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Patient Information:

**20000, Donor**

**DOB:** [REDACTED]

Sex: M

MR#: 20000

Patient#: FT-PT8768623

Partner Information:

**Not Tested**

Physician:

**Kuan, James**

ATTN: Kuan, James

Las Vegas 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: **Jul 12, 2024**

Accession:

**FT-7041054**

Test#: FT-TS14875473

Specimen Type: Blood (EDTA)

Collected: Jun 21, 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	20000, Donor	Partner
<b>Spinal muscular atrophy silent carrier</b> <i>SMN1</i>	AR	⊕ Possible Carrier c.*3+80T>G (p.?)	N/A
<b>Congenital adrenal hyperplasia due to 21-hydroxylase deficiency</b> <i>CYP21A2</i>	AR	⊕ Possible Carrier c.955C>T(:)*12C>T + CYP21A2 duplication p.(Gln319*)(:)(?)	N/A
<b>Lethal congenital contracture syndrome 1</b> <i>GLE1</i>	AR	⊕ Carrier c.1240C>T (p.Gln414*)	N/A

## INTERPRETATION:

### Notes and Recommendations:

- Based on these results, this individual is positive for carrier mutations in 3 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.
- 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>)

Patient: 20000, Donor; Sex: M;  
DOB: [REDACTED] MR#: 20000

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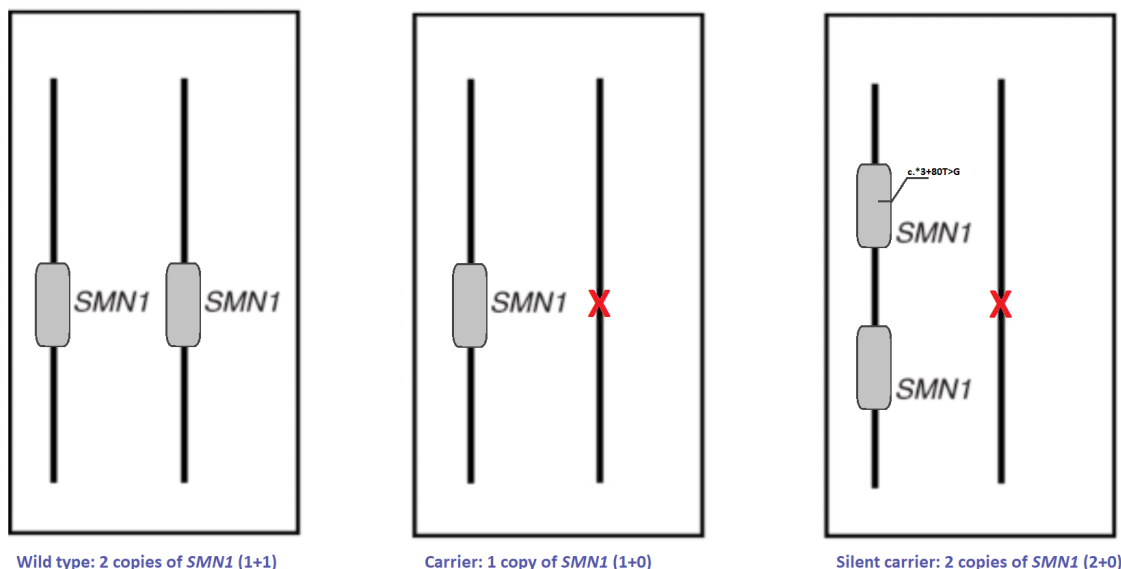
## SPINAL MUSCULAR ATROPHY SILENT CARRIER

Patient	20000, Donor	Partner
<b>Result</b>	<b>+</b> Possible Carrier	N/A
<b>Variant Details</b>	<b>SMN1</b> (NM_000344.3) c.*3+80T>G (p.?)	N/A

### *What is Spinal muscular atrophy silent carrier?*

Spinal muscular atrophy (SMA) affects nerve cells called motor neurons in the spinal cord and brainstem. The progressive degeneration of these nerve cells results in muscle weakness and atrophy (degeneration of muscle mass). Common symptoms include limited growth and poor weight gain, restrictive lung disease, and skeletal abnormalities, such as scoliosis or contractures of the joints.

