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Needham, MA 02494
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Lab Director: Arash Radfar M.D.
CLIA: 22D0957540



Patient Information:

N1001, Donor

DOB: [REDACTED]

Sex: M

MR#: N1001

Patient#: FT-PT8766744

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 08, 2024**

Accession:

FT-7117962

Test#: FT-TS14873596

Specimen Type: Blood (EDTA)

Collected: Jun 20, 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	N1001, Donor	Partner
Hepatocerebral mitochondrial DNA depletion syndrome, MPV17-related <i>MPV17</i>	AR	⊕ Carrier c.293C>T (p.Pro98Leu)	N/A
Zellweger syndrome, PEX6-related <i>PEX6</i>	AR	⊕ Carrier c.2663G>C (p.Arg888Pro)	N/A
Retinitis pigmentosa 25 <i>EYS</i>	AR	⊕ Carrier c.9036del (p.Leu3013Serfs*6)	N/A
Asparagine synthetase deficiency <i>ASNS</i>	AR	⊕ Carrier c.1210C>T (p.Arg404Cys)	N/A

INTERPRETATION:

Notes and Recommendations:

- **PLEASE NOTE:** While some heterozygous variants in the **PEX6** gene have been associated with autosomal dominant Peroxisome biogenesis disorder 4B, the reported variant has not been associated with those findings.
- Based on these results, this individual is positive for carrier mutations in 4 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

Patient: N1001, Donor; Sex: M;
DOB: [REDACTED] **MR#: N1001**

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Society of Genetic Counselors (NSGC; <https://www.nsgc.org>)



HEPATOCEREBRAL MITOCHONDRIAL DNA DEPLETION SYNDROME, MPV17-RELATED

Patient	N1001, Donor	Partner
Result	 Carrier	N/A
Variant Details	MPV17 (NM_002437.5) c.293C>T (p.Pro98Leu)	N/A

What is Hepatocerebral mitochondrial DNA depletion syndrome, MPV17-related?

MPV17-related hepatocerebral mitochondrial DNA depletion syndrome is an inherited disorder that can cause liver disease and neurological problems. The signs and symptoms of this condition begin in infancy and typically include vomiting, diarrhea, and failure to thrive. Many affected infants have a buildup of lactic acid in the body and hypoglycemia. Within the first weeks of life, infants develop liver disease that quickly progresses to liver failure. The neurological features are similar to other mitochondrial disorders and include developmental delay, hypotonia, ataxia, seizures, and motor and sensory peripheral neuropathy.

What is my risk of having an affected child?

Hepatocerebral mitochondrial DNA depletion syndrome, MPV17-related 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?

As the liver disease progresses, liver failure is inevitable and a transplant is required. However, because this is a multisystem disorder, a liver transplant is controversial. Management of the other symptoms is generally symptomatic and supportive.

What mutation was detected?

The detected heterozygous variant was NM_002437.5:c.293C>T (p.Pro98Leu). This missense variant, p.Pro98Leu, has been reported in the compound heterozygous state in at least eight unrelated individuals and in the homozygous state in at least five unrelated individuals with mitochondrial DNA depletion syndromes. This variant has been reported to segregate with disease in at least one family (PubMed: [20074988](#), [22508010](#), [27896091](#), [27536553](#), [24190800](#), [28776642](#), [23714749](#), [25129007](#)). In vitro functional study of this variant indicates that this change may affect gating properties of the non-selective channel formed by the protein MPV17 (PubMed: [25861990](#)). This variant is classified as "Pathogenic" in ClinVar, with multiple submitters in agreement (ClinVar: 38355). The laboratory classifies this variant as pathogenic.



ZELLWEGER SYNDROME, PEX6-RELATED

Patient	N1001, Donor	Partner
Result	 Carrier	N/A
Variant Details	PEX6 (NM_000287.4) c.2663G>C (p.Arg888Pro)	N/A

What is Zellweger syndrome, PEX6-related?

