15 Crawford St., STE 100
Needham, MA 02494
(p) 626-350-0537
(f) 626-454-1667
Lab Director: Arash Radfar M.D.
CLIA: 22D0957540

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Therapath Partners

Patient Information:
14723, Donor
DOB: [redacted]
Sex: M
MR#:
Patient#: FT-PT9138998

Partner Information:
Not Tested

Physician:
Kuan, James
ATTN: Martinez,Lupe
San Diego 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:
Dr. Amar Jariwala
Report Date: **Jul 16,2025**

Accession:
FT-7593632
Test#: FT-TS15253112
Specimen Type: Blood (EDTA)
Collected: Jul 01,2025

Accession:
N/A

FINAL RESULTS



Carrier for genetic conditions in **multiple** genes.

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	14723, Donor	Partner
Fanconi anemia, group L *FANCL*	AR	⊕ Carrier c.2T>C (p.?)	N/A
Congenital secretory chloride diarrhea *SLC26A3*	AR	⊕ Carrier c.386C>T (p.Pro129Leu)	N/A

INTERPRETATION:

Notes and Recommendations:

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

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FANCONI ANEMIA, GROUP L

Patient	14723, Donor	Partner
Result	Carrier	N/A
Variant Details	***FANCL*** (NM_018062.4) c.2T>C (p.?)	N/A

What is Fanconi anemia, group L?

Fanconi anemia, group L, is a severe autosomal recessive disorder. This condition is characterized by impaired bone marrow function, physical abnormalities, organ defects, and an increased risk of certain cancers including leukemia, myelodysplastic syndrome, and cancer of the head, neck, or urinary system. Affected individuals also have an increased risk for infections, anemia, and infertility. The first signs and symptoms typically appear in infancy with recurrent nosebleeds and easy bruising. Physical abnormalities may also be present at birth. Affected individuals with FANCL-associated Fanconi anemia present with multiple congenital anomalies including vertebral defects, anal atresia, tracheoesophageal fistula, esophageal atresia, radial or renal dysplasia, and hydrocephalus (referred to as VACTERL-H).

What is my risk of having an affected child?

Fanconi anemia, group L is inherited in an autosomal recessive manner. If the patient and the partner are both carriers, the risk for an affected child is 1 in 4 (25%).

What kind of medical management is available?

There is currently no cure for Fanconi anemia, group L. The majority of affected individuals with FANCL-Fanconi anemia do not survive past infancy.

What mutation was detected?

The detected heterozygous variant was NM_018062.4:c.2T>C (p.?). This variant is predicted to abolish the initiator methionine. The first downstream in-frame methionine is located at codon 74. At least one variant upstream of this alternative start codon has been determined to be pathogenic, suggesting the region between original and alternative codons is critical to protein function (PubMed: 27041517, 29335925, 29625052, 34008892, 36451132, 37865086). The N-terminal portion of the gene has been shown to be essential for efficient FANCL protein function (PubMed: 26149689, 27986371). This variant has been identified in the literature in patients with male and female breast cancers, and endometrial adenocarcinoma (PubMed: 29335925, 29625052, 31300551).Other variants that disrupt the initiator codon of FANCL have been reported as pathogenic in ClinVar (Variation ID:936826, 826861). This variant is classified as "Pathogenic" or "Likely Pathogenic" in ClinVar, with multiple submitters in agreement (Variation ID: 561859). This variant is represented in the Fanconi Anemia Mutation Database. The laboratory classifies this variant as likely pathogenic.

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CONGENITAL SECRETORY CHLORIDE DIARRHEA

Patient	14723, Donor	Partner
Result	⊕ Carrier	N/A
Variant Details	***SLC26A3*** (NM_000111.3) c.386C>T (p.Pro129Leu)	N/A

What is Congenital secretory chloride diarrhea?

Congenital secretory chloride diarrhea is an autosomal recessive form of severe chronic diarrhea characterized by excretion of large amounts of watery stool containing high levels of chloride, resulting in dehydration, hypokalemia, and metabolic alkalosis. Children affected are often premature presumably due to intrauterine diarrhea. This excess of watery stool can lead to severe dehydration and electrolyte imbalance.

What is my risk of having an affected child?

Congenital secretory chloride diarrhea 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?

In patients with congenital secretory chloride diarrhea, the oral intake of chloride, sodium, and potassium must exceed the amount lost. Careful monitoring of diet and electrolyte concentrations in blood and urine can help avoid complications of the condition.

What mutation was detected?

