# Donor 6747

## Genetic Testing Summary

Fairfax Cryobank recommends reviewing this genetic testing summary with your healthcare provider to determine suitability.

Last Updated: 04/05/24

Donor Reported Ancestry: English, Scottish, Irish  Jewish Ancestry: No

| Genetic Test* | Result | Comments/Donor's Residual Risk** |
|---|---|---|
| Chromosome analysis (karyotype) | Normal male karyotype | No evidence of clinically significant chromosome abnormalities |
| Hemoglobin evaluation | Normal hemoglobin fractionation and MCV/MCH results | Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies |
| Cystic Fibrosis (CF) carrier screening | Negative by gene sequencing in the CFTR gene | 1/440 |
| Spinal Muscular Atrophy (SMA) carrier screening | Negative for deletions of exon 7 and gene sequencing in the SMN1 gene | 1/1107 |
| Expanded Genetic Disease Carrier Screening Panel attached- 283 diseases by gene sequencing | Carrier: Primary Hyperoxaluria, Type 3 (HOGA1)<br><br>Negative for other genes sequenced | Partner testing recommended before using this donor. |
| **Special Testing** | | |
| Genes: POLG, AMN, MRE11, CC2D2A, NAGA, SERPINA1, GALNT3, MYO15A | Negative by gene sequencing | See attached reports |

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.

**Donor residual risk is the chance the donor is still a carrier after testing negative.

**Patient Information**
Name: Donor 6747
Date of Birth: [redacted]
Sema4 ID: [redacted]
Client ID: [redacted]
Indication: Carrier Screening

**Specimen Information**
Specimen Type: Blood
Date Collected: 11/05/2021
Date Received: 11/06/2021
Final Report: 11/22/2021

**Referring Provider**
[redacted]
Fairfax Cryobank, Inc.
[redacted]

# Expanded Carrier Screen Minus TSE (283 genes)

with Personalized Residual Risk

## SUMMARY OF RESULTS AND RECOMMENDATIONS

| ⊕ Positive | ⊖ Negative |
|---|---|
| **Carrier of Primary Hyperoxaluria, Type 3 (AR)**<br>Associated gene(s): *HOGA1*<br>Variant(s) Detected: c.208C>T, p.R70X, Pathogenic, Heterozygous (one copy) | **Negative for all other genes tested**<br>To view a full list of genes and diseases tested please see Table 1 in this report |

*AR=Autosomal recessive; XL=X-linked*

### Recommendations

- Testing the partner for the above positive disorder(s) and genetic counseling are recommended.
- Please note that for female carriers of X-linked diseases, follow-up testing of a male partner is not indicated.
- CGG repeat analysis of *FMR1* for fragile X syndrome is not performed on males as repeat expansion of premutation alleles is not expected in the male germline.
- Individuals of Asian, African, Hispanic and Mediterranean ancestry should also be screened for hemoglobinopathies by CBC and hemoglobin electrophoresis.
- Consideration of residual risk by ethnicity after a negative carrier screen is recommended for the other diseases on the panel, especially in the case of a positive family history for a specific disorder.

# Interpretation of positive results

### Primary Hyperoxaluria, Type 3 (AR)

**Results and Interpretation**

A heterozygous (one copy) pathogenic premature stop codon, c.208C>T, p.R70X, was detected in the *HOGA1* gene (NM_138413.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for primary hyperoxaluria, type 3. Therefore, this individual is expected to be at least a carrier for primary hyperoxaluria, type 3. Heterozygous carriers are not expected to exhibit symptoms of this disease.

**What is Primary Hyperoxaluria, Type 3?**

Primary hyperoxaluria, type 3 is an autosomal recessive disease caused by pathogenic variants in the *HOGA1* gene. While it has been diagnosed in patients of various ethnicities, it may be more prevalent in individuals of Ashkenazi Jewish descent due to the presence of a founder mutation. Age of onset is typically in childhood, and the disease is characterized by the accumulation of calcium oxalate in the kidney and urinary tract, leading to kidney stone formation. Some patients have a milder phenotype where they do not develop kidney stones. Life expectancy is not thought to be affected, and no genotype-phenotype correlation has been reported.

# Test description

This patient was tested for a panel of diseases using a combination of sequencing, targeted genotyping and copy number analysis. Please note that negative results reduce but do not eliminate the possibility that this individual is a carrier for one or more of the disorders tested. Please see Table 1 for a list of genes and diseases tested with the patient's personalized residual risk. If personalized residual risk is not provided, please see the complete residual risk table at **go.sema4.com/residualrisk**. Only variants determined to be pathogenic or likely pathogenic are reported in this carrier screening test.

Alice K Tanner

**Alice Tanner, Ph.D., M.S., CGC, FACMG, Laboratory Director**
Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D

# Genes and diseases tested

The personalized residual risks listed below are specific to this individual. The complete residual risk table is available at **go.sema4.com/residualrisk**

## Table 1: List of genes and diseases tested with detailed results

| Disease | Gene | Inheritance Pattern | Status | Detailed Summary |
|---|---|---|---|---|
| **Positive** | | | | |
| **Primary Hyperoxaluria, Type 3** | *HOGA1* | AR | Carrier | c.208C>T, p.R70X, Pathogenic, Heterozygous (one copy) |
| **Negative** | | | | |
| **3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency** | *HSD3B2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,300 |
| **3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC1*-Related)** | *MCCC1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,400 |
| **3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC2*-Related)** | *MCCC2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,200 |
| **3-Methylglutaconic Aciduria, Type III** | *OPA3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 50,000 |
| **3-Phosphoglycerate Dehydrogenase Deficiency** | *PHGDH* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 63,000 |
| **6-Pyruvoyl-Tetrahydropterin Synthase Deficiency** | *PTS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Abetalipoproteinemia** | *MTTP* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,200 |
| **Achromatopsia (*CNGB3*-related)** | *CNGB3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 8,600 |
| **Acrodermatitis Enteropathica** | *SLC39A4* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 12,000 |
| **Acute Infantile Liver Failure** | *TRMU* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 9,400 |
| **Acyl-CoA Oxidase I Deficiency** | *ACOX1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 39,000 |
| **Adenosine Deaminase Deficiency** | *ADA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,100 |
| **Adrenoleukodystrophy, X-Linked** | *ABCD1* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 19,000 |
| **Aicardi-Goutieres Syndrome (*SAMHD1*-Related)** | *SAMHD1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 10,000 |
| **Alpha-Mannosidosis** | *MAN2B1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,200 |
| **Alpha-Thalassemia** | *HBA1/HBA2* | AR | Reduced Risk | *HBA1* Copy Number: 2<br>*HBA2* Copy Number: 2<br>No pathogenic copy number variants detected<br>*HBA1/HBA2* Sequencing: Negative<br>**Personalized Residual Risk:** 1 in 10,000 |
| **Alpha-Thalassemia Intellectual Disability Syndrome** | *ATRX* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 48,000 |
| **Alport Syndrome (*COL4A3*-Related)** | *COL4A3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Alport Syndrome (*COL4A4*-Related)** | *COL4A4* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Alport Syndrome (*COL4A5*-Related)** | *COL4A5* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 150,000 |
| **Alstrom Syndrome** | *ALMS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,800 |
| **Andermann Syndrome** | *SLC12A6* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 151,000 |
| **Argininosuccinic Aciduria** | *ASL* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,200 |
| **Aromatase Deficiency** | *CYP19A1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,400 |
| **Arthrogryposis, Mental Retardation, and Seizures** | *SLC35A3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 454,000 |
| **Asparagine Synthetase Deficiency** | *ASNS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 202,000 |
| **Aspartylglycosaminuria** | *AGA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 13,000 |
| **Ataxia With Isolated Vitamin E Deficiency** | *TTPA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 61,000 |
| **Ataxia-Telangiectasia** | *ATM* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,300 |

