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Metroplex Pathology Associates
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Therapath Partners

Patient Information:
**11028, Donor**
**DOB:** [redacted]
Sex: M
MR#:
Patient#: FT-PT9193501

Partner Information:
**Not Tested**

Physician:
**Kuan, James**
ATTN: Kirk, Ashley
Phoenix Sperm Bank
4915 25th Avenue Northeast
Ste 204
Seattle, 98105
Phone: 3039705897

Laboratory:
**Fulgent Therapeutics LLC**
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Dr. Amar Jariwala
Report Date: **Aug 30,2025**

Accession:
**FT-7529024**
Test#: FT-TS15308825
Specimen Type: Blood (EDTA)
Collected: Aug 19,2025

Accession:
**N/A**

## FINAL RESULTS

Carrier for **ONE** genetic condition

## 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 | 11028, Donor | Partner |
|---|---|---|---|
| **EPG5-related disorder**<br>*EPG5* | AR | ⊕ Carrier<br>c.5869+1G>A (p.?) | N/A |

## INTERPRETATION:

**Notes and Recommendations:**

- Based on these results, this individual is positive for a carrier mutation in 1 gene. 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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# EPG5-RELATED DISORDER

| Patient | 11028, Donor | Partner |
|---|---|---|
| **Result** | ⊕ Carrier | N/A |
| **Variant Details** | ***EPG5*** (NM_020964.3)<br>c.5869+1G>A (p.?) | N/A |

## *What is EPG5-related disorder?*

Multiple conditions have been associated with the EPG5 gene including Vici Syndrome (the most severe EPG5-related disorder) and milder conditions.

- Vici Syndrome is a congenital multisystem disorder characterized by agenesis of the corpus callosum (ACC), cataracts, pigmentary defects, progressive cardiomyopathy, and variable immunodeficiency, microcephaly, and failure to thrive. Affected individuals also have profound psychomotor retardation and hypotonia due to a myopathy (PubMed: 21965116).
- The milder conditions on the EPG5-related include attenuated neurodevelopmental phenotypes with variable multisystem involvement.

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

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. There is no cure for EPG5-related disorders. However, supportive multidisciplinary care can be provided to enhance the quality of life, improve functionality, and reduce complications. Care may involve specialists in clinical genetics and pediatrics, as well as allied health professionals in neurology, audiology, ophthalmology, development, feeding, cardiology, pulmonology, gastroenterology, immunology, endocrinology, and nephrology. When invasive procedures are under consideration, experts in palliative care and medical ethics should be consulted, given the complexities of medical problems in affected individuals. It is important to note that rigorous and early antibacterial and antifungal treatment should be considered for chest infections to prevent episodes of life-threatening sepsis and organ failure due to primary immunodeficiency.

## *What mutation was detected?*

The detected heterozygous variant was NM_020964.3:c.5869+1G>A (p.?). This intronic variant alters the highly conserved consensus sequence for the canonical splice site and is predicted to abolish canonical splice activity. This variant is expected to result in a non-functional or absent gene product as a result of aberrant splicing. There's sufficient evidence that loss of function in this gene is a known disease mechanism for Vici syndrome (PubMed: 23222957, 26917586, 25331754, 28748650, 31216405). This variant has been reported in the compound heterozygous state in one individual with Vici syndrome (PubMed: 26917586). The laboratory classifies this variant as 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, 99.69% and 99.65% 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 **08/30/2025**
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 GENETIC RISK ASSESSMENT TESTING RESULTS

| | | | | | |
|---|---|---|---|---|---|
| **Patient name:** | Donor 11028 | **Sample type:** | Blood | **Report date:** | 27-AUG-2025 |
| **DOB:** | [redacted] | **Sample collection date:** | 19-AUG-2025 | **Invitae #:** | RQ7502429 |
| **Sex assigned at birth:** | Male | **Sample accession date:** | 20-AUG-2025 | **Clinical team:** | Ashley Kirk<br>Dr. James Kuan |
| **Gender:** | | | | | |
| **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 BTD gene, which is associated with being a carrier for a hereditary condition.**

| GENE | VARIANT | ZYGOSITY | VARIANT CLASSIFICATION |
|---|---|---|---|
| BTD | c.1330G>C (p.Asp444His) | heterozygous | PATHOGENIC |

**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.

**Laboratory Director:** Jeana DaRe, PhD, FACMG
**Labcorp Genetics** 1400 16th Street, San Francisco, CA 94103 · clientservices@invitae.com · 800.436.3037
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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7502429

## Clinical summary

A Pathogenic variant, c.1330G>C (p.Asp444His), was identified in BTD.

