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CLIA: 22D0957540



Patient Information:

10960, Donor

DOB: [REDACTED]

Sex: M

MR#:

Patient#: FT-PT8907308

Partner Information:

Not Tested

Physician:

Kuan, James

Phoenix Sperm Bank

4915 25th Avenue NE, Ste 204W

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Laboratory:

Fulgent Therapeutics LLC

CAP#: 8042697

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Laboratory Director:

Dr. Amar Jariwala

Report Date: **Dec 17, 2024**

Accession:

FT-7414266

Test#: FT-TS15014218

Specimen Type: Blood (EDTA)

Collected: Nov 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	10960, Donor	Partner
Microcephalic osteodysplastic primordial dwarfism, type II <i>PCNT</i>	AR	⊕ Carrier c.8917C>T (p.Arg2973*)	N/A
ADAMTSL4-related eye disorders <i>ADAMTSL4</i>	AR	⊕ Carrier c.268del (p.Arg90Aspfs*43)	N/A
Alpha thalassemia <i>HBA2</i>	AR	⊕ Carrier Whole Gene Deletion (αα/α-)	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.
- 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>)

Patient: 10960, Donor; Sex: M;
DOB: [REDACTED] **MR#:**

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DocID: FT-TS15014218AA; **PAGE 1 of 8**



MICROCEPHALIC OSTEODYSPLASTIC PRIMORDIAL DWARFISM, TYPE II

Patient	10960, Donor	Partner
Result	 Carrier	N/A
Variant Details	PCNT (NM_006031.6) c.8917C>T (p.Arg2973*)	N/A

What is Microcephalic osteodysplastic primordial dwarfism, type II?

Microcephalic osteodysplastic primordial dwarfism, type II (MOPDII) is a condition characterized by short stature with osteodysplasia and microcephaly. The growth problems in MOPDII are primordial, meaning they begin before birth, with affected individuals showing slow prenatal growth. The final adult height of people with this condition ranges from 20 inches to 40 inches. Intellectual development is typically normal. Many individuals with MOPDII have blood vessel abnormalities and develop brain aneurysms which may be treatable, but increase the risk of stroke. Life expectancy is generally decreased, but individuals with this condition live into their 30s.

What is my risk of having an affected child?

Microcephalic osteodysplastic primordial dwarfism type II 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?

Management of this condition is mainly symptomatic and includes early screening for medical complications related to hip and spine anomalies, anemia, insulin resistance, and abnormal lipid profiles. Screening for CNS vascular abnormalities with brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) is recommended at diagnosis and every 12 to 18 months.

What mutation was detected?

The detected heterozygous variant was NM_006031.6:c.8917C>T (p.Arg2973*). 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 Microcephalic osteodysplastic primordial dwarfism, type II (MOPD2) (PubMed: [18174396](#), [26231886](#)). This variant has been reported in the compound heterozygous state in two siblings with MOPD2 (PubMed: [21270239](#)) The laboratory classifies this variant as pathogenic.



ADAMTSL4-RELATED EYE DISORDERS

Patient	10960, Donor	Partner
Result	 Carrier	N/A
Variant Details	ADAMTSL4 (NM_019032.6) c.268del (p.Arg90Aspfs*43)	N/A

What is ADAMTSL4-related eye disorders?

Pathogenic mutations in the ADAMTSL4 gene are associated with eye-related disorders including autosomal recessive isolated ectopia lentis and ectopia lentis et pupillae, which refer to displacement of the lens and displacement of the lens and pupil, respectively. These conditions can cause acute or chronic visual impairment, can vary in severity, and are generally not associated with additional systemic manifestations; however, skeletal abnormalities have been observed in some individuals (PubMed: [22338190](#); OMIM: [610113](#)).

What is my risk of having an affected child?

Isolated ectopia lentis and ectopia lentis et pupillae are 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?

Medical management is specific to each individual and should be discussed with your doctor. Early correction of refractive errors with glasses, contact lenses, or patching is recommended to prevent amblyopia in children. Surgery may be required to correct vision if patching is unsuccessful, and for individuals with cataracts, risk for complications, and significant astigmatism.

What mutation was detected?