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|---|---|---|---|---|
| **Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay** | *SACS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,600 |
| **Bardet-Biedl Syndrome (*BBS10*-Related)** | *BBS10* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,700 |
| **Bardet-Biedl Syndrome (*BBS12*-Related)** | *BBS12* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 9,900 |
| **Bardet-Biedl Syndrome (*BBS1*-Related)** | *BBS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,400 |
| **Bardet-Biedl Syndrome (*BBS2*-Related)** | *BBS2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,200 |
| **Bare Lymphocyte Syndrome, Type II** | *CIITA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 35,000 |
| **Bartter Syndrome, Type 4A** | *BSND* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 91,000 |
| **Bernard-Soulier Syndrome, Type A1** | *GP1BA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 42,000 |
| **Bernard-Soulier Syndrome, Type C** | *GP9* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,300 |
| **Beta-Globin-Related Hemoglobinopathies** | *HBB* | AR | Reduced Risk | **Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies):** 1 in 2,000<br>**Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant):** 1 in 790,000<br>**Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant):** 1 in 2,107,000 |
| **Beta-Ketothiolase Deficiency** | *ACAT1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,400 |
| **Bilateral Frontoparietal Polymicrogyria** | *GPR56* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 203,000 |
| **Biotinidase Deficiency** | *BTD* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 500 |
| **Bloom Syndrome** | *BLM* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 7,400 |
| **Canavan Disease** | *ASPA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,000 |
| **Carbamoylphosphate Synthetase I Deficiency** | *CPS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,100 |
| **Carnitine Palmitoyltransferase IA Deficiency** | *CPT1A* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 24,000 |
| **Carnitine Palmitoyltransferase II Deficiency** | *CPT2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 670 |
| **Carpenter Syndrome** | *RAB23* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 21,000 |
| **Cartilage-Hair Hypoplasia** | *RMRP* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 960 |
| **Cerebral Creatine Deficiency Syndrome 1** | *SLC6A8* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 208,000 |
| **Cerebral Creatine Deficiency Syndrome 2** | *GAMT* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,100 |
| **Cerebrotendinous Xanthomatosis** | *CYP27A1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,900 |
| **Charcot-Marie-Tooth Disease, Type 4D** | *NDRG1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 730,000 |
| **Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome** | *PRPS1* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 114,000 |
| **Charcot-Marie-Tooth Disease, X-Linked** | *GJB1* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 11,000 |
| **Choreoacanthocytosis** | *VPS13A* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 13,000 |
| **Choroideremia** | *CHM* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 125,000 |
| **Chronic Granulomatous Disease (*CYBA*-Related)** | *CYBA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,000 |
| **Chronic Granulomatous Disease (*CYBB*-Related)** | *CYBB* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 294,000 |
| **Citrin Deficiency** | *SLC25A13* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 12,000 |
| **Citrullinemia, Type 1** | *ASS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,500 |
| **Cohen Syndrome** | *VPS13B* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,400 |
| **Combined Malonic and Methylmalonic Aciduria** | *ACSF3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,400 |
| **Combined Oxidative Phosphorylation Deficiency 1** | *GFM1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 13,000 |
| **Combined Oxidative Phosphorylation Deficiency 3** | *TSFM* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 27,000 |
| **Combined Pituitary Hormone Deficiency 2** | *PROP1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,800 |
| **Combined Pituitary Hormone Deficiency 3** | *LHX3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 140,000 |
| **Combined SAP Deficiency** | *PSAP* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 44,000 |
| **Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency** | *CYP17A1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |

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|---|---|---|---|---|
| **Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency** | *CYP21A2* | AR | Reduced Risk | *CYP21A2* copy number: 2<br>*CYP21A2* sequencing: Negative<br>**Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)):** 1 in 200<br>**Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)):** 1 in 1,300 |
| **Congenital Amegakaryocytic Thrombocytopenia** | *MPL* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,100 |
| **Congenital Disorder of Glycosylation, Type Ia** | *PMM2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 540 |
| **Congenital Disorder of Glycosylation, Type Ib** | *MPI* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,600 |
| **Congenital Disorder of Glycosylation, Type Ic** | *ALG6* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,100 |
| **Congenital Insensitivity to Pain with Anhidrosis** | *NTRK1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,700 |
| **Congenital Myasthenic Syndrome (*CHRNE*-Related)** | *CHRNE* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,100 |
| **Congenital Myasthenic Syndrome (*RAPSN*-Related)** | *RAPSN* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,900 |
| **Congenital Neutropenia (*HAX1*-Related)** | *HAX1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 82,000 |
| **Congenital Neutropenia (*VPS45*-Related)** | *VPS45* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 163,000 |
| **Corneal Dystrophy and Perceptive Deafness** | *SLC4A11* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,600 |
| **Corticosterone Methyloxidase Deficiency** | *CYP11B2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,500 |
| **Cystic Fibrosis** | *CFTR* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 440 |
| **Cystinosis** | *CTNS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 7,700 |
| **D-Bifunctional Protein Deficiency** | *HSD17B4* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,000 |
| **Deafness, Autosomal Recessive 77** | *LOXHD1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,700 |
| **Duchenne Muscular Dystrophy / Becker Muscular Dystrophy** | *DMD* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 10,000 |
| **Dyskeratosis Congenita (*RTEL1*-Related)** | *RTEL1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 9,800 |
| **Dystrophic Epidermolysis Bullosa** | *COL7A1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 900 |
| **Ehlers-Danlos Syndrome, Type VIIC** | *ADAMTS2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 243,000 |
| **Ellis-van Creveld Syndrome (*EVC*-Related)** | *EVC* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,200 |
| **Emery-Dreifuss Myopathy 1** | *EMD* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 833,000 |
| **Enhanced S-Cone Syndrome** | *NR2E3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,600 |
| **Ethylmalonic Encephalopathy** | *ETHE1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,400 |
| **Fabry Disease** | *GLA* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 7,700 |
| **Factor IX Deficiency** | *F9* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 5,100 |
| **Factor XI Deficiency** | *F11* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,500 |
| **Familial Autosomal Recessive Hypercholesterolemia** | *LDLRAP1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 136,000 |
| **Familial Dysautonomia** | *IKBKAP* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 51,000 |
| **Familial Hypercholesterolemia** | *LDLR* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 280 |
| **Familial Hyperinsulinism (*ABCC8*-Related)** | *ABCC8* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 450 |
| **Familial Hyperinsulinism (*KCNJ11*-Related)** | *KCNJ11* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,300 |
| **Familial Mediterranean Fever** | *MEFV* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,200 |
| **Fanconi Anemia, Group A** | *FANCA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,100 |
| **Fanconi Anemia, Group C** | *FANCC* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 12,000 |
| **Fanconi Anemia, Group G** | *FANCG* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 28,000 |
| **Fragile X Syndrome** | *FMR1* | XL | Reduced Risk | *FMR1* CGG repeat sizes: Not Performed<br>*FMR1* Sequencing: Negative<br>Fragile X CGG triplet repeat expansion testing was not performed at this time, as the patient has either been previously tested or is a male.<br>**Personalized Residual Risk:** 1 in 19,000 |
| **Fumarase Deficiency** | *FH* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,500 |
| **GRACILE Syndrome and Other *BCS1L*-Related Disorders** | *BCS1L* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,900 |

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|---|---|---|---|---|
| **Galactokinase Deficiency** | *GALK1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,700 |
| **Galactosemia** | *GALT* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,200 |
| **Gaucher Disease** | *GBA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,300 |
| **Gitelman Syndrome** | *SLC12A3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 290 |
| **Glutaric Acidemia, Type I** | *GCDH* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,700 |
| **Glutaric Acidemia, Type IIa** | *ETFA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,700 |
| **Glutaric Acidemia, Type IIc** | *ETFDH* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,700 |
| **Glycine Encephalopathy (*AMT*-Related)** | *AMT* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,700 |
| **Glycine Encephalopathy (*GLDC*-Related)** | *GLDC* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 760 |
| **Glycogen Storage Disease, Type II** | *GAA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 520 |
| **Glycogen Storage Disease, Type III** | *AGL* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,600 |
| **Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease** | *GBE1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,400 |
| **Glycogen Storage Disease, Type Ia** | *G6PC* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,300 |
| **Glycogen Storage Disease, Type Ib** | *SLC37A4* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 7,300 |
| **Glycogen Storage Disease, Type V** | *PYGM* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,200 |
| **Glycogen Storage Disease, Type VII** | *PFKM* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,300 |
| **HMG-CoA Lyase Deficiency** | *HMGCL* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,700 |
| **Hemochromatosis, Type 2A** | *HFE2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 12,000 |
| **Hemochromatosis, Type 3** | *TFR2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 11,000 |
| **Hereditary Fructose Intolerance** | *ALDOB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,900 |
| **Hereditary Spastic Paraparesis 49** | *TECPR2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 116,000 |
| **Hermansky-Pudlak Syndrome, Type 1** | *HPS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,500 |
| **Hermansky-Pudlak Syndrome, Type 3** | *HPS3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 49,000 |
| **Holocarboxylase Synthetase Deficiency** | *HLCS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,500 |
| **Homocystinuria (*CBS*-Related)** | *CBS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,400 |
| **Homocystinuria due to *MTHFR* Deficiency** | *MTHFR* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,300 |
| **Homocystinuria, cblE Type** | *MTRR* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 9,600 |
| **Hydrolethalus Syndrome** | *HYLS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 52,000 |
| **Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome** | *SLC25A15* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,700 |
| **Hypohidrotic Ectodermal Dysplasia 1** | *EDA* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 22,000 |
| **Hypophosphatasia** | *ALPL* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 790 |
| **Inclusion Body Myopathy 2** | *GNE* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,000 |
| **Infantile Cerebral and Cerebellar Atrophy** | *MED17* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 129,000 |
| **Isovaleric Acidemia** | *IVD* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,000 |
| **Joubert Syndrome 2** | *TMEM216* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 152,000 |
| **Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome** | *RPGRIP1L* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 32,000 |
| **Junctional Epidermolysis Bullosa (*LAMA3*-Related)** | *LAMA3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 21,000 |
| **Junctional Epidermolysis Bullosa (*LAMB3*-Related)** | *LAMB3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,900 |
| **Junctional Epidermolysis Bullosa (*LAMC2*-Related)** | *LAMC2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 77,000 |
| **Krabbe Disease** | *GALC* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 860 |
| **Lamellar Ichthyosis, Type 1** | *TGM1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,500 |
| **Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies** | *CEP290* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,100 |
| **Leber Congenital Amaurosis 13** | *RDH12* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,500 |
| **Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20** | *RPE65* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,500 |
| **Leber Congenital Amaurosis 5** | *LCA5* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 14,000 |