- If a person carries two clinically significant genetic changes, one in each copy of the BTD gene, this may result in an autosomal recessive condition known as biotinidase deficiency. The c.1330G>C (p.Asp444His) gene change in BTD is associated with a mild form of biotinidase deficiency, known as partial biotinidase deficiency.
- This result is associated with being a carrier of partial biotinidase deficiency. Carriers typically do not have symptoms of the condition, but may be at risk to have a child with the condition.

- Biotinidase deficiency is an inherited condition in which the body has difficulty recycling a vitamin called biotin. Symptoms can range from mild to severe, and typically affect the brain and skin. In severe cases (profound biotinidase deficiency), affected individuals present with acid accumulation in the body (metabolic acidosis), developmental delay, poor muscle tone (hypotonia), seizures, uncoordinated movements (ataxia), skin rashes and hair loss (alopecia). The milder partial biotinidase deficiency is caused by having one or two copies of the c.1330G>C (p.Asp444His) gene change in addition to another clinically significant gene change in the BTD gene. Affected individuals typically have no signs or symptoms of the condition (asymptomatic); however, if untreated, symptoms may appear during times of illness or stress and may include low muscle tone (hypotonia), skin rashes, and hair loss (alopecia). Early treatment, including biotin supplementation, may prevent or reduce the severity of symptoms (PMID: 20129807).

  Some individuals have two copies of the c.1330G>C (p.Asp444His) gene change (homozygous) but no other clinically significant BTD gene changes; while this is associated with some degree of defective biotin recycling, it is not expected to cause clinical symptoms of partial biotinidase deficiency.

- 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 biotinidase deficiency and could consider testing. The chance of having a child with autosomal recessive biotinidase deficiency depends on whether this individual's partner is also a carrier of the same condition. The form of biotinidase deficiency depends on the specific BTD gene changes the child inherits from the reproductive parents.

## Variant details

BTD, Exon 4, c.1330G>C (p.Asp444His), heterozygous, PATHOGENIC

- This sequence change replaces aspartic acid, which is acidic and polar, with histidine, which is basic and polar, at codon 444 of the BTD protein (p.Asp444His).
- This variant is present in population databases (rs13078881, gnomAD 6%), and has an allele count higher than expected for a pathogenic variant.
- In the homozygous state this variant does not cause biotinidase deficiency or partial biotinidase deficiency (PMID: 28682309, 9654207). However, this variant in conjunction with another pathogenic variant is a common cause of partial biotinidase deficiency (PMID: 10206677, 9654207, 12227467, 23644139). This variant has also been observed in individuals affected with profound biotinidase deficiency when this variant is in cis with the p.A171T variant and in trans with a third variant (PMID: 10206677, 9654207).
- In individuals affected with partial biotinidase deficiency who harbor this variant in combination with another BTD variant, serum biotinidase activity was approximately 24% of the mean normal control activity (PMID: 9654207). In individuals affected with profound biotinidase deficiency who harbor this variant in cis with p.A171T and in trans with another BTD variant, serum biotinidase activity was <10% of the mean normal control activity (PMID: 10206677, 9654207). Individuals who are homozygous for this variant typically have an enzyme activity that is approximately 50% of normal (PMID: 20539236, 28682309, 9654207), similar to what is seen for a carrier of a profound allele.
- ClinVar contains an entry for this variant (Variation ID: 1900).
- 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) indicates that this missense variant is expected to disrupt BTD protein function with a positive predictive value of 95%.
- For these reasons, this variant has been classified as Pathogenic.


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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7502429

# 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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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7502429

| 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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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7502429

## 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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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7502429

## 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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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7502429

## 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, gnomAD, and dbSNP.
- 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

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


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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 Amendments (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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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7502429

## This report has been reviewed and approved by:



Matteo Vatta, Ph.D., FACMG
Clinical Molecular Geneticist

mv_6bdc_pr


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# INVITAE GENETIC RISK ASSESSMENT TESTING RESULTS

| | | | | | |
|---|---|---|---|---|---|
| **Patient name:** | Donor 11028 | **Sample type:** | Blood | **Report date:** | 23-JUL-2025 |
| **DOB:** | [redacted] | **Sample collection date:** | 16-JUL-2025 | **Invitae #:** | RQ7428504 |
| **Sex assigned at birth:** | Male | **Sample accession date:** | 17-JUL-2025 | **Clinical team:** | Guadalupe Martinez<br>Dr. James Kuan |
| **Gender:** | | | | | |
| **Patient ID (MRN):** | | | | | |

**Test performed**

Sequence analysis and deletion/duplication testing of the 64 genes listed in the Genes Analyzed section.

