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Lab Director: Arash Radfar M.D.
CLIA: 22D0957540

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Metroplex Pathology Associates
Lakewood Pathology Associates
Cohen Dermatopathology
Therapath Partners

Patient Information:
**N8010, Donor**
**DOB:** [redacted]
Sex: M
MR#:
Patient#: FT-PT8705338

Partner Information:
**Not Tested**

Physician:
**Kuan, James**
ATTN: Kuan, James
Denver Sperm Bank
4915 25th Avenue NE, Ste 204W
Seattle, WA 98105
Phone: (206) 588-1484

Laboratory:
**Fulgent Therapeutics LLC**
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Lawrence M. Weiss, MD
Report Date: **May 03,2024**

Accession:
**FT-7133876**
Test#: FT-TS14811992
Specimen Type: Blood (EDTA)
Collected: Apr 11,2024

Accession:
**N/A**

## FINAL RESULTS

Carrier for genetic conditions in **multiple** genes.
Genetic counseling is recommended.

## TEST PERFORMED

**Beacon Preconception Carrier Screening - 515 Genes (without X-linked Disorders)**
(515 Gene Panel; gene sequencing with deletion and duplication analysis)

| Condition and Gene | Inheritance | N8010, Donor | Partner |
|---|---|---|---|
| **Mitochondrial complex I deficiency, nuclear type 4** *NDUFV1* | AR | ⊕ Carrier c.1162+4A>C (p.?) | N/A |
| **Cystic Fibrosis** *CFTR* | AR | ⊕ Carrier c.3209G>A (p.Arg1070Gln) | N/A |

## INTERPRETATION:

**Notes and Recommendations:**

- Based on these results, this individual is positive for carrier mutations in 2 genes. Carrier screening for the reproductive partner is recommended to accurately assess the risk for any autosomal recessive conditions. A negative result reduces, but does not eliminate, the chance to be a carrier for any condition included in this screen. Please see the supplemental table for details.
- Testing for copy number changes in the SMN1 gene was performed to screen for the carrier status of Spinal Muscular Atrophy. The results for this individual are within the normal range for non-carriers. See Limitations section for more information.
- This carrier screening test does not screen for all possible genetic conditions, nor for all possible mutations in every gene tested. This report does not include variants of uncertain significance; only variants classified as pathogenic or likely pathogenic at the time of testing, and considered relevant for reproductive carrier screening, are reported. Please see the gene specific notes for details. Please note that the classification of variants can change over time.
- Patients may wish to discuss any carrier results with blood relatives, as there is an increased chance that they are also carriers. These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.
- X-linked genes are not routinely analyzed for male carrier screening tests. Gene specific notes and limitations may be present. See below.
- Genetic counseling is recommended. Available genetic counselors and additional resources can be found at the National Society of Genetic Counselors (NSGC; https://www.nsgc.org).

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# MITOCHONDRIAL COMPLEX I DEFICIENCY, NUCLEAR TYPE 4

| Patient | N8010, Donor | Partner |
|---|---|---|
| **Result** | Carrier | N/A |
| **Variant Details** | ***NDUFV1*** (NM_007103.4) c.1162+4A>C (p.?) | N/A |

## *What is Mitochondrial complex I deficiency, nuclear type 4?*

Mitochondrial complex I deficiency, also known as Leigh syndrome, is a severe neurodegenerative disorder that usually becomes apparent in the first year of life. This condition typically results in death within two to three years, usually due to respiratory failure. In rare cases, individuals do not develop symptoms until adulthood or have symptoms that worsen more slowly. The first signs of disease are seen in infancy include vomiting, diarrhea, difficulty feeding, and failure to thrive. Affected individuals may develop poor muscle tone, involuntary muscle contractions, and problems with movement and balance due to mitochondrial encephalopathy. Additionally, many individuals with this condition have ocular problems, respiratory failure, cardiomyopathy, and abnormal lactic acid build-up.