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| **Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy** | *CRB1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 990 |
| **Leigh Syndrome, French-Canadian Type** | *LRPPRC* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 32,000 |
| **Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease** | *GLE1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 10,000 |
| **Leukoencephalopathy with Vanishing White Matter** | *EIF2B5* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,300 |
| **Limb-Girdle Muscular Dystrophy, Type 2A** | *CAPN3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 960 |
| **Limb-Girdle Muscular Dystrophy, Type 2B** | *DYSF* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,100 |
| **Limb-Girdle Muscular Dystrophy, Type 2C** | *SGCG* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,900 |
| **Limb-Girdle Muscular Dystrophy, Type 2D** | *SGCA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,500 |
| **Limb-Girdle Muscular Dystrophy, Type 2E** | *SGCB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 31,000 |
| **Limb-Girdle Muscular Dystrophy, Type 2I** | *FKRP* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,400 |
| **Lipoamide Dehydrogenase Deficiency** | *DLD* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 14,000 |
| **Lipoid Adrenal Hyperplasia** | *STAR* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,600 |
| **Lipoprotein Lipase Deficiency** | *LPL* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,400 |
| **Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency** | *HADHA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,900 |
| **Lysinuric Protein Intolerance** | *SLC7A7* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,000 |
| **Maple Syrup Urine Disease, Type 1a** | *BCKDHA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,100 |
| **Maple Syrup Urine Disease, Type 1b** | *BCKDHB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,100 |
| **Meckel Syndrome 1 / Bardet-Biedl Syndrome 13** | *MKS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,700 |
| **Medium Chain Acyl-CoA Dehydrogenase Deficiency** | *ACADM* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Megalencephalic Leukoencephalopathy with Subcortical Cysts** | *MLC1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,300 |
| **Menkes Disease** | *ATP7A* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 172,000 |
| **Metachromatic Leukodystrophy** | *ARSA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,000 |
| **Methylmalonic Acidemia (*MMAA*-Related)** | *MMAA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 15,000 |
| **Methylmalonic Acidemia (*MMAB*-Related)** | *MMAB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 12,000 |
| **Methylmalonic Acidemia (*MUT*-Related)** | *MUT* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,300 |
| **Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type** | *MMACHC* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,800 |
| **Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type** | *MMADHC* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 219,000 |
| **Microphthalmia / Anophthalmia** | *VSX2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 40,000 |
| **Mitochondrial Complex I Deficiency (*ACAD9*-Related)** | *ACAD9* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Mitochondrial Complex I Deficiency (*NDUFAF5*-Related)** | *NDUFAF5* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 98,000 |
| **Mitochondrial Complex I Deficiency (*NDUFS6*-Related)** | *NDUFS6* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 353,000 |
| **Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy** | *MPV17* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,400 |
| **Mitochondrial Myopathy and Sideroblastic Anemia 1** | *PUS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 449,000 |
| **Mucolipidosis II / IIIA** | *GNPTAB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,100 |
| **Mucolipidosis III Gamma** | *GNPTG* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 68,000 |
| **Mucolipidosis IV** | *MCOLN1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 9,400 |
| **Mucopolysaccharidosis Type I** | *IDUA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,300 |
| **Mucopolysaccharidosis Type II** | *IDS* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 76,000 |
| **Mucopolysaccharidosis Type IIIA** | *SGSH* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,700 |
| **Mucopolysaccharidosis Type IIIB** | *NAGLU* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 950 |
| **Mucopolysaccharidosis Type IIIC** | *HGSNAT* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,200 |
| **Mucopolysaccharidosis Type IIID** | *GNS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 137,000 |

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| **Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis** | *GLB1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,700 |
| **Mucopolysaccharidosis type IX** | *HYAL1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 149,000 |
| **Mucopolysaccharidosis type VI** | *ARSB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,300 |
| **Multiple Sulfatase Deficiency** | *SUMF1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 69,000 |
| **Muscle-Eye-Brain Disease and Other *POMGNT1*-Related Congenital Muscular Dystrophy-Dystroglycanopathies** | *POMGNT1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,200 |
| **Myoneurogastrointestinal Encephalopathy** | *TYMP* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,100 |
| **Myotubular Myopathy 1** | *MTM1* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 192,000 |
| **N-Acetylglutamate Synthase Deficiency** | *NAGS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,200 |
| **Nemaline Myopathy 2** | *NEB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,400 |
| **Nephrogenic Diabetes Insipidus, Type II** | *AQP2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,400 |
| **Nephrotic Syndrome (*NPHS1*-Related) / Congenital Finnish Nephrosis** | *NPHS1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 920 |
| **Nephrotic Syndrome (*NPHS2*-Related) / Steroid-Resistant Nephrotic Syndrome** | *NPHS2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 780 |
| **Neuronal Ceroid-Lipofuscinosis (*CLN3*-Related)** | *CLN3* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 9,200 |
| **Neuronal Ceroid-Lipofuscinosis (*CLN5*-Related)** | *CLN5* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,300 |
| **Neuronal Ceroid-Lipofuscinosis (*CLN6*-Related)** | *CLN6* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 8,600 |
| **Neuronal Ceroid-Lipofuscinosis (*CLN8*-Related)** | *CLN8* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,100 |
| **Neuronal Ceroid-Lipofuscinosis (*MFSD8*-Related)** | *MFSD8* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,200 |
| **Neuronal Ceroid-Lipofuscinosis (*PPT1*-Related)** | *PPT1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 7,500 |
| **Neuronal Ceroid-Lipofuscinosis (*TPP1*-Related)** | *TPP1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,300 |
| **Niemann-Pick Disease (*SMPD1*-Related)** | *SMPD1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Niemann-Pick Disease, Type C (*NPC1*-Related)** | *NPC1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 690 |
| **Niemann-Pick Disease, Type C (*NPC2*-Related)** | *NPC2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,600 |
| **Nijmegen Breakage Syndrome** | *NBN* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 14,000 |
| **Non-Syndromic Hearing Loss (*GJB2*-Related)** | *GJB2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 600 |
| **Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome** | *WNT10A* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,900 |
| **Omenn Syndrome (*RAG2*-Related)** | *RAG2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 17,000 |
| **Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type** | *DCLRE1C* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,500 |
| **Ornithine Aminotransferase Deficiency** | *OAT* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,400 |
| **Ornithine Transcarbamylase Deficiency** | *OTC* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 103,000 |
| **Osteopetrosis 1** | *TCIRG1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,700 |
| **Pendred Syndrome** | *SLC26A4* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 390 |
| **Phenylalanine Hydroxylase Deficiency** | *PAH* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 340 |
| **Polycystic Kidney Disease, Autosomal Recessive** | *PKHD1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 450 |
| **Polyglandular Autoimmune Syndrome, Type 1** | *AIRE* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,300 |
| **Pontocerebellar Hypoplasia, Type 1A** | *VRK1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 25,000 |
| **Pontocerebellar Hypoplasia, Type 6** | *RARS2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 8,600 |
| **Primary Carnitine Deficiency** | *SLC22A5* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,500 |
| **Primary Ciliary Dyskinesia (*DNAH5*-Related)** | *DNAH5* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,500 |
| **Primary Ciliary Dyskinesia (*DNAI1*-Related)** | *DNAI1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,000 |
| **Primary Ciliary Dyskinesia (*DNAI2*-Related)** | *DNAI2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 76,000 |
| **Primary Hyperoxaluria, Type 1** | *AGXT* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,900 |
| **Primary Hyperoxaluria, Type 2** | *GRHPR* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 11,000 |
| **Progressive Cerebello-Cerebral Atrophy** | *SEPSECS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,400 |
| **Progressive Familial Intrahepatic Cholestasis, Type 2** | *ABCB11* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 950 |