Individuals typically have one copy of the *SMN1* gene on each chromosome, with carriers having a mutation in one copy that prevents normal function. A spinal muscular atrophy silent carrier is an individual who has two functional copies of the *SMN1* gene on one chromosome and zero copies of the *SMN1* gene on the other chromosome. This is a special scenario because the overall number of copies of *SMN1* may appear normal (i.e. two total copies of *SMN1*), however, that same person is considered a carrier for SMA since there are no functional copies of the *SMN1* gene on one chromosome. A person with this specific configuration of the *SMN1* genes is considered to be a "silent carrier".



For technical reasons, the chromosome with zero copies of *SMN1* cannot always be directly observed in the DNA sequencing data (PubMed: [20301526](#), [32915251](#)). Instead, silent carriers are observed based on the presence of two copies of the *SMN1* gene and the specific variant c.\*3+80T>G, which commonly occurs on the same chromosome with a duplication of the *SMN1* gene. For individuals of Ashkenazi Jewish descent, c.\*3+80T>G with two copies of *SMN1* is considered as a positive finding for SMA carrier status (PubMed: [23788250](#), [36140824](#)). While the positive predictive value of c.\*3+80T>G with two copies of *SMN1* can vary, nonetheless, for all other ethnic groups this variant is associated with an increased likelihood of being a carrier for SMA (PubMed: [36140824](#), [32066871](#), [36669496](#)). Alternatively, in some individuals with c.\*3+80T>G and two copies of *SMN1* there is a possibility that these variants occur with a single copy of the *SMN1* gene on each chromosome, and in that case the individual would not be considered a silent carrier for spinal muscular atrophy. In some cases, follow-up genetic testing of the parents of the *SMN1* silent carrier may be helpful in further resolving the mutation status.

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

Patient: 20000, Donor; Sex: M;  
DOB: [REDACTED] MR#: 20000

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SMA is inherited in an autosomal recessive manner. This means that when both parents are carriers for the condition, there is a 25% (1 in 4) risk of having an affected child.

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

There is currently no cure for SMA, but management can include supportive, rehabilitative, and palliative care to manage symptoms and prevent complications. Treatment is designed to address the primary and secondary effects of muscle weakness and may include dietary management and placement of a gastrostomy tube, breathing exercises or machines to help with breathing problems, and surgical repair for scoliosis. Exercises and stretches help with mobility and assistive equipment such as wheelchairs or splints may also be necessary. There have also been recent drug therapies developed to treat SMA such as Spinraza and Zolgensma. For SMA, it is important to provide proactive care and deliver timely intervention.


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### *What mutation was detected?*

The detected heterozygous variant was NM\_000344.3:c.\*3+80T>G (p.?). The detected variant NM\_000344.3:c.\*3+80T>G (p.?) is part of a SMN1 haplotype. In individuals with Ashkenazi Jewish heritage, the detection of this variant in concert with normal copy number of the SMN1 gene is considered positive for carrier status (PubMed: [23788250](#)). For all other ethnic groups this variant is associated with an increased likelihood of being a carrier for SMA (PubMed: [36140824](#), [32066871](#), [36669496](#)). This variant is located within the 3-prime untranslated region of the SMN1 gene, and has been linked with "silent carrier" status (or "[2+0]" configuration) where two copies of the SMN1 gene are present on the same chromosome and zero copies are present on the opposite chromosome. As this individual was detected as having two copies of the SMN1 gene by copy number analysis, these results indicate that this individual may be a carrier for an SMN1 deletion on the other chromosome ("silent" carrier). The laboratory classifies this variant as pathogenic.



## CONGENITAL ADRENAL HYPERPLASIA DUE TO 21-HYDROXYLASE DEFICIENCY

Patient	20000, Donor	Partner
Result	 Possible Carrier	N/A
Variant Details	<b>CYP21A2</b> (NM_000500.9) c.955C>T(;)*12C>T + CYP21A2 duplication p.(Gln319*)(;)(?)	N/A

### *What is Congenital adrenal hyperplasia due to 21-hydroxylase deficiency?*

Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is an inherited disorder that affects the adrenal glands and hormone production. Approximately 75 percent of individuals with classic 21-hydroxylase deficiency have the salt-wasting type, whereby the body excretes too much salt in urine. Affected infants present with poor feeding, weight loss, dehydration, and vomiting, all of which can be life-threatening. Females with this condition typically have ambiguous genitalia, while males usually have normal genitalia, but with small testes. Individuals with the simple virilizing form and the non-classic form of the disease do not experience salt loss. Males and females with either the classic or non-classic forms of 21-hydroxylase deficiency tend to have an early growth spurt, but their final adult height is usually shorter than others in their family, and affected individuals may have reduced fertility. Additionally, individuals may have excessive body hair growth, hair loss, and irregular menstruation. Some individuals (male or female) with the non-classic form of the disease may have mild, non-life-threatening symptoms, while others may never develop symptoms of the disorder at all.