## *What is my risk of having an affected child?*

Mitochondrial complex I deficiency, nuclear type 4 is inherited in an autosomal recessive manner. If the patient and the partner are both carriers, the risk for an affected child is 1 in 4 (25%).

## *What kind of medical management is available?*

There is currently no cure for mitochondrial complex I deficiency, nuclear type 4. The prognosis can be poor; Leigh syndrome is lethal in most cases. Various therapeutic interventions, including coenzyme-Q, riboflavin, a ketogenic diet, and L-carnitine, have been attempted in individuals with NDUFV1-related mitochondrial complex I deficiency with mixed results.

## *What mutation was detected?*

The detected heterozygous variant was NM_007103.4:c.1162+4A>C (p.?). This intronic variant, c.1162+4A>C, is predicted by multiple splice site models (3 of 5), to reduce the strength of the canonical splice donor site of exon 8. Functional studies, in patient derived mRNA, have demonstrated that this variant results in exon 8 skipping (PubMed: 11349233, 27344648). Further functional work in patient fibroblasts has demonstrated that this variant results in decreased NDUFV1 protein expression, decreased complex CI and complex IV assembly and consequential reductions in the enzymatic activities of both complexes (PubMed: 27344648)This variant has been reported in the compound heterozygous state in several unrelated individuals with Mitochondrial complex I deficiency (PubMed: 11349233, 26024641, 27344648, 34134969).This variant is classified as "Pathogenic" or "Likely Pathogenic" in ClinVar, with multiple submitters in agreement (Variation ID: 372716). The laboratory classifies this variant as pathogenic.

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# CYSTIC FIBROSIS

| Patient | N8010, Donor | Partner |
|---|---|---|
| **Result** | ⊕ Carrier | N/A |
| **Variant Details** | ***CFTR*** (NM_000492.4)<br>c.3209G>A (p.Arg1070Gln) | N/A |

## *What is Cystic Fibrosis?*

Cystic fibrosis (CF) is a progressive lung disease caused by the body producing mucus that is abnormally thick and sticky. This results in a buildup of mucus in the lungs and the digestive system. This buildup can lead to chronic respiratory infections, lung damage, and malabsorption of nutrients, resulting in poor growth, diarrhea, and a form of diabetes known as cystic fibrosis-related diabetes mellitus. The symptoms are highly variable among individuals, from severe to mild, and may also include complications in pregnancy and male infertility. While CF used to be considered a fatal disease of childhood, many people with CF now live into adulthood.

## *What is my risk of having an affected child?*

Cystic fibrosis is inherited in an autosomal recessive manner. This means that if both parents are carriers, their risk of having an affected child is 1 in 4 (25%).

## *What kind of medical management is available?*

Medical advancements have significantly improved the longevity of patients with CF with the median predicted survival age now close to 40 years. Treatments vary depending on severity but may include nebulizers (machines that deliver liquid medicine to the lungs in the form of a fine mist), inhalers, antibiotics, and enzymatic supplementation. Men with congenital absence of the vas deferens (CAVD) may require fertility treatments to father children.

## *What mutation was detected?*

The detected heterozygous variant was NM_000492.4:c.3209G>A (p.Arg1070Gln). This variant, p.Arg1070Gln (also reported as c.3341G>A), has been previously detected in a compound heterozygous state in at least 20 individuals presenting with cystic fibrosis (PubMed: 23891399, 25087612, 7683628).Additionally, this variant has also been detected in the heterozygous and compound heterozygous states in multiple individuals presenting with chronic pancreatitis, a known CFTR-related disorder (PubMed: 18456578, 22658665, 27171515).While rare, the allele frequency of this variant in the general population is not consistent with it being highly penetrant for autosomal dominant pancreatitis. In vitro experiments have indicated that this variant causes defects in the processing and function of the CFTR protein, resulting in significantly lower chloride transport than wildtype (PubMed: 23891399). Of note, the CFTR potentiator ivacaftor was shown to increase chloride transport through the p.Arg1070Gln CFTR protein from 20% to 33% of wildtype when tested in vitro (PubMed: 23891399). The laboratory classifies this variant as likely pathogenic.