The detected heterozygous variant was NM_000111.3:c.386C>T (p.Pro129Leu). SLC26A3 c.386C>T (p.Pro129Leu) results in a non-conservative amino acid change located in the SLC26A/SulP transporter domain (IPR011547) of the encoded protein sequence. Five of five in-silico tools predict a damaging effect of the variant on protein function. The variant allele was found at a frequency of 8e-06 in 251422 control chromosomes (gnomAD). c.386C>T has been reported in the literature as a biallelic genotype in at least three individuals affected with Congenital secretory diarrhea, chloride type, including one case of a homozygous individual who also had a diagnosis of Cystic Fibrosis, however pseudo-Bartters syndrome was ruled out in favor of congenital chloride diarrhea following urine and electrolyte stool studies and genetic analysis (e.g. Wedenoja_2011, Canani_2013, Masip_2020, Heinz-Erian_2021 (no PMID)). These data indicate that the variant is likely to be associated with disease. To our knowledge, no experimental evidence demonstrating an impact on protein function has been reported. The following publications have been ascertained in the context of this evaluation (PMID: 24350656, 31976143, 21394828) Two submitters have cited clinical-significance assessments for this variant to ClinVar after 2014. One submitter classified the variant as likely pathogenic, and the other classified the variant as uncertain significance. Based on the evidence outlined above, the variant was classified as likely pathogenic. The laboratory classifies this variant as likely pathogenic.

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GENES TESTED:

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

This analysis was run using the Beacon Preconception Carrier Screening - 515 Genes (without X-linked Disorders) gene list. 515 genes were tested with 99.7% of targets sequenced at >20x coverage. For more gene-specific information and assistance with residual risk calculation, see the SUPPLEMENTAL TABLE.

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

METHODS:

Genomic DNA was isolated from the submitted specimen indicated above (if cellular material was submitted). DNA was barcoded, and enriched for the coding exons of targeted genes using hybrid capture technology. Prepared DNA libraries were then sequenced using a Next Generation Sequencing technology. Following alignment to the human genome reference sequence (assembly GRCh37), variants were detected in regions of at least 10x coverage. For this specimen, 99.73% and 99.69% 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 FPLMv2.0 pipeline was used to analyze this specimen.

LIMITATIONS:

General Limitations

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

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

Gene Specific Notes and Limitations

ALG1: Due to the interference by highly homologous regions, our current testing method has less sensitivity to detect variants in exons 6-13 of the ALG1 gene (NM_019109.4). *CEP290:* Copy number analysis for exons 8-13 and exons 39-42 may have reduced sensitivity in the CEP290 gene. Confirmation of these exons are limited to individuals with a positive personal history of CEP290-related conditions and/or individuals carrying a pathogenic/likely pathogenic sequence variant. *CFTR:* Analysis of the intron 8 polymorphic region (e.g. IVS8-5T allele) is only performed if the p.Arg117His (R117H) mutation is detected. Single exon deletion/duplication analysis is limited to deletions of previously reported exons: 1, 2, 3, 11, 19, 20, 21. Analysis of the intron 8 polymorphic region (e.g. IVS8-5T allele) is only performed if the p.Arg117His (R117H) mutation is detected. 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, 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.

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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 21-29 (NM_144672.4) 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). *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 **07/16/2025**
Laboratory Director, Fulgent

DISCLAIMER:

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

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

INVITAE

INVITAE GENETIC RISK ASSESSMENT TESTING RESULTS

Patient name:	DONOR 14723	**Sample type:**	Blood	**Report date:**	15-JUL-2025
DOB:	[redacted]	**Sample collection date:**	01-JUL-2025	**Invitae #:**	RQ7406599
Sex assigned at birth:	Male	**Sample accession date:**	02-JUL-2025	**Clinical team:**	Eric Victoria Dr. James Kuan
Gender:	Man				
Patient ID (MRN):					

Test performed

Sequence analysis and deletion/duplication testing of the 163 genes listed in the Genes Analyzed section.

- Invitae Comprehensive Genetic Risk Panel

RESULT: CARRIER

A single clinically significant genetic change was found in the HFE gene, which is associated with being a carrier for a hereditary condition.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
HFE	c.187C>G (p.His63Asp)	heterozygous	Pathogenic (low penetrance)

About this test

This test evaluates 163 genes for variants (genetic changes) that indicate a significantly increased risk of developing certain types of hereditary cancer, heart-related conditions, or other types of genetic health conditions. These are disorders for which early detection may enable effective medical interventions and preventive measures. Genetic changes of uncertain significance are not included in this report; however, if additional evidence becomes available to indicate that a previously uncertain genetic change is clinically significant, the laboratory will update this report and provide notification.

Next steps

- A carrier result is medically important and you should consider discussing this with an appropriate healthcare provider. While this result indicates you do not have any personal genetic risk factors for the conditions associated with the tested genes, it is important to note that at least a baseline, population-level risk remains for developing these types of disorders and age-appropriate screenings are still recommended. A complete family history may point to health risks not evaluated by this test. Genetic counseling is recommended to discuss the implications of this result and potential next steps.
- Consider sharing this result with relatives as they may also be at risk. Details on our Family Variant Testing program can be found at **www.invitae.com/family**.
- Register your test at **www.invitae.com/patients** to download a digital copy of your results. You can also access educational resources about how your results can help inform your health.

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INVITAE

Patient name: DONOR 14723 **DOB:** [redacted]

Invitae #: RQ7406599

Clinical summary

A Pathogenic (low penetrance) variant, c.187C>G (p.His63Asp), was identified in HFE.