Zellweger syndrome is a spectrum of disorders, also known as peroxisome biogenesis disorders, that have overlapping symptoms caused by degeneration of the myelin. Myelin is an insulating material that covers nerve fibers and is important in brain and central nervous system function. At the severe end of the spectrum, symptoms begin in the newborn period and include weak muscle tone, feeding difficulties, hearing and vision loss, liver and kidney dysfunction, dysmorphic facial features, and seizures. Children with the severe form typically do not live past infancy. On the other end of the spectrum, affected individuals do not typically develop symptoms until late infancy or early childhood, and the progression of disease occurs more slowly. Other intermediate and mild forms of *PEX6*-related disease include neonatal adrenoleukodystrophy (NALD), infantile Refsum disease, and Heimler syndrome.

What is my risk of having an affected child?

PEX6-related Zellweger syndrome is inherited in an autosomal recessive manner. This means that if you and your partner are both carriers, the risk of having a child affected with Zellweger syndrome is 1 in 4 (25%).

What kind of medical management is available?

There is currently no cure for Zellweger spectrum disorders, but treatment options are available. Treatment involves supportive therapy, management of symptoms, and palliative care. Children with a severe form typically do not live past infancy. Milder forms of the spectrum may be variable and progress slowly, however, life expectancy is reduced.

What mutation was detected?

The detected heterozygous variant was NM_000287.4:c.2663G>C (p.Arg888Pro). This variant has been reported with a pathogenic variant in one individual with Zellweger syndrome spectrum (PubMed: [19877282](#)). Other variant at this position in the gene (p.R999H) has been associated with Zellweger spectrum disorders, suggesting that a change at this position adversely affects protein structure and/or function and is potentially disease-causing (PubMed: [29419819](#)). The laboratory classifies this variant as likely pathogenic.



RETINITIS PIGMENTOSA 25

Patient	N1001, Donor	Partner
Result	 Carrier	N/A
Variant Details	EYS (NM_001142800.2) c.9036del (p.Leu3013Serfs*6)	N/A

What is Retinitis pigmentosa 25?

Retinitis pigmentosa, also known as RP, refers to a group of inherited diseases causing retinal degeneration. People with RP experience a gradual decline in their vision because photoreceptor cells in the retina degenerate. Night blindness is one of the earliest and most frequent symptoms of RP, and most people with RP are legally blind by age 40. Symptoms of RP are most often recognized in children, adolescents, and young adults with the progression of the disease continuing throughout the individual's life. The pattern and degree of visual loss are variable, depending on the various types of genes that cause RP.

What is my risk of having an affected child?

Retinitis pigmentosa 25 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 no known cure for retinitis pigmentosa. However, there are few treatment options such as light avoidance and/or the use of low-vision aids to slow down the progression of RP. A number of services and devices are available to help people with vision loss carry out daily activities and maintain their independence.

What mutation was detected?

The detected heterozygous variant was NM_001142800.2:c.9036del (p.Leu3013Serfs*6). This frameshift variant is the result of the deletion of one base pair, which leads to an out of frame transcript and the introduction of a premature stop codon in the last exon of the EYS mRNA. The position of the premature stop codon introduced by this variant near the terminus of this gene has unknown functional and clinical consequences. However, truncating variants downstream of this position have been reported to be pathogenic (PubMed: [20333770](#), [22581970](#), [30337596](#)). This variant has been reported in the compound heterozygous state in two unrelated individuals with retinal dystrophy (PubMed: [27735924](#), [31074760](#)). The laboratory classifies this variant as pathogenic.



ASPARAGINE SYNTHETASE DEFICIENCY

Patient	N1001, Donor	Partner
Result	 Carrier	N/A
Variant Details	ASNS (NM_133436.3) c.1210C>T (p.Arg404Cys)	N/A

What is Asparagine synthetase deficiency?

Asparagine Synthetase deficiency is a severe neurological disorder. The condition is caused by mutations in the ASNS gene, which normally creates a protein involved in the synthesis of asparagine, an amino acid that is crucial for brain development. Symptoms or features can begin in utero or at birth and include microcephaly, delayed psychomotor development, progressive encephalopathy, cortical atrophy of the brain, and seizures. The disease may cause death in infancy, due to failure to thrive, poor feeding, and respiratory insufficiency.

What is my risk of having an affected child?

Asparagine synthetase 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?

