMCHD1*):c.1647+103A>G, NM_015295.2(*SMCHD1*):c.1843-15A>G, NM_015295.2(*SMCHD1*):c.3634-19A>G, NM_000540.2(*RYR1*):c.8692+131G>A, NM_000540.2(*RYR1*):c.14647-1449A>G, NM_024301.4(*FKRP*):c.-272G>A, NM_003494.3(*DYSF*):c.3443-33A>G, NM_003494.3(*DYSF*):c.4410+13T>G, NM_003494.3(*DYSF*):c.4886+1249G>T, NM_003494.3(*DYSF*):c.5668-824C>T,

NM_003494.3(*DYSF*):c.*107T>A, NM_080916.2(*DGUOK*):c.444-62C>A, NM_080916.2(*DGUOK*):c.444-11C>G, NM_001271208.1(*NEB*):c.24220-151C>A, NM_001271208.1(*NEB*):c.19429-381_19429-379delTTTinsA, NM_004369.3(*COL6A3*):c.6283-15C>A, NM_001848.2(*COL6A1*):c.859-22A>G, NM_001848.2(*COL6A1*):c.904-39A>G, NM_001848.2(*COL6A1*):c.930+189C>T, NM_001848.2(*COL6A1*):c.1336-146C>T, NM_001849.3(*COL6A2*):c.1117-35_1118dupAAAAGACGTGAGGCTGATTCTGCAAACCCTTCCAGGG, NM_001849.3(*COL6A2*):c.1459-63G>A, NM_013334.3(*GMPPB*):c.-87C>T, NM_000158.3(*GBE1*):c.2053-3358_2053-3350delGTGTGGTGGinsTGTTTTTTACATGACAGGT, NM_004130.3(*GYG1*):c.481+3276C>G, NM_003060.3(*SLC22A5*):c.394-16T>A, NM_003060.3(*SLC22A5*):c.825-52G>A, NM_022464.4(*SIL1*):c.1030-18G>A, NM_000426.3(*LAMA2*):c.3175-22G>A, NM_000426.3(*LAMA2*):c.3556-13T>A, NM_000426.3(*LAMA2*):c.5235-18G>A, NM_000426.3(*LAMA2*):c.8989-12C>G, NM_182961.3(*SYNE1*):c.16237-13C>G, NM_182961.3(*SYNE1*):c.15918-12A>G, NM_006731.2(*FKTN*):c.648-1243G>T, NM_007171.3(*POMT1*):c.-30-2A>G, NM_004006.2(*DMD*):c.10554-18C>G, NM_004006.2(*DMD*):c.9974+175T>A, NM_004006.2(*DMD*):c.9564-30A>T, NM_004006.2(*DMD*):c.9564-427T>G, NM_004006.2(*DMD*):c.9563+1215A>G, NM_004006.2(*DMD*):c.9362-1215A>G, NM_004006.2(*DMD*):c.9361+117A>G, NM_004006.2(*DMD*):c.9225-160A>G, NM_004006.2(*DMD*):c.9225-285A>G, NM_004006.2(*DMD*):c.9225-287C>A, NM_004006.2(*DMD*):c.9225-647A>G, NM_004006.2(*DMD*):c.9225-648A>G, NM_004006.2(*DMD*):c.9224+9192C>A, NM_004006.2(*DMD*):c.9085-15519G>T, NM_004006.2(*DMD*):c.8217+32103G>T, NM_004006.2(*DMD*):c.8217+18052A>G, NM_004006.2(*DMD*):c.7661-11T>C, NM_004006.2(*DMD*):c.6913-4037T>G, NM_004006.2(*DMD*):c.6614+3310G>T, NM_004006.2(*DMD*):c.6290+30954C>T, NM_004006.2(*DMD*):c.6118-15A>G, NM_004006.2(*DMD*):c.5740-15G>T, NM_004006.2(*DMD*):c.5326-215T>G, NM_004006.2(*DMD*):c.5325+1743_5325+1760delTATTAAAAAATGGGTAGA, NM_004006.2(*DMD*):c.4675-11A>G, NM_004006.2(*DMD*):c.3787-843C>A, NM_004006.2(*DMD*):c.3603+2053G>C, NM_004006.2(*DMD*):c.3432+2240A>G, NM_004006.2(*DMD*):c.3432+2036A>G, NM_004006.2(*DMD*):c.961-5831C>T, NM_004006.2(*DMD*):c.961-5925A>C, NM_004006.2(*DMD*):c.832-15A>G, NM_004006.2(*DMD*):c.650-39498A>G, NM_004006.2(*DMD*):c.531-16T>A/G, NM_004006.2(*DMD*):c.531-16T>A, NM_004006.2(*DMD*):c.531-16T>G, NM_004006.2(*DMD*):c.265-463A>G, NM_004006.2(*DMD*):c.93+5590T>A, NM_004006.2(*DMD*):c.31+36947G>A, NM_004006.2(*DMD*):c.-54T>A, NM_000291.3(*PGK1*):c.1214-25T>G, NM_000252.2(*MTM1*):c.137-19_137-16delACTT, NM_000252.2(*MTM1*):c.137-11T>A, NM_000252.2(*MTM1*):c.232-26_232-23delGACT, NM_000252.2(*MTM1*):c.529-909A>G, NM_000252.2(*MTM1*):c.868-13T>A, NM_001017980.3(*VMA21*):c.54-27A>C/T, NM_001017980.3(*VMA21*):c.54-27A>C, NM_001017980.3(*VMA21*):c.54-27A>T, NM_001017980.3(*VMA21*):c.54-16_54-8delGTTTACTTT, NM_000117.2(*EMD*):c.266-27_266-10delTCTGCTACCGCTGCCCCC

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.