- If a person carries two clinically significant genetic changes, one in each copy of the HFE gene, this may increase the risk for hereditary hemochromatosis (HH).
- This result is associated with being a carrier of autosomal recessive HFE-HH. Carriers typically do not have symptoms of the condition, but may be at risk to have a child with the condition.
- HH is characterized by excessive storage of iron in the skin, liver, pancreas, heart, and joints. Clinical symptoms are usually mild, but in cases of severe or untreated iron depositions, findings may include progressive increase in skin pigmentation, diabetes mellitus, congestive heart failure and/or arrhythmias, arthritis, hypogonadism, osteoporosis, and liver disease, including cirrhosis and/or subsequent liver cancer. It is important to recognize that the genetic changes in HFE, the gene that most commonly causes HH, are known to have reduced penetrance. Reduced penetrance means that not all individuals with these genetic changes will show signs or symptoms of the condition. Penetrance is often higher in men than in women, and increases with age.
- Since genetic changes are often shared within families, there is a chance that biological relatives may be a carrier or at risk for autosomal recessive HFE-HH and could consider testing. The chance of having a child with autosomal recessive HFE-HH depends on whether this individual's partner is also a carrier of the same condition.

Variant details

HFE, Exon 2, c.187C>G (p.His63Asp), heterozygous, Pathogenic (low penetrance)

- This sequence change replaces histidine, which is basic and polar, with aspartic acid, which is acidic and polar, at codon 63 of the HFE protein (p.His63Asp).
- This variant is present in population databases (rs1799945, gnomAD 14%), and has an allele count higher than expected for a pathogenic variant.
- This is a very common, low penetrance variant that is known to contribute to hemochromatosis when present with a second pathogenic allele in HFE. An estimated 1.5% of individuals of European descent who are affected with hemochromatosis are homozygous for this variant (PMID: 11479183), however, penetrance of the homozygous genotype is very low and is associated with variable phenotypes (PMID: 24729993, 11399207, 16132052, 11358905).
- ClinVar contains an entry for this variant (Variation ID: 10).
- Invitae Evidence Modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) has been performed for this missense variant. However, the output from this modeling did not meet the statistical confidence thresholds required to predict the impact of this variant on HFE protein function.
- Experimental studies have shown that this missense change affects HFE function (PMID: 9162021, 9356458, 12429850, 14673107).
- In summary, this variant is reported to cause disease. However, as this variant is associated with a lower penetrance than other pathogenic alleles in the HFE gene, it has been classified as Pathogenic (low penetrance).

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INVITAE

Patient name: DONOR 14723 **DOB:** [redacted]

Invitae #: RQ7406599

Genes analyzed

This table represents a complete list of genes analyzed for this individual. Genes listed in this table may also have additional reported clinical associations outside of the conditions listed. Additional information about gene-condition associations can be found at http://www.omim.org. An asterisk (*) indicates that this gene has a limitation. Please see the Limitations section for details.

Cancer-related genes

GENE	TRANSCRIPT	ASSOCIATED CONDITION(S)
APC*	NM_000038.5	Gastrointestinal, endocrine, nervous system/brain cancer, and sarcoma
ATM*	NM_000051.3	Breast, gynecologic, gastrointestinal, and prostate cancer
AXIN2	NM_004655.3	Gastrointestinal cancer
BAP1	NM_004656.3	Renal/urinary tract and skin cancer
BARD1	NM_000465.3	Breast cancer
BMPR1A	NM_004329.2	Gastrointestinal cancer
BRCA1	NM_007294.3	Breast, gynecologic, gastrointestinal, and prostate cancer
BRCA2	NM_000059.3	Breast, gynecologic, gastrointestinal, prostate, and skin cancer
BRIP1	NM_032043.2	Gynecologic cancer
CDC73	NM_024529.4	Endocrine and renal/urinary tract cancer
CDH1	NM_004360.3	Breast and gastrointestinal cancer, blepharocheilodontic syndrome
CDK4	NM_000075.3	Skin cancer
CDKN1B	NM_004064.4	Endocrine and gastrointestinal cancer
CDKN2A (p14ARF)	NM_058195.3	Skin and nervous system/brain cancer
CDKN2A (p16INK4a)	NM_000077.4	Skin and gastrointestinal cancer
CHEK2	NM_007194.3	Breast, endocrine, and prostate cancer
DICER1*	NM_177438.2	Endocrine, gynecologic, lung, nervous system/brain, renal/urinary tract cancer, and sarcoma
EGFR	NM_005228.3	Lung cancer
EPCAM*	NM_002354.2	Gastrointestinal, gynecologic, renal/urinary tract, nervous system/brain, prostate, and skin cancer
FH*	NM_000143.3	Renal/urinary tract, endocrine, nervous system/brain cancer, and sarcoma
FLCN	NM_144997.5	Renal/urinary tract cancer
GREM1*	NM_013372.6	Gastrointestinal cancer
HOXB13	NM_006361.5	Prostate cancer
KIT	NM_000222.2	Gastrointestinal cancer and sarcoma, immune condition, skin condition
LZTR1	NM_006767.3	Nervous system/brain cancer, Noonan spectrum disorders
MAX*	NM_002382.4	Endocrine and nervous system/brain cancer, polydactyly-macrocephaly syndrome
MEN1*	NM_130799.2	Endocrine, gastrointestinal, and nervous system/brain cancer, endocrine condition
MET*	NM_001127500.1	Renal/urinary tract cancer, skeletal condition
MITF	NM_000248.3	Skin cancer, Waardenburg syndrome
MLH1*	NM_000249.3	Gastrointestinal, gynecologic, renal/urinary tract, nervous system/brain, prostate, and skin cancer
MSH2*	NM_000251.2	Gastrointestinal, gynecologic, renal/urinary tract, nervous system/brain, prostate, and skin cancer
MSH3*	NM_002439.4	Gastrointestinal cancer
MSH6*	NM_000179.2	Gastrointestinal, gynecologic, renal/urinary tract, nervous system/brain, prostate, and skin cancer
MUTYH	NM_001128425.1	Gastrointestinal cancer
NF1*	NM_000267.3	Breast, endocrine, gastrointestinal, nervous system/brain cancer, and sarcoma
NF2	NM_000268.3	Nervous system/brain cancer
NTHL1	NM_002528.6	Gastrointestinal cancer
PALB2	NM_024675.3	Breast, gynecologic, gastrointestinal, and prostate cancer
PDGFRA	NM_006206.4	Gastrointestinal cancer and sarcoma
PMS2*	NM_000535.5	Gastrointestinal, gynecologic, renal/urinary tract, nervous system/brain, prostate, and skin cancer
POLD1*	NM_002691.3	Gastrointestinal cancer and MDPL syndrome
POLE	NM_006231.3	Gastrointestinal cancer
POT1	NM_015450.2	Skin and nervous system/brain cancer, and sarcoma
PRKAR1A	NM_002734.4	Endocrine, nervous system/brain cancer, and sarcoma, acrodysostosis
PTCH1	NM_000264.3	Skin, nervous system/brain cancer, and sarcoma
PTEN*	NM_000314.4	Breast, gynecologic, gastrointestinal, endocrine, renal/urinary tract, nervous system/brain, and skin cancer
RAD51C	NM_058216.2	Breast and gynecologic cancer
RAD51D	NM_002878.3	Breast and gynecologic cancer
RB1*	NM_000321.2	Retinoblastoma, skin cancer, and sarcoma
RET	NM_020975.4	Endocrine and nervous system/brain cancer, gastrointestinal condition