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## GENES TESTED:

**Beacon Preconception Carrier Screening - 515 Genes (without X-linked Disorders) - 515 Genes**

This analysis was run using the Beacon Preconception Carrier Screening - 515 Genes (without X-linked Disorders) gene list. 515 genes were tested with 99.4% of targets sequenced at >20x coverage. For more gene-specific information and assistance with residual risk calculation, see the SUPPLEMENTAL TABLE.

*AAAS, ABCA12, ABCA3, ABCA4, ABCB11, ABCB4, ABCC2, ABCC8, ACAD9, ACADM, ACADVL, ACAT1, ACOX1, ACSF3, ADA, ADAMTS2, ADAMTSL4, ADGRG1, ADGRV1, AGA, AGL, AGPS, AGXT, AHI1, AIPL1, AIRE, ALDH3A2, ALDH7A1, ALDOB, ALG1, ALG6, ALMS1, ALPL, AMN, AMT, ANO10, AP1S1, AQP2, ARG1, ARL6, ARSA, ARSB, ASL, ASNS, ASPA, ASS1, ATM, ATP6V1B1, ATP7B, ATP8B1, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, BCKDHA, BCKDHB, BCS1L, BLM, BLOC1S3, BLOC1S6, BMP1, BRIP1, BSND, CAD, CANT1, CAPN3, CASQ2, CBS, CC2D1A, CC2D2A, CCDC103, CCDC39, CCDC88C, CD3D, CD3E, CD40, CD59, CDH23, CEP152, CEP290, CERKL, CFTR, CHAT, CHRNE, CHRNG, CIITA, CLCN1, CLN3, CLN5, CLN6, CLN8, CLRN1, CNGB3, COL11A2, COL17A1, COL27A1, COL4A3, COL4A4, COL7A1, COX15, CPS1, CPT1A, CPT2, CRB1, CRTAP, CRYL1, CTNS, CTSA, CTSC, CTSD, CTSK, CYBA, CYP11A1, CYP11B1, CYP11B2, CYP17A1, CYP19A1, CYP1B1, CYP21A2, CYP27A1, CYP27B1, CYP7B1, DBT, DCAF17, DCLRE1C, DDX11, DGAT1, DGUOK, DHCR7, DHDDS, DLD, DLL3, DNAH11, DNAH5, DNAI1, DNAI2, DNMT3B, DOK7, DUOX2, DYNC2H1, DYSF, EIF2AK3, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, ELP1, EPG5, ERCC2, ERCC6, ERCC8, ESCO2, ETFA, ETFB, ETFDH, ETHE1, EVC, EVC2, EXOSC3, EYS, FAH, FAM161A, FANCA, FANCC, FANCD2, FANCE, FANCG, FANCI, FANCL, FBP1, FBXO7, FH, FKBP10, FKRP, FKTN, FMO3, FOXN1, FOXRED1, FRAS1, FREM2, FUCA1, G6PC, G6PC3, GAA, GALC, GALE, GALK1, GALNS, GALNT3, GALT, GAMT, GATM, GBA, GBE1, GCDH, GCH1, GDF5, GFM1, GHR, GJB2, GJB6, GLB1, GLDC, GLE1, GNE, GNPAT, GNPTAB, GNPTG, GNS, GORAB, GRHPR, GRIP1, GSS, GUCY2D, GUSB, HADH, HADHA, HADHB, HAMP, HAX1, HBA1, HBA2, HBB, HEXA, HEXB, HGSNAT, HJV, HLCS, HMGCL, HMOX1, HOGA1, HPD, HPS1, HPS3, HPS4, HPS5, HPS6, HSD17B3, HSD17B4, HSD3B2, HYAL1, HYLS1, IDUA, IGHMBP2, IKBKB, IL7R, INVS, ITGA6, ITGB3, ITGB4, IVD, JAK3, KCNJ1, KCNJ11, LAMA2, LAMA3, LAMB3, LAMC2, LARGE1, LCA5, LDLR, LDLRAP1, LHX3, LIFR, LIG4, LIPA, LMBRD1, LOXHD1, LPL, LRAT, LRP2, LRPPRC, LYST, MAK, MAN2B1, MANBA, MCEE, MCOLN1, MCPH1, MECR, MED17, MESP2, MFSD8, MKKS, MKS1, MLC1, MLYCD, MMAA, MMAB, MMACHC, MMADHC, MOCS1, MOCS2, MPI, MPL, MPV17, MRE11, MTHFR, MTR, MTRR, MTTP, MUSK, MUT, MVK, MYO15A, MYO7A, NAGA, NAGLU, NAGS, NBN, NCF2, NDRG1, NDUFAF2, NDUFAF5, NDUFS4, NDUFS6, NDUFS7, NDUFV1, NEB, NEU1, NGLY1, NPC1, NPC2, NPHP1, NPHS1, NPHS2, NR2E3, NSMCE3, NTRK1, OAT, OCA2, OPA3, OSTM1, OTOA, OTOF, P3H1, PAH, PANK2, PC, PCBD1, PCCA, PCCB, PCDH15, PCNT, PDHB, PEPD, PET100, PEX1, PEX10, PEX12, PEX13, PEX16, PEX2, PEX26, PEX5, PEX6, PEX7, PFKM, PGM3, PHGDH, PHKB, PHKG2, PHYH, PIGN, PJVK, PKHD1, PLA2G6, PLEKHG5, PLOD1, PMM2, PNPO, POLG, POLH, POMGNT1, POMT1, POMT2, POR, POU1F1, PPT1, PRCD, PRDM5, PRF1, PROP1, PSAP, PTPRC, PTS, PUS1, PYGM, QDPR, RAB23, RAG1, RAG2, RAPSN, RARS2, RDH12, RLBP1, RMRP, RNASEH2A, RNASEH2B, RNASEH2C, RPE65, RPGRIP1L, RTEL1, RXYLT1, RYR1, SACS, SAMD9, SAMHD1, SCO2, SEC23B, SEPSECS, SGCA, SGCB, SGCD, SGCG, SGSH, SKIV2L, SLC12A1, SLC12A3, SLC12A6, SLC17A5, SLC19A2, SLC19A3, SLC1A4, SLC22A5, SLC25A13, SLC25A15, SLC25A20, SLC26A2, SLC26A3, SLC26A4, SLC27A4, SLC35A3, SLC37A4, SLC38A8, SLC39A4, SLC45A2, SLC4A11, SLC5A5, SLC7A7, SMARCAL1, SMN1, SMPD1, SNAP29, SPG11, SPR, SRD5A2, ST3GAL5, STAR, STX11, STXBP2, SUMF1, SUOX, SURF1, SYNE4, TANGO2, TAT, TBCD, TBCE, TCIRG1, TCN2, TECPR2, TERT, TF, TFR2, TG, TGM1, TH, TK2, TMC1, TMEM216, TMEM67, TMPRSS3, TPO, TPP1, TREX1, TRIM32, TRIM37, TRMU, TSEN54, TSFM, TSHB, TSHR, TTC37, TTPA, TULP1, TYMP, TYR, TYRP1, UBR1, UNC13D, USH1C, USH2A, VDR, VLDLR, VPS11, VPS13A, VPS13B, VPS45, VPS53, VRK1, VSX2, WISP3, WNT10A, WRN, XPA, XPC, ZBTB24, ZFYVE26, ZNF469*