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| **Propionic Acidemia (*PCCA*-Related)** | *PCCA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,600 |
| **Propionic Acidemia (*PCCB*-Related)** | *PCCB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 12,000 |
| **Pycnodysostosis** | *CTSK* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,100 |
| **Pyruvate Dehydrogenase E1-Alpha Deficiency** | *PDHA1* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 139,000 |
| **Pyruvate Dehydrogenase E1-Beta Deficiency** | *PDHB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 15,000 |
| **Renal Tubular Acidosis and Deafness** | *ATP6V1B1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,600 |
| **Retinitis Pigmentosa 25** | *EYS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Retinitis Pigmentosa 26** | *CERKL* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 13,000 |
| **Retinitis Pigmentosa 28** | *FAM161A* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 34,000 |
| **Retinitis Pigmentosa 59** | *DHDDS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 601,000 |
| **Rhizomelic Chondrodysplasia Punctata, Type 1** | *PEX7* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 10,000 |
| **Rhizomelic Chondrodysplasia Punctata, Type 3** | *AGPS* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 620,000 |
| **Roberts Syndrome** | *ESCO2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 139,000 |
| **Salla Disease** | *SLC17A5* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 8,400 |
| **Sandhoff Disease** | *HEXB* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Schimke Immunoosseous Dysplasia** | *SMARCAL1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,800 |
| **Segawa Syndrome** | *TH* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,100 |
| **Sjogren-Larsson Syndrome** | *ALDH3A2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 5,500 |
| **Smith-Lemli-Opitz Syndrome** | *DHCR7* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 750 |
| **Spinal Muscular Atrophy** | *SMN1* | AR | Reduced Risk | *SMN1* copy number: 2<br>*SMN2* copy number: 2<br>c.*3+80T>G: Negative<br>*SMN1* Sequencing: Negative<br>**Personalized Residual Risk:** 1 in 1,107 |
| **Spondylothoracic Dysostosis** | *MESP2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 382,000 |
| **Steel Syndrome** | *COL27A1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 93,000 |
| **Stuve-Wiedemann Syndrome** | *LIFR* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,000 |
| **Sulfate Transporter-Related Osteochondrodysplasia** | *SLC26A2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,800 |
| **Tay-Sachs Disease** | *HEXA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,400 |
| **Tyrosinemia, Type I** | *FAH* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,900 |
| **Usher Syndrome, Type IB** | *MYO7A* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,000 |
| **Usher Syndrome, Type IC** | *USH1C* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,600 |
| **Usher Syndrome, Type ID** | *CDH23* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,400 |
| **Usher Syndrome, Type IF** | *PCDH15* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,800 |
| **Usher Syndrome, Type IIA** | *USH2A* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 290 |
| **Usher Syndrome, Type III** | *CLRN1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,300 |
| **Very Long Chain Acyl-CoA Dehydrogenase Deficiency** | *ACADVL* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 920 |
| **Walker-Warburg Syndrome and Other *FKTN*-Related Dystrophies** | *FKTN* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 4,200 |
| **Wilson Disease** | *ATP7B* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 350 |
| **Wolman Disease / Cholesteryl Ester Storage Disease** | *LIPA* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 3,200 |
| **X-Linked Juvenile Retinoschisis** | *RS1* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 40,000 |
| **X-Linked Severe Combined Immunodeficiency** | *IL2RG* | XL | Reduced Risk | **Personalized Residual Risk:** 1 in 250,000 |
| **Zellweger Syndrome Spectrum (*PEX10*-Related)** | *PEX10* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 6,300 |
| **Zellweger Syndrome Spectrum (*PEX1*-Related)** | *PEX1* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 2,000 |
| **Zellweger Syndrome Spectrum (*PEX2*-Related)** | *PEX2* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 77,000 |
| **Zellweger Syndrome Spectrum (*PEX6*-Related)** | *PEX6* | AR | Reduced Risk | **Personalized Residual Risk:** 1 in 1,600 |

*AR=Autosomal recessive; XL=X-linked*

# Test methods and comments

Genomic DNA isolated from this patient was analyzed by one or more of the following methodologies, as applicable:

**Fragile X CGG Repeat Analysis (Analytical Detection Rate >99%)**

PCR amplification using Asuragen, Inc. AmplideX® *FMR1* PCR reagents followed by capillary electrophoresis for allele sizing was performed. Samples positive for *FMR1* CGG repeats in the premutation and full mutation size range were further analyzed by Southern blot analysis to assess the size and methylation status of the *FMR1* CGG repeat.

**Genotyping (Analytical Detection Rate >99%)**

Multiplex PCR amplification and allele specific primer extension analyses using the MassARRAY® System were used to identify certain recurrent variants that are complex in nature or are present in low copy repeats. Rare sequence variants may interfere with assay performance.

**Multiplex Ligation-Dependent Probe Amplification (MLPA) (Analytical Detection Rate >99%)**

MLPA® probe sets and reagents from MRC-Holland were used for copy number analysis of specific targets versus known control samples. False positive or negative results may occur due to rare sequence variants in target regions detected by MLPA probes. Analytical sensitivity and specificity of the MLPA method are both 99%.

For alpha thalassemia, the copy numbers of the *HBA1* and *HBA2* genes were analyzed. Alpha-globin gene deletions, triplications, and the Constant Spring (CS) mutation are assessed. This test is expected to detect approximately 90% of all alpha-thalassemia mutations, varying by ethnicity. carriers of alpha-thalassemia with three or more *HBA* copies on one chromosome, and one or no copies on the other chromosome, may not be detected. With the exception of triplications, other benign alpha-globin gene polymorphisms will not be reported. Analyses of *HBA1* and *HBA2* are performed in association with long-range PCR of the coding regions followed by short-read sequencing.