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GENE	TRANSCRIPT	ASSOCIATED CONDITION(S)
SDHA*	NM_004168.3	Endocrine, nervous system/brain, and gastrointestinal cancer, sarcoma, mitochondrial disorder
SDHAF2	NM_017841.2	Endocrine and nervous system/brain cancer
SDHB	NM_003000.2	Endocrine, nervous system/brain, renal/urinary tract, and gastrointestinal cancer, sarcoma
SDHC*	NM_003001.3	Endocrine, nervous system/brain, renal/urinary tract, and gastrointestinal cancer, sarcoma
SDHD	NM_003002.3	Endocrine, nervous system/brain, and gastrointestinal cancer, sarcoma
SMAD4	NM_005359.5	Gastrointestinal cancer, hereditary hemorrhagic telangiectasia, aortopathy, Myhre syndrome
SMARCA4	NM_001128849.1	Gynecologic, nervous system/brain, and renal/urinary tract cancer, Coffin-Siris syndrome
SMARCB1	NM_003073.3	Nervous system/brain and renal/urinary tract cancer, Coffin-Siris syndrome
STK11	NM_000455.4	Breast, gynecologic, gastrointestinal, lung, and testicular cancer
TMEM127	NM_017849.3	Endocrine and nervous system/brain cancer
TP53	NM_000546.5	Breast, gynecologic, gastrointestinal, endocrine, nervous system/brain, renal/urinary tract, prostate, skin, and hematologic cancer, sarcoma
TSC1*	NM_000368.4	Endocrine, gastrointestinal, renal/urinary tract, and nervous system/brain cancer
TSC2	NM_000548.3	Endocrine, gastrointestinal, renal/urinary tract, and nervous system/brain cancer
VHL	NM_000551.3	Endocrine, gastrointestinal, renal/urinary tract, and nervous system/brain cancer
WT1	NM_024426.4	Renal/urinary tract cancer

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Cardiovascular-related genes