## METHODS:

Genomic DNA was isolated from the submitted specimen indicated above (if cellular material was submitted). DNA was barcoded, and enriched for the coding exons of targeted genes using hybrid capture technology. Prepared DNA libraries were then sequenced using a Next Generation Sequencing technology. Following alignment to the human genome reference sequence (assembly GRCh37), variants were detected in regions of at least 10x coverage. For this specimen, 99.50% and 99.44% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). All genes listed were evaluated for large deletions and/or duplications. However, single exon deletions or duplications will not be detected in this assay, nor will copy number alterations in regions of genes with significant pseudogenes. Putative deletions or duplications are analyzed using Fulgent Germline proprietary pipeline for this specimen. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

## LIMITATIONS:

**General Limitations**

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or

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otherwise, to future pregnancies, and negative results do not rule out the genetic risk to a pregnancy. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions other than specified genes. DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution of pseudogene sequences or other highly-homologous sequences, sometimes these may still interfere with the technical ability of the assay to identify pathogenic alterations in both sequencing and deletion/duplication analyses. Deletion/duplication analysis can identify alterations of genomic regions which include one whole gene (buccal swab specimens and whole blood specimens) and are two or more contiguous exons in size (whole blood specimens only); single exon deletions or duplications may occasionally be identified, but are not routinely detected by this test. When novel DNA duplications are identified, it is not possible to discern the genomic location or orientation of the duplicated segment, hence the effect of the duplication cannot be predicted. Where deletions are detected, it is not always possible to determine whether the predicted product will remain in-frame or not. Unless otherwise indicated, deletion/duplication analysis has not been performed in regions that have been sequenced by Sanger.

**Gene Specific Notes and Limitations**

*ALG1:* Due to the interference by highly homologous regions, our current testing method has less sensitivity to detect variants in exons 6-13 of the ALG1 gene (NM_019109.4). *CEP290:* Copy number analysis for exons 8-13 and exons 39-42 may have reduced sensitivity in the CEP290 gene. Confirmation of these exons are limited to individuals with a positive personal history of CEP290-related conditions and/or individuals carrying a pathogenic/likely pathogenic sequence variant. *CFTR:* Analysis of the intron 8 polymorphic region (e.g. IVS8-5T allele) is only performed if the p.Arg117His (R117H) mutation is detected. Single exon deletion/duplication analysis is limited to deletions of previously reported exons: 1, 2, 3, 11, 19, 20, 21. Analysis of the intron 8 polymorphic region (e.g. IVS8-5T allele) is only performed if the p.Arg117His (R117H) mutation is detected. Single exon deletion/duplication analysis is limited to deletions of previously reported exons: 1, 2, 3, 11, 19, 20, 21. CFTR variants primarily associated with CFTR-related isolated congenital bilateral absence of the vas deferens and CFTR-related pancreatitis are not included in this analysis. CFTR variants with insufficient evidence of being cystic fibrosis mutations will not be reported either. *CRYL1:* As mutations in the CRYL1 gene are not known to be associated with any clinical condition, sequence variants in this gene are not analyzed. However, to increase copy number detection sensitivity for large deletions including this gene and a neighboring on gene on the panel (GJB6, also known as connexin 30), this gene was evaluated for copy number variation. *CYP11B1:* The current testing method is not able to reliably detect certain pathogenic variants in this gene due to the interference by highly homologous regions. This analysis is not designed to detect or rule-out copy-neutral chimeric CYP11B1/CYP11B2 gene. *CYP11B2:* The current testing method is not able to reliably detect certain pathogenic variants in this gene due to the interference by highly homologous regions. This analysis is not designed to detect or rule-out copy-neutral chimeric CYP11B1/CYP11B2 gene. *CYP21A2:* Significant pseudogene interference and/or reciprocal exchanges between the CYP21A2 gene and its pseudogene, CYP21A1P, have been known to occur and may impact results. As such, the relevance of variants reported in this gene must be interpreted clinically in the context of the clinical findings, biochemical profile, and family history of each patient. LR-PCR is not routinely ordered for NM_000500.9:c.955C>T (p.Gln319Ter). Individuals with c.955C>T (p.Gln319Ter) will be reported as a Possible Carrier indicating that the precise nature of the variant has not been determined by LR-PCR and that the variant may occur in the CYP21A2 wild-type gene or in the CYP21A1P pseudogene. The confirmation test is recommended if the second reproductive partner is tested positive for variants associated with classic CAH. *DDX11:* Due to the interference by highly homologous regions, our current testing method has less sensitivity to detect variants in the DDX11 gene. *DUOX2:* The current testing method is not able to reliably detect variants in exons 6-8 of the DUOX2 gene (NM_014080.5) due to significant interference by the highly homologous gene, DUOX1. *FANCD2:* Due to pseudogene interference, copy-number-variants within exon 14-17 of the FANCD2 gene (NM _033084.4) are not evaluated and detection of single-nucleotide variants and small insertions/deletions in this region is not guaranteed. *GALT:* In general, the D2 "Duarte" allele is not reported if detected, but can be reported upon request. While this allele can cause positive newborn screening results, it is not known to cause clinical symptoms in any state. See GeneReviews for more information: https://www.ncbi.nlm.nih.gov/books/NBK1518/ *GBA:* Significant pseudogene interference and/or reciprocal exchanges between the GBA gene and its pseudogene, GBAP1, have been known to occur and may impact results. As such, the relevance of variants reported in this gene must be interpreted clinically in the context of this individual's clinical findings, biochemical profile, and family history. The current testing method cannot detect copy-neutral rearrangements between the pseudogene and the functional gene, which have been reported in very rare cases of Gaucher disease (PubMed: 21704274). *HBA1:* Significant interference