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

CAH due to 21-hydroxylase deficiency 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?*

Treatment consists of early initiation of hormone replacement therapy and/or surgery for females. Prognosis is good for patients with appropriate medical management and psychological support.


### *What mutation was detected?*

The heterozygous variants c.955C>T (p.Gln319\*) and a whole gene duplication of CYP21A2 were detected in this sample. In addition, the benign polymorphism c.\*12C>T was also detected. The phase of these variants is unknown but could be determined through parental testing.

The nonsense variant, p.Gln319\*, introduces a premature stop codon and is expected to result in the loss of function of the protein product of the CYP21A2 gene, either as the result of protein truncation or of nonsense-mediated mRNA decay. This variant, also reported as Q318\*, is a classic 21-hydroxylase-deficient congenital adrenal hyperplasia mutation and has been reported in multiple affected individuals (PubMed: [3267225](#), [12220458](#), [12915679](#)). The variant, p.Gln319\*, and the polymorphism c.\*12C>T are known to frequently occur in a duplicated copy of the CYP21A2 gene coexisting with a normal copy of CYP21A2 on the same chromosome. This haplotype was identified in approximately 2% of the general population and in ~80% of carriers of p.Gln319\*, and such a configuration may represent a benign allele (PubMed: [28401898](#), [19773403](#)). Nonetheless, there is a possibility that p.Gln319\* occurs on a chromosome with only a single copy of CYP21A2, in which case it results in a pathogenic allele. If multiple copies of CYP21A2 are present, we cannot be certain if this p.Gln319\* variant occurs on a chromosome with one (i.e. pathogenic state) or two (i.e. benign state) copies of CYP21A2. While this combination of variants may represent a benign allele, the laboratory classifies the variant p.Gln319\* as likely pathogenic.



## LETHAL CONGENITAL CONTRACTURE SYNDROME 1

Patient	20000, Donor	Partner
Result	 Carrier	N/A
Variant Details	<b>GLE1</b> (NM_001003722.2) c.1240C>T (p.Gln414*)	N/A

### *What is Lethal congenital contracture syndrome 1?*

Lethal congenital contracture syndrome 1 is a disorder characterized by degeneration of neurons in the spinal cord and malformations due to stiffening of muscles and tendons. Affected fetuses show a complete absence of movement. Other indications may be abnormally thin ribs, a malformed jaw, as well as fluid buildup in the lungs. Death occurs either during pregnancy or within the first hours of life. To date, cases of lethal congenital contracture syndrome 1 have only been reported in individuals of Finnish ancestry.

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

Lethal congenital contracture syndrome 1 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?*

Lethal congenital contracture syndrome 1 always results in death during or shortly after birth.

### *What mutation was detected?*

The detected heterozygous variant was NM\_001003722.2:c.1240C>T (p.Gln414\*). This nonsense variant is predicted to introduce a premature stop codon at least 50 nucleotides upstream of the canonical donor splice site of the penultimate exon and to result in the loss of function of the protein product due to nonsense-mediated mRNA decay (PubMed: [25741868](#), [30192042](#), [27618451](#), [11532962](#), [18066079](#)). There's sufficient evidence that loss of function in this gene is a known disease mechanism for GLE1-related conditions (PubMed: [32954510](#), [34025336](#)). The laboratory classifies this variant as likely pathogenic.



## 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 99.5% 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, CHRNA, 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, FKBP, FKTN, FMO3, FOXN1, FOXRED1, FRAS1, FREM2, FUCA1, G6PC, G6PC3, GAA, GALT, GALE, GALK1, GALNS, GALNT3, GALT, GAMT, GATM, GBA, GBE1, GCDH, GCH1, GDF5, GFM1, GHR, GJB2, GJB6, GJB1, GLDC, GLE1, GNE, GNPAT, GNPTAB, GNPTG, GNS, GORAB, GRHRP, 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, IKBK, 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, MECP, MED17, MESF2, MFSDB, MKKS, MKS1, MLC1, MLYCD, MMAA, MMAB, MMACHC, MMADHC, MOCS1, MOCS2, MPI, MPL, MPV17, MRE11, MTHFR, MTR, MTRR, MTPP, 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, PJKV, 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, RARSN, 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, SMARCA1, 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, TMPPRS3, 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, 99.55% and 99.51% 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





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 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