GENE	TRANSCRIPT	ASSOCIATED CONDITION(S)
ACTA2	NM_001613.2	Aortopathy
ACTC1*	NM_005159.4	Cardiomyopathy, congenital heart disease, skeletal condition
ACTN2*	NM_001103.3	Cardiomyopathy, neuromuscular condition
ACVRL1	NM_000020.2	Hereditary hemorrhagic telangiectasia, pulmonary arterial hypertension
APOB	NM_000384.2	Familial hypercholesterolemia, familial hypobetalipoproteinemia
BAG3	NM_004281.3	Cardiomyopathy, neuromuscular condition
BMPR2	NM_001204.6	Pulmonary arterial hypertension
CACNA1C*	NM_000719.6;NM_001129840.1	Arrhythmia, Timothy syndrome
CALM1	NM_006888.4	Arrhythmia
CALM2	NM_001743.4	Arrhythmia
CALM3	NM_005184.2	Arrhythmia
CASQ2	NM_001232.3	Arrhythmia
CAV1	NM_001753.4	Pulmonary arterial hypertension, lipodystrophy
COL3A1*	NM_000090.3	Aortopathy
COL5A1	NM_000093.4	Connective tissue disorder
COL5A2	NM_000393.3	Connective tissue disorder
CSRP3	NM_003476.4	Cardiomyopathy
DES	NM_001927.3	Arrhythmia, cardiomyopathy, neuromuscular condition
DMD	NM_004006.2	Cardiomyopathy, neuromuscular condition
DSC2	NM_024422.4	Arrhythmia, cardiomyopathy
DSG2	NM_001943.3	Arrhythmia, cardiomyopathy
DSP	NM_004415.2	Arrhythmia, cardiomyopathy
ENG*	NM_000118.3	Hereditary hemorrhagic telangiectasia
FBN1	NM_000138.4	Marfan syndrome, lipodystrophy, connective tissue disorder, skeletal conditions
FHL1	NM_001449.4	Cardiomyopathy, neuromuscular condition
FLNC*	NM_001458.4	Arrhythmia, cardiomyopathy, neuromuscular conditions
GDF2	NM_016204.2	Hereditary hemorrhagic telangiectasia, pulmonary arterial hypertension
GLA	NM_000169.2	Fabry disease
HCN4	NM_005477.2	Arrhythmia, cardiomyopathy, aortopathy
JUP	NM_002230.2	Arrhythmia, cardiomyopathy
KCNE1	NM_000219.5	Arrhythmia
KCNH2	NM_000238.3	Arrhythmia
KCNJ2	NM_000891.2	Arrhythmia, Andersen-Tawil syndrome
KCNQ1	NM_000218.2	Arrhythmia
LAMP2	NM_002294.2	Danon disease
LDLR	NM_000527.4	Familial hypercholesterolemia
LDLRAP1	NM_015627.2	Familial hypercholesterolemia
LMNA	NM_170707.3	Arrhythmia, cardiomyopathy, neuromuscular conditions, progeria, lipodystrophy, and others
MYBPC3	NM_000256.3	Cardiomyopathy
MYH11	NM_001040113.1	Aortopathy
MYH7	NM_000257.3	Cardiomyopathy, neuromuscular condition
MYL2	NM_000432.3	Cardiomyopathy
MYL3	NM_000258.2	Cardiomyopathy
MYLK	NM_053025.3	Aortopathy
PCSK9*	NM_174936.3	Familial hypercholesterolemia
PKP2	NM_004572.3	Arrhythmia, cardiomyopathy
PLN	NM_002667.3	Arrhythmia, cardiomyopathy
PRKAG2	NM_016203.3	Arrhythmia, cardiomyopathy
PRKG1	NM_006258.3	Aortopathy
PROC	NM_000312.3	Hereditary thrombophilia
PROS1	NM_000313.3	Hereditary thrombophilia
RBM20	NM_001134363.2	Arrhythmia, cardiomyopathy
RYR2	NM_001035.2	Arrhythmia, cardiomyopathy
SCN5A	NM_198056.2	Arrhythmia, cardiomyopathy
SERPINC1	NM_000488.3	Hereditary thrombophilia
SGCD	NM_000337.5	Neuromuscular condition
SMAD3	NM_005902.3	Aortopathy
SMAD9	NM_001127217.2	Pulmonary arterial hypertension
TCAP	NM_003673.3	Cardiomyopathy
TGFB2	NM_003238.3	Aortopathy, skeletal condition
TGFB3	NM_003239.3	Aortopathy
TGFBR1	NM_004612.2	Aortopathy, skin tumors
TGFBR2	NM_003242.5	Aortopathy
TMEM43	NM_024334.2	Arrhythmia, cardiomyopathy
TNNC1	NM_003280.2	Cardiomyopathy
TNNI3	NM_000363.4	Cardiomyopathy
TNNT2	NM_001001430.2	Cardiomyopathy
TPM1	NM_001018005.1	Cardiomyopathy
TRDN	NM_006073.3	Arrhythmia
TTN*	NM_001267550.2	Cardiomyopathy, neuromuscular condition
TTR	NM_000371.3	Hereditary transthyretin-mediated amyloidosis
VCL	NM_014000.2	Cardiomyopathy

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INVITAE

Patient name: DONOR 14723 **DOB:** [redacted]