The detected heterozygous variant was NM_019032.6:c.268del (p.Arg90Aspfs*43). This 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 Ectopia lentis (PubMed: [28642162](#), [22736615](#), [20564469](#), [20564469](#)). The laboratory classifies this variant as likely pathogenic.



ALPHA THALASSEMIA

Patient	10960, Donor	Partner
Result	⊕ Carrier	N/A
Variant Details	HBA2 (NM_000517.5) Whole Gene Deletion ($\alpha\alpha/\alpha-$)	N/A

What is Alpha thalassemia?

Alpha thalassemia is a blood disorder that reduces the production of a protein called hemoglobin. This reduction in the amount of hemoglobin can prevent enough oxygen from reaching the body's tissues. Affected individuals may have anemia, which can cause pale skin, weakness, fatigue, and more serious complications. There are two distinct types of alpha thalassemia: the more severe type is known as Hb Bart syndrome, and the milder form is called HbH disease. Hb Bart syndrome is characterized by hydrops fetalis, a condition in which excess fluid builds up in the body before birth. Additional signs and symptoms can include severe anemia, hepatosplenomegaly (swollen liver and spleen), heart defects, and abnormalities of the urinary system or genitalia. As a result of these serious health problems, most babies with this condition are stillborn or die soon after birth. Hb Bart syndrome can also cause serious complications for women during pregnancy, including preeclampsia, premature delivery, and abnormal bleeding. HbH disease causes mild to moderate anemia, hepatosplenomegaly, and jaundice. Some affected individuals also have bone changes such as overgrowth of the upper jaw and an unusually prominent forehead.

See the table below for a description of the diseases associated with different combinations of HBA1 and HBA2 mutations.

Carrier Status of Partner 1	Carrier Status of Partner 2	Risk for a child with HbH disease (-/-/- α)	Risk for a child with Hb Bart syndrome (-/-/-)
alpha thalassemia trait cis ($\alpha\alpha/-$)	alpha thalassemia trait trans ($\alpha/-$) or ($-\alpha/-$)	50%	No risk
	alpha thalassemia trait cis ($\alpha\alpha/-$)	Residual Risk	25%
	silent carrier ($\alpha\alpha/\alpha-$) or ($\alpha\alpha/\alpha-$)	25%	Residual Risk
alpha thalassemia trait trans ($\alpha/-$) or ($-\alpha/-$)	alpha thalassemia trait trans ($\alpha/-$) or ($-\alpha/-$)	Residual Risk	Residual Risk
	silent carrier ($\alpha\alpha/\alpha-$) or ($\alpha\alpha/\alpha-$)	Residual Risk	Residual Risk
silent carrier ($\alpha\alpha/\alpha-$) or ($\alpha\alpha/\alpha-$)	silent carrier ($\alpha\alpha/\alpha-$) or ($\alpha\alpha/\alpha-$)	Residual Risk	Residual Risk

Note that carriers for single heterozygous deletions of HBA1 or HBA2 are commonly referred to as silent carriers (PubMed: [20301608](#)).

What is my risk of having an affected child?

Generally, each person has two copies of the *HBA1* gene and two copies of the *HBA2* gene, or four copies (alleles) in total. The different forms of alpha thalassemia result from the loss of some or all of these alleles: Hb Bart syndrome results from the loss of all four alleles, while HbH disease results from the loss of three alleles. Alpha thalassemia is inherited in an autosomal recessive manner, which means that if one parent is a carrier for a loss of two alleles on one chromosome and a second parent is a carrier of a loss of one or more alleles on one chromosome, there is a 1 in 4 (25%) risk of having an affected child.

What kind of medical management is available?

There is currently no cure for alpha thalassemia. Medical management of Hb Bart syndrome is limited but may include blood transfusions or a stem cell transplant. For HbH disease, management can vary based on the severity of symptoms. Mild forms may have little effect on daily life, and management for such cases can include supplementation of iron or folic acid. Management for more severe cases usually requires regular transfusions. Untreated, the prognosis for HbH disease is poor, with a shortened lifespan of up to age 5 years. However, when treated, individuals with HbH disease may have a lifespan that approaches normal.

What mutation was detected?