For Duchenne muscular dystrophy, the copy numbers of all *DMD* exons were analyzed. Potentially pathogenic single exon deletions and duplications are confirmed by a second method. Analysis of *DMD* is performed in association with sequencing of the coding regions.

For congenital adrenal hyperplasia, the copy number of the *CYP21A2* gene was analyzed. This analysis can detect large deletions typically due to unequal meiotic crossing-over between *CYP21A2* and the pseudogene *CYP21A1P*. Classic 30-kb deletions make up approximately 20% of *CYP21A2* pathogenic alleles. This test may also identify certain point mutations in *CYP21A2* caused by gene conversion events between *CYP21A2* and *CYP21A1P*. Some carriers may not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *CYP21A2* gene on one chromosome and loss of *CYP21A2* (deletion) on the other chromosome. Analysis of *CYP21A2* is performed in association with long-range PCR of the coding regions followed by short-read sequencing.

For spinal muscular atrophy (SMA), the copy numbers of the *SMN1* and *SMN2* genes were analyzed. The individual dosage of exons 7 and 8 as well as the combined dosage of exons 1, 4, 6 and 8 of *SMN1* and *SMN2* were assessed. Copy number gains and losses can be detected with this assay. Depending on ethnicity, 6 - 29 % of carriers will not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *SMN1* gene on one chromosome and loss of *SMN1* (deletion) on the other chromosome (silent 20 carrier) or individuals that carry an intragenic mutation in *SMN1*. Please also note that 2% of individuals diagnosed with SMA have a causative *SMN1* variant that occurred *de novo*, and therefore cannot be picked up by carrier screening in the parents. Analysis of *SMN1* is performed in association with short-read sequencing of exons 2a-7, followed by confirmation using long-range PCR (described below).

The presence of the c.*380T>G (chr5:70,247,901T>G) variant allele in an individual with Ashkenazi Jewish or Asian ancestry is typically indicative of a duplication of *SMN1*. When present in an Ashkenazi Jewish or Asian individual with two copies of *SMN1*, c.*380T>G is likely indicative of a silent (20) carrier. In individuals with two copies of *SMN1* with African American, Hispanic or Caucasian ancestry, the presence or absence of c.*380T>G significantly increases or decreases, respectively, the likelihood of being a silent 20 silent carrier.

MLPA for Gaucher disease (*GBA*), cystic fibrosis (*CFTR*), and non-syndromic hearing loss (*GJB2/GJB6*) will only be performed if indicated for confirmation of detected CNVs. If *GBA* analysis was performed, the copy numbers of exons 1, 3, 4, and 6 - 10 of the *GBA* gene (of 11 exons total)

were analyzed. If *CFTR* analysis was performed, the copy numbers of all 27 *CFTR* exons were analyzed. If *GJB2/GJB6* analysis was performed, the copy number of the two *GJB2* exons were analyzed, as well as the presence or absence of the two upstream deletions of the *GJB2* regulatory region, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854).

**Next Generation Sequencing (NGS) (Analytical Detection Rate >95%)**

NGS was performed on a panel of genes for the purpose of identifying pathogenic or likely pathogenic variants.

Agilent SureSelect$^{TM}$XT Low Input technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Libraries were pooled and sequenced on the Illumina NovaSeq 9000 platform, using paired-end 100 bp reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house.

The coding exons and splice junctions of the known protein-coding RefSeq genes were assessed for the average depth of coverage (minimum of 20X) and data quality threshold values. Most exons not meeting a minimum of >20X read depth across the exon are further analyzed by Sanger sequencing. Please note that several genomic regions present difficulties in mapping or obtaining read depth >20X. These regions, which are described below, will not be reflexed to Sanger sequencing if the mapping quality or coverage is poor. Any variants identified during testing in these regions are confirmed by a second method and reported if determined to be pathogenic or likely pathogenic. However, as there is a possibility of false negative results within these regions, detection rates and residual risks for these genes have been calculated with the presumption that variants in these exons will not be detected, unless included in the MassARRAY® genotyping platform.

This test will detect variants within the exons and the intron-exon boundaries of the target regions. Variants outside these regions may not be detected, including, but not limited to, UTRs, promoters, and deep intronic areas, or regions that fall into the Exceptions mentioned above. This technology may not detect all small insertion/deletions and is not diagnostic for repeat expansions and structural genomic variation. In addition, a mutation(s) in a gene not included on the panel could be present in this patient.

Variant interpretation and classification was performed based on the American College of Medical Genetics Standards and Guidelines for the Interpretation of Sequence Variants (Richards et al, 2015). All potentially pathogenic variants may be confirmed by either a specific genotyping assay or Sanger sequencing, if indicated. Any benign variants, likely benign variants or variants of uncertain significance identified during this analysis will not be reported.

**Next Generation Sequencing for SMN1**

Exonic regions and intron/exon splice junctions of *SMN1* and *SMN2* were captured, sequenced, and analyzed as described above. Any variants located within exons 2a-7 and classified as pathogenic or likely pathogenic were confirmed to be in either *SMN1* or *SMN2* using gene-specific long-range PCR analysis followed by Sanger sequencing. Variants located in exon 1 cannot be accurately assigned to either *SMN1* or *SMN2* using our current methodology, and so these variants are considered to be of uncertain significance and are not reported.

**Copy Number Variant Analysis (Analytical Detection Rate >95%)**

Large duplications and deletions were called from the relative read depths on an exon-by-exon basis using a custom exome hidden Markov model (XHMM) algorithm. Deletions or duplications determined to be pathogenic or likely pathogenic were confirmed by either a custom arrayCGH platform, quantitative PCR, or MLPA (depending on CNV size and gene content). While this algorithm is designed to pick up deletions and duplications of 2 or more exons in length, potentially pathogenic single-exon CNVs will be confirmed and reported, if detected.

**Exon Array (Confirmation method) (Accuracy >99%)**

The customized oligonucleotide microarray (Oxford Gene Technology) is a highly-targeted exon-focused array capable of detecting medically relevant microdeletions and microduplications at a much higher resolution than traditional aCGH methods. Each array matrix has approximately 180,000 60-mer oligonucleotide probes that cover the entire genome. This platform is designed based on human genome NCBI Build 37 (hg19) and the CGH probes are enriched to target the exonic regions of the genes in this panel.