Invitae #: RQ7406599

Other genes

GENE	TRANSCRIPT	ASSOCIATED CONDITION(S)
ABCD1	NM_000033.3	X-linked adrenoleukodystrophy
ATP7B	NM_000053.3	Wilson disease
BTD	NM_000060.3	Biotinidase deficiency
CACNA1S	NM_000069.2	Malignant hyperthermia susceptibility, neuromuscular conditions
CAV3	NM_033337.2	Neuromuscular condition
CRYAB	NM_001885.2	Cataracts, neuromuscular condition
EMD	NM_000117.2	Neuromuscular condition
F11	NM_000128.3	Bleeding condition
F2	NM_000506.3	Bleeding condition
F5	NM_000130.4	Bleeding condition
F9	NM_000133.3	Bleeding condition
G6PD	NM_001042351.2	Glucose-6-phosphate dehydrogenase deficiency
GAA	NM_000152.3	Glycogen storage disease
GCH1	NM_000161.2	Neuromuscular condition
HAMP	NM_021175.2	Hereditary hemochromatosis
HFE	NM_000410.3	Hereditary hemochromatosis
HJV	NM_213653.3	Hereditary hemochromatosis
HMBS	NM_000190.3	Acute intermittent porphyria
HNF1A	NM_000545.5	Maturity-onset diabetes of the young
HNF1B	NM_000458.3	Renal cysts and diabetes syndrome
MEFV	NM_000243.2	Familial Mediterranean fever
OTC	NM_000531.5	Ornithine transcarbamylase deficiency
RPE65	NM_000329.2	Retinal dystrophy
RYR1	NM_000540.2	Malignant hyperthermia susceptibility, neuromuscular conditions
SERPINA1	NM_000295.4	Alpha-1 antitrypsin deficiency
SLC40A1	NM_014585.5	Hereditary hemochromatosis
TFR2	NM_003227.3	Hereditary hemochromatosis

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INVITAE

Patient name: DONOR 14723 **DOB:** [redacted]

Invitae #: RQ7406599

Methods

- Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol, and sequenced using Illumina technology. Unless otherwise indicated, all targeted regions are sequenced with ≥50x depth or are supplemented with additional analysis. Reads are aligned to a reference sequence (GRCh37), and sequence changes are identified and interpreted in the context of a single clinically relevant transcript, indicated in the Genes Analyzed table. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 20bp of flanking intronic sequence, and other specific genomic regions demonstrated to be causative of disease at the time of assay design. Promoters, untranslated regions, and other non-coding regions are not otherwise interrogated. For some genes only targeted loci are analyzed. Exonic deletions and duplications are called using an in-house algorithm that determines copy number at each target by comparing the read depth for each target in the proband sequence with both mean read-depth and read-depth distribution, obtained from a set of clinical samples. Markers across the X and Y chromosomes are analyzed for quality control purposes and may detect deviations from the expected sex chromosome complement. Such deviations may be included in the report in accordance with internal guidelines. Variants are reported according to the Human Genome Variation Society (HGVS) guidelines. Confirmation of the presence and location of reportable variants is performed as needed based on stringent criteria using one of several validated orthogonal approaches (PubMed ID 30610921). Sequencing is performed by Labcorp Genetics, Inc (1400 16th Street, San Francisco, CA 94103, #05D2040778). Confirmatory sequencing is performed by Labcorp Genetics, Inc (1400 16th Street, San Francisco, CA 94103, #05D2040778). RNA sequencing is performed by Labcorp Genetics, Inc (1400 16th Street, San Francisco, CA 94103, #05D2040778).

  The following additional analyses are performed if relevant to the requisition. For PMS2 exons 12-15, the reference genome has been modified to force all sequence reads derived from PMS2 and the PMS2CL pseudogene to align to PMS2, and variant calling algorithms are modified to support an expectation of 4 alleles. If a rare SNP or indel variant is identified by this method, both PMS2 and the PMS2CL pseudogene are amplified by long-range PCR and the location of the variant is determined by Pacific Biosciences (PacBio) SMRT sequencing of the relevant exon in both long-range amplicons. If a CNV is identified, MLPA or MLPA-seq is run to confirm the variant. If confirmed, both PMS2 and PMS2CL are amplified by long-range PCR, and the identity of the fixed differences between PMS2 and PMS2CL are sequenced by PacBio from the long-range amplicon to disambiguate the location of the CNV. For C9orf72 repeat expansion testing, hexanucleotide repeat units are detected by repeat-primed PCR (RP-PCR) with fluorescently labeled primers followed by capillary electrophoresis. Interpretation Reference Ranges: Benign (Normal Range): <25 repeat units, Uncertain: 25-30 repeat units, Pathogenic (Full Mutation): >=31 repeat units (PMID: 21944779, 22406228, 23111906, 28689190, 31315673, 33168078, 33575483). A second round of RP-PCR utilizing a non-overlapping set of primers is used to confirm the initial call in the case of suspected allele sizes of 22 or more repeats. For RNA analysis of the genes indicated in the Genes Analyzed table, complementary DNA is synthesized by reverse transcription from RNA derived from a blood specimen and enriched for specific gene sequences using capture hybridization. After high-throughput sequencing using Illumina technology, the output reads are aligned to a reference sequence (genome build GRCh37; custom derivative of the RefSeq transcriptome) to identify the locations of exon junctions through the detection of split reads. The relative usage of exon junctions in a test specimen is assessed quantitatively and compared to the usage seen in control specimens. Abnormal exon junction usage is evaluated as evidence in the Sherloc variant interpretation framework. If an abnormal splicing pattern is predicted based on a DNA variant outside the typical reportable range, as described above, the presence of the variant is confirmed by targeted DNA sequencing.