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, CGMB** on 7/12/2024  
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](tel:626-350-0537) or by email at [info@fulgentgenetics.com](mailto: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](#)







Patient Information	Specimen Information	Client Information
<b>20000, DONOR</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] Gender: M      Fasting: U Phone: 725.257.0900 Patient ID: 20000	Specimen: LV973907W Requisition: 0000013  Collected: 06/21/2024 / 09:33 PDT Received: 06/21/2024 / 21:42 PDT Reported: 07/02/2024 / 13:41 PDT	Client #: 88807473      MAIL500 FOORD, DYLAN R LAS VEGAS SPERM BANK 2870 S MARYLAND PKWY STE 250 LAS VEGAS, NV 89109-1548

**COMMENTS:**      FASTING:UNKNOWN

## Cytogenetic Report

### CHROMOSOME ANALYSIS, BLOOD - 14596

**Lab:EZ**

### CHROMOSOME ANALYSIS, BLOOD

Order ID: 24-295478  
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

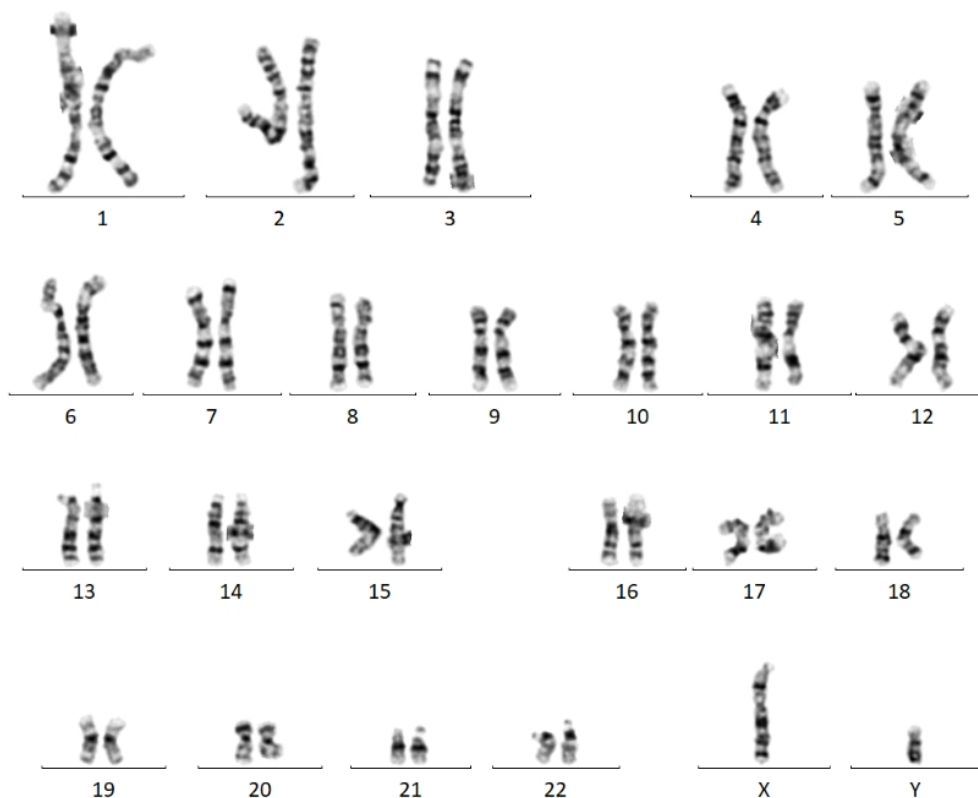
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

Lauren Walters-Sen, PhD, FACMG (800) NICHOLS-4307, [

Electronic Signature: 7/2/2024 3:50 PM



Patient Information	Specimen Information	Client Information
<b>20000, DONOR</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] <b>Gender:</b> M <b>Fasting:</b> U <b>Patient ID:</b> 20000	<b>Specimen:</b> LV973907W <b>Collected:</b> 06/21/2024 / 09:33 PDT <b>Received:</b> 06/21/2024 / 21:42 PDT <b>Reported:</b> 07/02/2024 / 13:41 PDT	<b>Client #:</b> 88807473 <b>FOORD, DYLAN R</b>



**PERFORMING SITE:**

EZ QUEST DIAGNOSTICS/NICHOLS SJC, 33608 ORTEGA HWY, SAN JUAN CAPISTRANO, CA 92675-2042 Laboratory Director: IRINA MARAMICA,MD,PHD,MBA, CLIA: 05D0643352