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from highly homologous regions in exons 1-2 of the HBA1 gene has been recognized to occur, potentially impeding the assay's technical capability to detect pathogenic alterations during sequencing analyses. *HBA2:* Significant interference from highly homologous regions in exons 1-2 of the HBA2 gene has been recognized to occur, potentially impeding the assay's technical capability to detect pathogenic alterations during sequencing analyses. *HSD17B4:* Copy number analysis for exons 4-6 may have reduced sensitivity in the HSD17B4 gene. Confirmation of these exons are limited to individuals with a positive personal history of D-bifunctional protein deficiency and Perrault syndrome and/or individuals carrying a pathogenic/likely pathogenic sequence variant. *LMBRD1:* Copy number analysis for exons 9-12 may have reduced sensitivity in the LMBRD1 gene. Confirmation of these exons are limited to individuals with a positive personal history of combined methylmalonic aciduria and homocystinuria and/or individuals carrying a pathogenic/likely pathogenic sequence variant. *MTHFR:* As recommended by ACMG, the two common polymorphisms in the MTHFR gene - c.1286A>C (p.Glu429Ala, also known as c.1298A>C) and c.665C>T (p.Ala222Val, also known as c.677C>T) - are not reported in this test due to lack of sufficient clinical utility to merit testing (PubMed: 23288205). *NEB:* This gene contains a 32-kb triplicate region (exons 82-105) which is not amenable to sequencing and deletion/duplication analysis. *NPHS2:* If detected, the variant NM_014625.3:c.686G>A (p.Arg229Gln) will not be reported as this variant is not significantly associated with disease when homozygous or in the compound heterozygous state with variants in exons 1-6 of NPHS2. *OTOA:* Due to pseudogene interference, our current testing method is not able to reliably detect variants in exons 20-28 (NM_144672.3) in the OTOA gene. *SMN1:* The current testing method detects sequencing variants in exon 7 and copy number variations in exons 7-8 of the SMN1 gene (NM_022874.2). Sequencing and deletion/duplication analysis are not performed on any other region in this gene. About 5%-8% of the population have two copies of SMN1 on a single chromosome and a deletion on the other chromosome, known as a [2+0] configuration (PubMed: 20301526). The current testing method cannot directly detect carriers with a [2+0] SMN1 configuration but can detect linkage between the silent carrier allele and certain population-specific single nucleotide changes. As a result, a negative result for carrier testing greatly reduces but does not eliminate the chance that a person is a carrier. Only abnormal results will be reported. *TERT:* The TERT promoter region is analyzed for both sequencing and copy number variants. *TYR:* Due to the interference by highly homologous regions, our current testing method has less sensitivity to detect variants in exons 4-5 of the TYR gene (NM_000372.5). *VPS45:* LoF is not a known disease mechanism *WRN:* Due to the interference by highly homologous regions within the WRN gene, our current testing method has less sensitivity to detect variants in exons 10-11 of WRN (NM_000553.6).