- A PMID is a unique identifier referring to a published, scientific paper. Search by PMID at **http://www.ncbi.nlm.nih.gov/pubmed**.
- An rsID is a unique identifier referring to a single genomic position, and is used to associate population frequency information with sequence changes at that position. Reported population frequencies are derived from a number of public sites that aggregate data from large-scale population sequencing projects, including ExAC (**http://exac.broadinstitute.org**), gnomAD (**http://gnomad.broadinstitute.org**), and dbSNP (**http://ncbi.nlm.nih.gov/SNP**).
- A MedGen ID is a unique identifier referring to an article in MedGen, NCBI's centralized database of information about genetic disorders and phenotypes. Search by MedGen ID at **http://www.ncbi.nlm.nih.gov/medgen**. An OMIM number is a unique identifier referring to a comprehensive entry in Online Mendelian Inheritance in Man (OMIM). Search by OMIM number at **http://omim.org/**.
- The laboratory uses information from individuals undergoing testing to inform variant interpretation. If "internal data" is cited as a reference in the variant details this may refer to the individual in this requisition and/or historical internal observations.

Limitations

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Based on validation study results, this assay achieves >99% analytical sensitivity and specificity for single nucleotide variants, insertions and deletions <15bp in length, and exon-level deletions and duplications. This test detects insertions and deletions larger than 15bp but smaller than a full exon but sensitivity for these may be marginally reduced. Deletion/duplication analysis for this test determines copy number at a single exon resolution at virtually all targeted exons. However, in rare situations, single-exon copy number events may not be analyzed due to inherent sequence properties or isolated reduction in data quality. Certain types of variants, such as structural rearrangements (e.g. inversions, gene conversion events, translocations, etc.) or variants embedded in sequence with complex architecture (e.g. short tandem repeats or segmental duplications), may not be detected. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity. Unless explicitly guaranteed, sequence changes in the promoter, non-coding exons, and other non-coding regions are not covered by this assay. Please consult the test definition on our website for details regarding regions or types of variants that are covered or excluded for this test. This report reflects the analysis of an extracted genomic DNA sample. While this test is intended to reflect the analysis of extracted genomic DNA from a referred patient, in very rare cases the analyzed DNA may not represent that individual's constitutional genome, such as in the case of a circulating hematolymphoid neoplasm, bone marrow transplant, blood transfusion, chimerism, culture artifact or maternal cell contamination. Interpretations are made on the assumption that any clinical information provided, including specimen identity, is accurate. RNA analysis is not designed for use as a stand-alone diagnostic method and cannot determine absolute RNA levels. Results from the RNA analysis may not be informative for interpreting copy number events. Additionally, sensitivity to detect RNA splicing events may be reduced for variants in the first donor site of each gene and for complex rearrangements or events.

ACTC1: Sequencing analysis for exons 6 includes only cds +/- 10 bp. ACTN2: Deletion/duplication analysis is not offered for exon 9. APC: Sequencing analysis for exons 5 includes only cds +/- 10 bp. ATM: Sequencing analysis for exons 6, 24, 43 includes only cds +/- 10 bp. CACNA1C: Deletion/duplication and sequencing analysis is not offered for exons 44-45. COL3A1: Deletion/duplication analysis is not offered for exons 23-24. DICER1: Sequencing analysis for exons 22 includes only cds +/- 10 bp. ENG: Sequencing analysis for exons 7 includes only cds +/- 10 bp. EPCAM: Sequencing analysis is not offered for this gene. FH: Sequencing analysis for exons 9 includes only cds +/- 10 bp. MAX: Sequencing analysis for exons 2 includes only cds +/- 10 bp. MEN1: Sequencing analysis for exons 2 includes only cds +/- 10 bp. MET: Sequencing analysis for exons 12 includes only cds +/- 10 bp. MLH1: Sequencing analysis for exons 12 includes only cds +/- 10 bp. MSH2: Analysis includes the exon 1-7 inversion (Boland mutation). Sequencing analysis for exons 2, 5 includes only cds +/- 10 bp. MSH6: Sequencing analysis for exons 7, 10 includes only cds +/- 10 bp. PCSK9: Sequencing analysis for exons 9 includes only cds +/- 10 bp. PMS2: Sequencing analysis for exons 7 includes only cds +/- 10 bp. PTEN: Sequencing analysis for exons 8 includes only cds +/- 10 bp. RB1: Sequencing analysis for exons 15-16 includes only cds +/- 10 bp. SDHA: Deletion/duplication analysis is not offered for this gene and sequencing analysis is not offered for exon 14. Sequencing analysis for exons 6-8 includes only cds +/- 10 bp. SDHC: Sequencing analysis for exons 2, 6 includes only cds +/- 10 bp. TSC1: Sequencing analysis for exons 21 includes only cds +/- 10 bp. GREM1: Promoter region duplication testing only. POLD1: Sequencing analysis for exon 22 includes only cds +/- 10 bp and exon 27 includes only cds +-0 bp. FLNC: Deletion/duplication analysis is not offered for exon 47. Sensitivity and specificity for single nucleotide variants, insertions and deletions in exons 47-48 may be reduced due to the presence of segmental duplications overlapping the region. MSH3: Sequencing analysis of the repeat region of exon 1 (5:79950697-79950765) is not offered. NF1: Sequencing analysis for exons 2, 7, 25, 41, 48 includes only cds +/- 10 bp. TTN: Exons 45-46, 147, 149, 164, 172-201 (NM_001267550.2) are excluded from analysis. TTN variants are included in the primary report based on functional effect and/or location. A complete list of variants of uncertain significance, likely benign and benign variants in TTN is available upon request. Variants are named relative to the NM_001267550.2 (meta) transcript. Variants in the coding sequence and intronic boundaries of the clinically relevant NM_133378.4 (N2A) and fetal isoforms are reported (PMID: 25589632, 29598826, 29691892, 31660661), with the exception of the PEVK tandem repeat region (172-198) (PMID: 28040389).