- Invitae Cancer Genetic Risk Panel

## RESULT: NEGATIVE

**This test did not identify any genetic variation that is currently recognized as clinically significant.**

**About this test**

This test evaluates 64 genes for variants (genetic changes) that indicate a significantly increased risk of developing certain types of hereditary cancer. 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

- You can request a referral for genetic counseling to further discuss this test result and to review your family health history. A complete family history may point to health risks not evaluated by this test. It is important to note that while this test has found no genetic risk factors for certain types of conditions, at least a baseline, population-level risk remains for developing these types of disorders and age-appropriate screenings are still recommended.

- 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.

**Laboratory Director:** Jeana DaRe, PhD, FACMG
**Labcorp Genetics** 1400 16th Street, San Francisco, CA 94103 · clientservices@invitae.com · 800.436.3037
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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7428504

## Clinical summary

There were no known, clinically significant genetic changes identified that confer a genetic predisposition to, or carrier status for, certain types of hereditary cancer tested with this panel (see complete list of genes and conditions evaluated below). However, other types of risk based on factors including personal and family history, genetic causes not evaluated with this test, lifestyle, or other environmental influences may still be of clinical significance.

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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7428504

# 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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# INVITAE GENETIC RISK ASSESSMENT TESTING RESULTS

**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7428504

| 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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**Patient name:** Donor 11028 **DOB:** [redacted]
**Invitae #:** RQ7428504

## 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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**Invitae #:** RQ7428504

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.

APC: Sequencing analysis for exons 5 includes only cds +/- 10 bp. ATM: Sequencing analysis for exons 6, 24, 43 includes only cds +/- 10 bp. DICER1: Sequencing analysis for exons 22 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. 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. 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.

## 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.

## This report has been reviewed and approved by:



Jennifer Sanmann, Ph.D., FACMG
Clinical Molecular Geneticist, Clinical Cytogeneticist

js_dfe1_pr


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INVITAE®

GENERAL GUIDELINES
# NEGATIVE RESULTS GUIDE

This document is not part of the Invitae® clinical report and does not represent medical advice. These are general guidelines that are not specific to your result and may not represent all relevant international recommendations. You can use this guide to talk to your healthcare provider about your test results, clinical history, and the most current guidelines. We recognize that individuals have diverse gender and sexual identities. In this guide, the terms female, male, women, and men refer to sex assigned at birth.

## What is a negative result?



A negative test result means that no significant genetic changes ("pathogenic" or "likely pathogenic" variants) were found. Risk for disease can still be influenced by a combination of personal, lifestyle, environmental, and/or unidentified genetic factors.

## Create a plan with a healthcare provider



It is important to share these results with a healthcare provider to determine appropriate next steps. The chance for an individual to develop a disease is not usually determined by genetic test results alone.

## What does this result mean for family members?



Parents, siblings, children, and other relatives have their own genetic makeup. Although these results did not find a significant genetic change, family members can discuss their own potential health and/or reproductive risks and the option of genetic testing with their own healthcare providers.

## Resources



Genetic counseling can help individuals understand their genetic test results and options for next steps. Reviewing test results with a genetic counselor or other healthcare provider is recommended. Local or telehealth genetic counselors can be identified using the Find a Genetic Counselor search tool at nsgc.org (US and Canada). Individuals with an Invitae test result can also log in to their patient portal (invitae.com) to view their results, contact a genetic counselor, or join Invitae's Patient Insights Network (PIN) (pin.invitae.com), an online platform where individuals can share information about their health and experiences to help advance research and drug development.