## SIGNATURE:

**Geetu Mendiratta-Vij, PhD, FACMG, CGMBS** on **5/3/2024**
Laboratory Director, Fulgent

## DISCLAIMER:

This test was developed and its performance characteristics determined by Fulgent Therapeutics LLC CAP #8042697 CLIA #05D2043189; 4399 Santa Anita Ave., El Monte, CA, 91731. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Since genetic variation, as well as systematic and technical factors, can affect the accuracy of testing, the results of testing should always be interpreted in the context of clinical and familial data. For assistance with interpretation of these results, healthcare professionals may contact us directly at **626-350-0537** or by email at **info@fulgentgenetics.com**. It is recommended that patients receive appropriate genetic counseling to explain the implications of the test result, including its residual risks, uncertainties and reproductive or medical options.

**To view the supplemental table describing the carrier frequencies, detection rates, and residual risks associated with the genes on this test please visit the following link:**
**Beacon Expanded Carrier Screening Supplemental Table**

# N8010,DONOR

DOB: [redacted]
Sex: M
Phone: (303) 970-5897
Patient ID: N8010

Age [redacted]
Fasting: U

Specimen: DV767066M
Requisition: 0000095
Report Status: FINAL / SEE REPORT

Collected: 04/11/2024 10:11
Received: 04/11/2024 22:03
Reported: 04/23/2024 16:07

Client #: 70413924
BERRY,ANDREW
DENVER SPERM BANK
1601 E 19TH AVE STE 4500
DENVER, CO 80218-1289
Phone: (303) 970-5897

FASTING:UNKNOWN

## CHROMOSOME ANALYSIS, BLOOD

FINAL

Lab: EZ

| Analyte | Value | |
|---|---|---|
| **CHROMOSOME ANALYSIS, BLOOD** (29770-5) | **See Below** | FINAL |

```
Order ID:                 24-171642

Specimen Type:            Blood

Clinical Indication:      GAMETE DONOR

RESULT:
NORMAL MALE KARYOTYPE

INTERPRETATION:
Chromosome analysis revealed normal G-band patterns within
the limits of standard cytogenetic analysis.

Please expect the results of any other concurrent study in a
separate report.


NOMENCLATURE:
46,XY

ASSAY INFORMATION:
Method:                   G-Band (Digital Analysis: MetaSyst
Cells Counted:            20
Band Level:               450
Cells Analyzed:           5
Cells Karyotyped:         5

This test does not address genetic disorders that cannot be
detected by standard cytogenetic methods or rare events such
as low level mosaicism or subtle rearrangements.

Morteza Hemmat, PhD, FACMG     (800) NICHOLS-4307

Electronic Signature:            4/23/2024 5:22 PM
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**Performing Sites**

EZ Quest Diagnostics/Nichols SJC-San Juan Capistrano,, 33608 Ortega Hwy, San Juan Capistrano, CA 92675-2042 Laboratory Director: Irina Maramica MD,PhD,MBA

**Key**

Priority Out of Range  Out of Range  PEND Pending Result  PRE Preliminary Result  FINAL Final Result  RE Reissued Result