Disclaimer

DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of many aspects used by the healthcare provider to help with a diagnosis and treatment plan, but it is not a diagnosis itself. This test was developed and its performance characteristics determined by Labcorp Genetics. It has not been cleared or approved by the FDA. The laboratory is regulated under the Clinical Laboratory Improvement Act (CLIA) as qualified to perform high-complexity clinical tests (CLIA ID: 05D2040778). This test is used for clinical purposes. It should not be regarded as investigational or for research.

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INVITAE

Patient name: DONOR 14723 **DOB:** [redacted]

Invitae #: RQ7406599

This report has been reviewed and approved by:



Fatimah Nahhas-Alwan, PhD, FACMG
Clinical Molecular Geneticist

fn_017b_pr

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Patient Information	Specimen Information	Client Information
14723, DONOR **DOB:** [redacted] **AGE:** [redacted] Gender: M Fasting: U Phone: 206.588.1484 Patient ID: 14723 Health ID: 8573036833869302	Specimen: OW309003E Requisition: 0000821 Collected: 07/01/2025 / 12:00 PDT Received: 07/04/2025 / 01:31 PDT Reported: 07/16/2025 / 16:22 PDT	Client #: 98105026 VNLZR00 KUAN, JAMES K SEATTLE SPERM BANK 4915 25TH AVE NE STE 204W SEATTLE, WA 98105-5668

COMMENTS: FASTING:UNKNOWN

Cytogenetic Report

CHROMOSOME ANALYSIS, BLOOD - 14596 Lab:EZ

CHROMOSOME ANALYSIS, BLOOD

Order ID: 25-358627
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

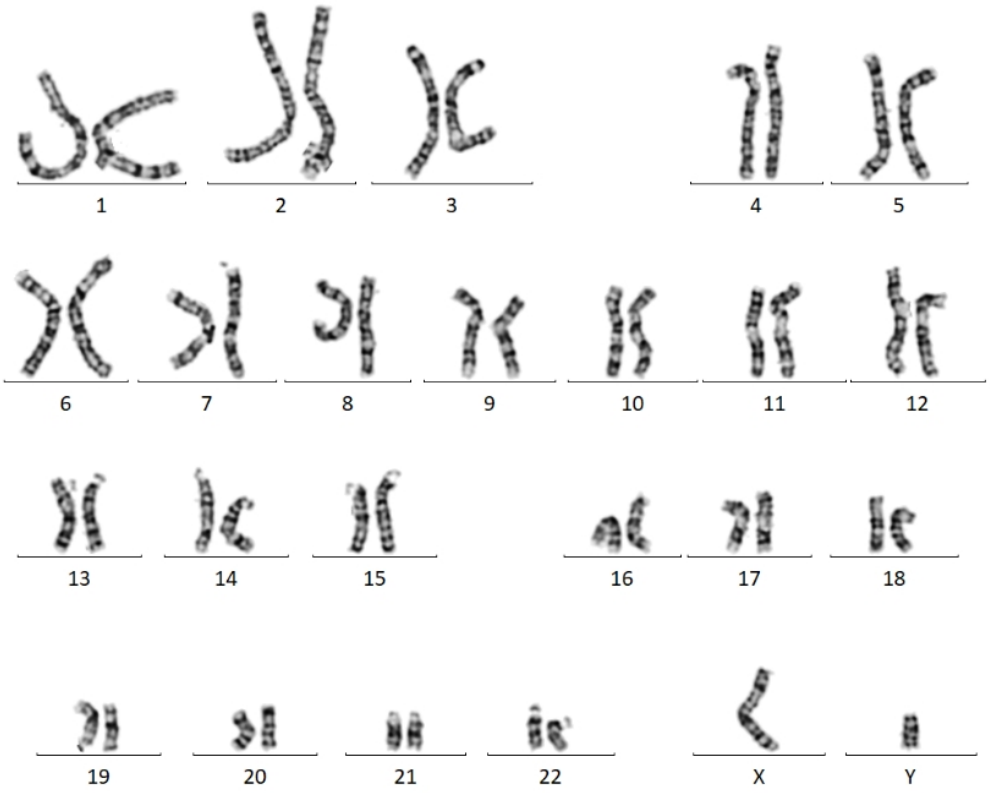
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements. A portion of the testing was performed at SJC47

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

Electronic Signature: 7/16/2025 4:41 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

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