**Quantitative PCR (Confirmation method) (Accuracy >99%)**

The relative quantification PCR is utilized on a Roche Universal Library Probe (UPL) system, which relates the PCR signal of the target region in one group to another. To test for genomic imbalances, both sample DNA and reference DNA is amplified with primer/probe sets that specific to the target region and a control region with known genomic copy number. Relative genomic copy numbers are calculated based on the standard ΔΔCt formula.

**Long-Range PCR (Analytical Detection Rate >99%)**

Long-range PCR was performed to generate locus-specific amplicons for *CYP21A2*, *HBA1* and *HBA2* and *GBA*. The PCR products were then prepared for short-read NGS sequencing and sequenced. Sequenced reads were mapped back to the original genomic locus and run through the bioinformatics pipeline. If indicated, copy number from MLPA was correlated with the sequencing output to analyze the results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where two copies of a gene are located on the same chromosome in tandem, only the second copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in the tandem allele and this patient is therefore less likely to be a carrier. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to determine the phase (cisrans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing is required to determine the carrier status.

**Residual Risk Calculations**

Carrier frequencies and detection rates for each ethnicity were calculated through the combination of internal curations of >30,000 variants and genomic frequency data from >138,000 individuals across seven ethnic groups in the gnomAD database. Additional variants in HGMD and novel deleterious variants were also incorporated into the calculation. Residual risk values are calculated using a Bayesian analysis combining the *a priori* risk of being a pathogenic mutation carrier (carrier frequency) and the detection rate. They are provided only as a guide for assessing approximate risk given a negative result, and values will vary based on the exact ethnic background of an individual. This report does not represent medical advice but should be interpreted by a genetic counselor, medical geneticist or physician skilled in genetic result interpretation and the relevant medical literature.

**Personalized Residual Risk Calculations**

Agilent SureSelect$^{TM}$XT Low-Input technology was utilized in order to create whole-genome libraries for each patient sample. Libraries were then pooled and sequenced on the Illumina NovaSeq platform. Each sequencing lane was multiplexed to achieve 0.4-2x genome coverage, using paired-end 100 bp reads. The sequencing data underwent ancestral analysis using a customized, licensed bioinformatics algorithm that was validated in house. Identified sub-ethnic groupings were binned into one of 7 continental-level groups (African, East Asian, South Asian, Non-Finnish European, Finnish, Native American, and Ashkenazi Jewish) or, for those ethnicities that matched poorly to the continental-level groups, an 8$^{th}$ "unassigned" group, which were then used to select residual risk values for each gene. For individuals belonging to multiple high-level ethnic groupings, a weighting strategy was used to select the most appropriate residual risk. For genes that had insufficient data to calculate ethnic-specific residual risk values, or for sub-ethnic groupings that fell into the "unassigned" group, a "worldwide" residual risk was used. This "worldwide" residual risk was calculated using data from all available continental-level groups.

**Sanger Sequencing (Confirmation method) (Accuracy >99%)**

Sanger sequencing, as indicated, was performed using BigDye Terminator chemistry with the ABI 3730 DNA analyzer with target specific amplicons. It also may be used to supplement specific guaranteed target regions that fail NGS sequencing due to poor quality or low depth of coverage (<20 reads) or as a confirmatory method for NGS positive results. False negative results may occur if rare variants interfere with amplification or annealing.

Please note these tests were developed and their performance characteristics were determined by Mount Sinai Genomics, Inc. They have not been cleared or approved by the FDA. These analyses generally provide highly accurate information regarding the patient's carrier or affected status. Despite this high level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, or other rare genetic variants that interfere with analysis. Families should understand that rare diagnostic errors may occur for these reasons.

Exceptions:

| Gene | Transcript | Exceptions |
|---|---|---|
| *ABCD1* | NM_000033.3 | Exons 8 and 9 |
| *ADA* | NM_000022.2 | Exon 1 |
| *ADAMTS2* | NM_014244.4 | Exon 1 |
| *AGPS* | NM_003659.3 | chr2:178,257,512 - 178,257,649 (partial exon 1) |
| *ALMS1* | NM_015120.4 | chr2:73,612,990 - 73,613,041 (partial exon 1) |
| *CEP290* | NM_025114.3 | Exon 5, exon 7, chr12:88,519,017 - 88,519,039 (partial exon 13), chr12:88,514,049 - 88,514,058 (partial exon 15), chr12:88,502,837 - 88,502,841 (partial exon 23), chr12:88,481,551 - 88,481,589 (partial exon 32), chr12:88,471,605 - 88,471,700 (partial exon 40) |
| *CFTR* | NM_000492.3 | Exon 10 |
| *COL4A4* | NM_000092.4 | chr2:227,942,604 - 227,942,619 (partial exon 25) |
| *CYP11B2* | NM_000498.3 | Exons 3 - 7 |
| *DNAI2* | NM_023036.4 | chr17:72,308,136 - 72,308,147 (partial exon 12) |
| *EVC* | NM_153717.2 | Exon 1 |
| *FH* | NM_000143.3 | Exon 1 |
| *GAMT* | NM_000156.5 | Exon 1 |
| *GLDC* | NM_000170.2 | Exon 1 |
| *GNPTAB* | NM_024312.4 | chr17:4,837,000 - 4,837,400 (partial exon 2) |
| *GNPTG* | NM_032520.4 | Exon 1 |
| *HGSNAT* | NM_152419.2 | Exon 1 |
| *IDS* | NM_000202.6 | Exon 3 |
| *LIFR* | NM_002310.5 | Exon 19 |
| *NEB* | NM_001271208.1 | Exons 82 - 105 |

| | | |
|---|---|---|
| *NPC1* | NM_000271.4 | chr18:21,123,519 - 21,123,538 (partial exon 14) |
| *PUS1* | NM_025215.5 | chr12:132,414,446 - 132,414,532 (partial exon 2) |
| *RPGRIP1L* | NM_015272.2 | Exon 23 |
| *SGSH* | NM_000199.3 | chr17:78,194,022 - 78,194,072 (partial exon 1) |
| *SLC6A8* | NM_005629.3 | Exons 3 and 4 |

**SELECTED REFERENCES**

**Carrier Screening**

Grody W et al. ACMG position statement on prenatal/preconception expanded carrier screening. *Genet Med.* 2013 15:482-3.

**Fragile X syndrome:**

Chen L et al. An information-rich CGG repeat primed PCR that detects the full range of Fragile X expanded alleles and minimizes the need for Southern blot analysis. *J Mol Diag* 2010 12:589-600.