There is no identified curative treatment for Asparagine Synthetase deficiency, and treatment is instead focused on symptom management. The prognosis is very poor. Most identified affected individuals died in infancy, and an effective treatment has not been found.

What mutation was detected?

The detected heterozygous variant was NM_133436.3:c.1210C>T (p.Arg404Cys). This missense variant has been reported in the compound heterozygous and homozygous state in multiple unrelated individuals with ASNS-related conditions (PubMed: [34490615](#), [36374791](#)). Additionally, another variant at this position in the gene (p.Arg404His) has been associated with ASNS-related conditions, suggesting that a change at this position adversely affects protein structure and/or function and is potentially disease-causing (PubMed: [27711071](#), [29405484](#), [30214071](#), [30214071](#)). 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 99.4% 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, 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, GRHR, 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, MKK5, 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, 99.49% 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



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:



Yan Meng, Ph.D., CGMB, FACMG on 7/8/2024
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. 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
N1001, DONOR DOB: [REDACTED] AGE: [REDACTED] Gender: M Fasting: U Phone: 725.257.0900 Patient ID: N1001	Specimen: LV963684W Requisition: 0000010 Collected: 06/20/2024 / 10:37 PDT Received: 06/20/2024 / 16:26 PDT Reported: 06/30/2024 / 14:12 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: 24-293100
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: 4

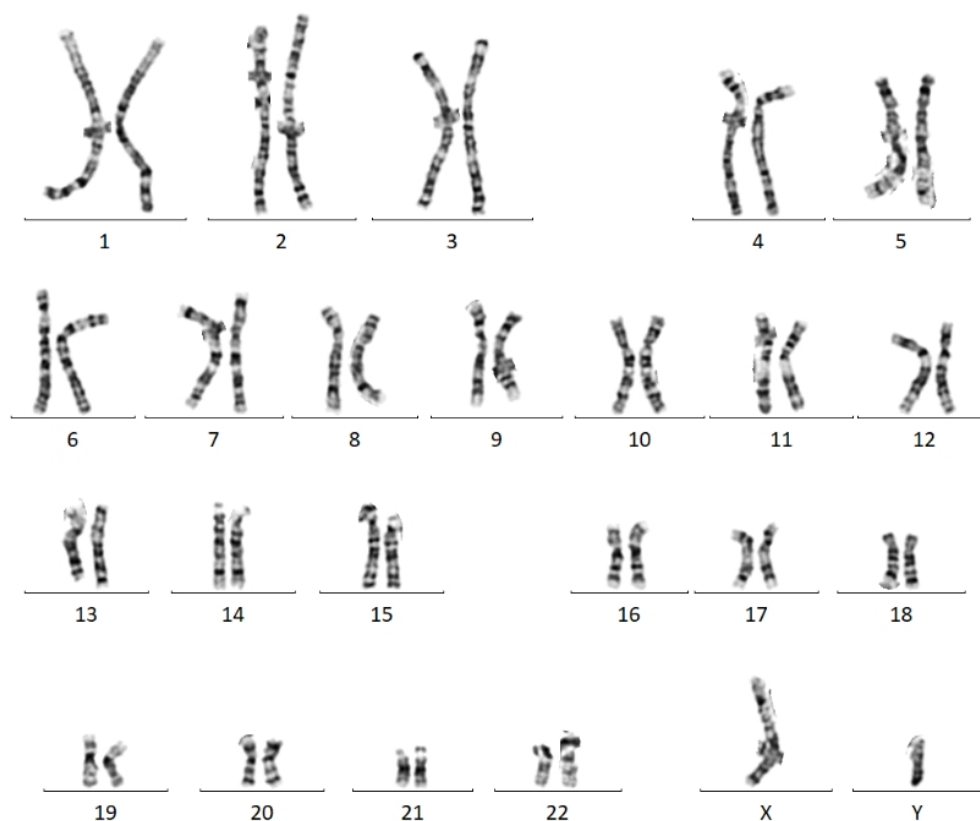
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements. A portion of the testing was performed at SJC3.

Peter H. Bui, PhD, FACMG (800) NICHOLS-4307

Electronic Signature: 6/30/2024 4:18 PM



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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