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**Report Status FINAL**
Route 2017 Ordered by:

**Phoenix Sperm Bank**
1492 S Mill Ave
Suite 306
Tempe, AZ 85281

**James Kuan, MD**

Sonora Quest Laboratories™
A Subsidiary of Laboratory Sciences of Arizona

Patient Information:
**11028, DONOR**

**Order #: 181 0 / NL1 48**

Account: 18131
**ID/MR#: 11028**
Patient Lab ID:
68a5f8fb092f314914a0c4ac

Collected: 08/19/2025 01:14 PM
Received: 08/20/2025 09:13 AM
Reported: 08/26/2025 02:59 PM

**DOB:** [redacted] Age: [redacted]
Sex: M
Patient Phone: 602-888-7255

[redacted] PL

GENETICS

**Accession #:**
CG250008918

**Cell Type/Source:**
Blood

**Clinician Provided Information:**
DONOR TESTING

**Chromosome Analysis: Routine Blood**

**Analysis Details:** PV

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

**Results:** PV

NORMAL MALE KARYOTYPE

46,XY

**Interpretation:** PV

**Normal**

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.

**Comments:** PV

remote: jmr

**Cytogenetics Director:** PV



Electronically signed by Liwen Lai R PhD, DABMGG, FACMG R
Verified 08/26/25


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**Report Status FINAL**
Route 2017 Ordered by:

**Phoenix Sperm Bank**
1492 S Mill Ave
Suite 306
Tempe, AZ 85281

**James Kuan, MD**

Sonora Quest Laboratories™
A Subsidiary of Laboratory Sciences of Arizona

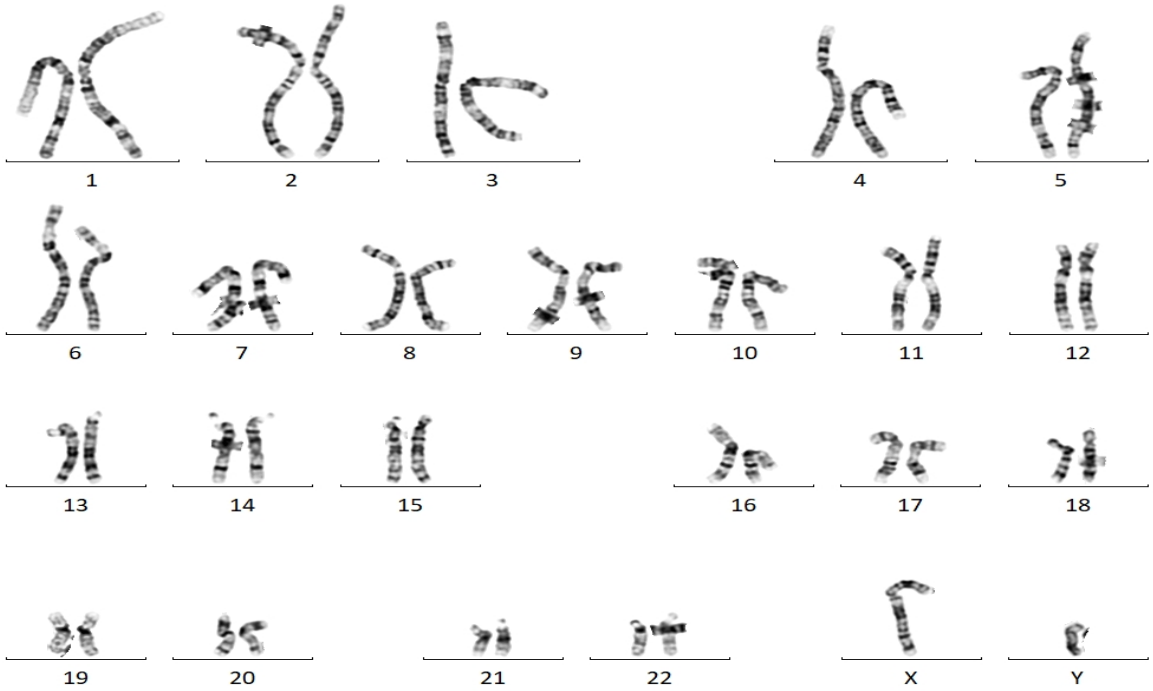
Patient Information: [redacted]
**11028, DONOR**

**Order #: 18[redacted]0 / NL1[redacted]48**

Account: 18131
**ID/MR#: 11028**
Patient Lab ID:
68a5f8fb092f314914a0c4ac

Collected: 08/19/2025 01:14 PM
Received: 08/20/2025 09:13 AM
Reported: 08/26/2025 02:59 PM

**DOB:** [redacted] Age: [redacted]
Sex:
Patient Phone: 602-888-7255




**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 Laboratory Director: Dr. Regina Van Buren
Testing noted as PV performed by: Genetics/Genomics Div., Sonora Quest Laboratories, 424 S. 56th St, Phoenix, AZ 85034 602.685.5700 Laboratory Director:

**End of Report**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