The detected variant was a whole gene deletion ($\alpha\alpha/\alpha-$) in the *HBA2* gene (NM_000517.5). The detected mutation was a whole

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gene deletion in one of four alleles comprising the alpha globin locus. These results are consistent with having three functional copies of alpha-globin ($\alpha\alpha/\alpha^-$). If your partner is also a carrier for alpha thalassemia, there is an increased risk to have a child with HbH disease, but not hydrops fetalis. Genetic counseling is recommended. Individuals with a single alpha globin gene defect ($\alpha\alpha/\alpha^-$) are carriers and clinically asymptomatic. Deletions of HBA2 are common in many human populations (PubMed: [20301608](#), [25390741](#)). The laboratory classifies this variant as 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, 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, RAPSN, RARS2, RDH12, RLBP1, RMRP, RNASEH2A, RNASEH2B, RNASEH2C, RPE65, RPGRIP1L, RTEL1, RXYLT1, RYR1, SACS, SAMD9, SAMHD1, SCQ2, 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, VRRK1, 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, 99.54% 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

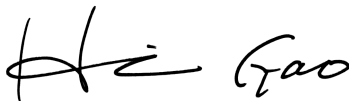


from highly homologous regions in exons 1-2 of the HBA1 gene has been recognized to occur, potentially impeding the assay's technical capability to detect pathogenic alterations during sequencing analyses. HBA2: Significant interference from highly homologous regions in exons 1-2 of the HBA2 gene has 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:



Shuxi Liu, Ph.D., FACMG
Laboratory Director, Fulgent



Dr. Harry Gao, DABMG, FACMG on 12/17/2024
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 tested on any Beacon panel, please visit the following link:

[Beacon Expanded Carrier Screening Supplemental Table](#)



Report Status FINAL

Route 2017 Ordered by:
Phoenix Sperm Bank
1492 S Mill Ave
Suite 306
Tempe, AZ 85281



**Sonora Quest
Laboratories™**

A Subsidiary of Laboratory Sciences of Arizona

James Kuan, MD

Patient Information:

10960, DONOR

Account: 18131
ID/MR#: 10960
Patient Lab ID:
673f65a468493062c7e9f45b

Collected: 11/20/2024 03:23 PM
Received: 11/21/2024 09:14 AM
Reported: 11/29/2024 03:27 PM

Order #: 181 **1 / NL1** **27**
DOB: **Age:**
Sex: M
Patient Phone: 602-888-7255

PL

GENETICS**Accession #:**

CG240012461

Cell Type/Source:

Blood

Clinician Provided Information:

DONOR TESTING

Chromosome Analysis: Routine Blood**Analysis Details:**

Metaphases/Cells Counted : 20
Metaphases/Cells Analyzed : 5
Metaphases Karyotyped : 3

PV

Results:

NORMAL MALE KARYOTYPE

PV

46,XY

Interpretation:

PV

Normal

PV

Normal karyotype at the band level 550 or above as determined by the trypsin-Giemsa method. There was no evidence for a chromosome abnormality within the limits of the band level and technology utilized in this study.

PHA-stimulated lymphocyte chromosome analysis is an accurate technique to detect many constitutional chromosome abnormalities. More extensive investigation may be required to detect mosaicism or subtle structural rearrangement. It also should be noted that this type of testing does not rule out the possibility of mendelian, mitochondrial, multifactorial or environmental etiologies.

Cytogenetics Director:

PV

Electronically signed by Guang Liu MD, ABMGG, FACMG, Genetics/Genomics
Director
Verified 11/29/24

Tests Ordered: Chromosome Analysis: Routine Blood

Unless otherwise noted, testing performed by: Sonora Quest Laboratories, 424 S 56th St, Phoenix, AZ 85034 800.766.6721

Testing noted as PV performed by: Genetics/Genomics Div., Sonora Quest Laboratories, 424 S. 56th St, Phoenix, AZ 85034 602.685.5700

End of Report**10960, DONOR Order #: 181310000161 / NL107074527 - FINAL Report**

L=Low, H=High, C=Critical Abnormal, CL=Critical Low, CH=Critical High, *=Comment

Distribution #: 759410789-41674327



Result Report

Produced by AutoDist On 11/29/2024 03:29 PM

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