**Spinal Muscular Atrophy:**

Luo M et al. An Ashkenazi Jewish SMN1 haplotype specific to duplication alleles improves pan-ethnic carrier screening for spinal muscular atrophy. *Genet Med.* 2014 16:149-56.

**Ashkenazi Jewish Disorders:**

Scott SA et al. Experience with carrier screening and prenatal diagnosis for sixteen Ashkenazi Jewish Genetic Diseases. *Hum. Mutat.* 2010 31:1-11.

**Duchenne Muscular Dystrophy:**

Flanigan KM et al. Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. *Hum Mutat.* 2009 30:1657-66.

**Variant Classification:**

Richards S et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-24

Additional disease-specific references available upon request.

| Patient Information | Specimen Information | Client Information |
|---|---|---|
| **6747, DONOR**<br><br>**DOB:** [redacted] **AGE:** [redacted]<br>Gender: M<br>Phone: NG<br>Patient ID: [redacted] | Specimen: [redacted]<br>Requisition: [redacted]<br>Lab Ref #: [redacted]<br><br>Collected: 11/05/2021<br>Received: 11/06/2021 / 23:06 EST<br>Reported: 11/16/2021 / 23:16 EST | Client #: 48041578 NYNJMAIL<br>GENOMICS, SEMA4<br>SEMA4<br>62 SOUTHFIELD AVE<br>STAMFORD, CT 06902-7229 |

Ward: FFAXCB

# Cytogenetic Report

## CHROMOSOME ANALYSIS, BLOOD - 14596 Lab:EZ

**CHROMOSOME ANALYSIS, BLOOD**

Order ID: 21-344705
Specimen Type: Blood
Clinical Indication: RULE OUT CHROMOSOME ABNORMALITY

**RESULT:**
NORMAL MALE KARYOTYPE

**INTERPRETATION:**
Chromosome analysis revealed normal G-band patterns within the limits of standard cytogenetic analysis.

Please expect the results of any other concurrent study in a separate report.

**NOMENCLATURE:**
46,XY

**ASSAY INFORMATION:**

Method: G-Band (Digital Analysis: MetaSyst
Cells Counted: 20
Band Level: 450
Cells Analyzed: 5
Cells Karyotyped: 4

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

Lakshmi J. Nemana, Ph.D., FACMG

Electronic Signature: 11/16/2021 10:18 PM



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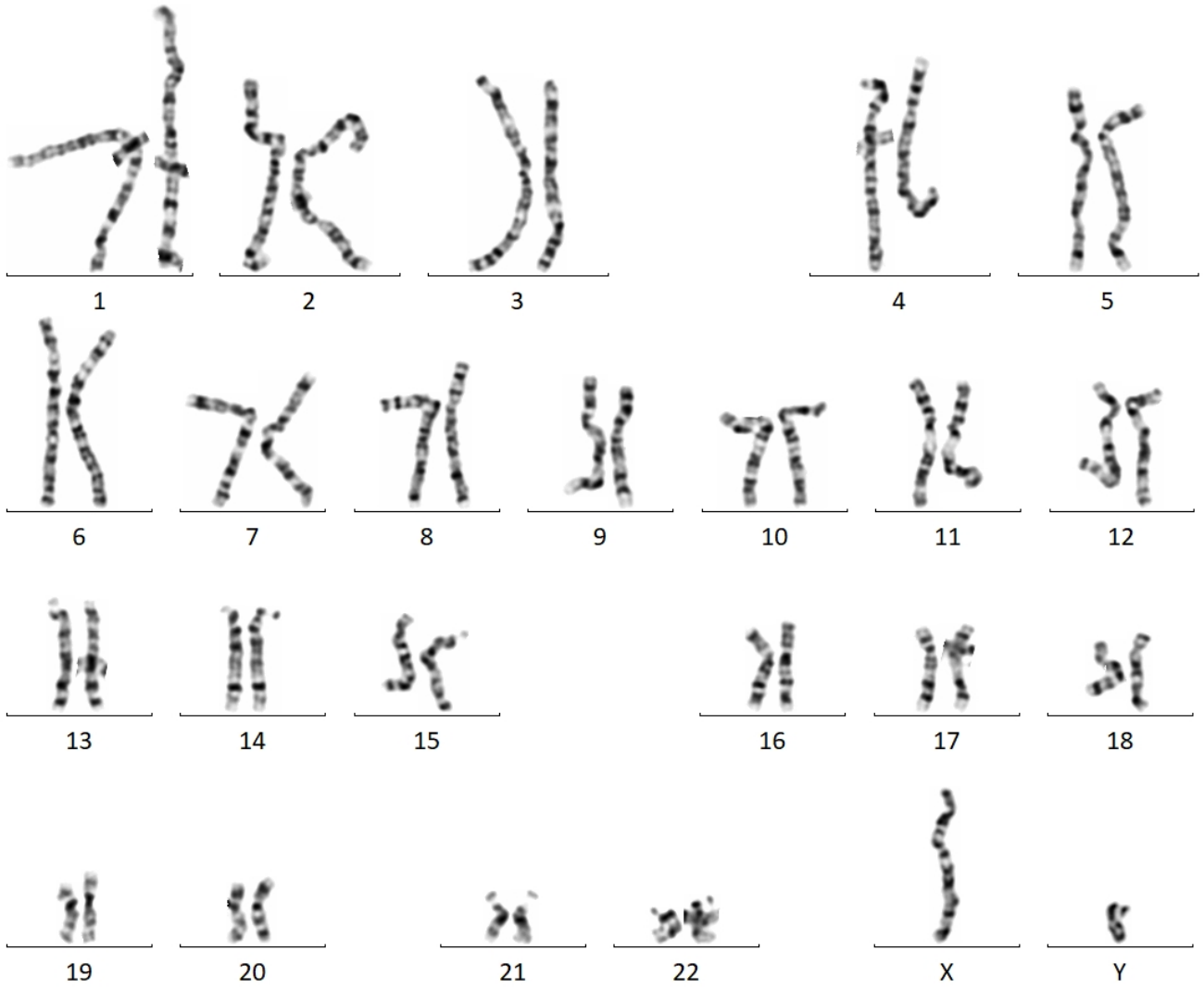
| Patient Information | Specimen Information | Client Information |
|---|---|---|
| **6747, DONOR**<br><br>**DOB:** [redacted] **AGE:** [redacted]<br>Gender: M<br>Patient ID: [redacted] | Specimen: [redacted]<br>Collected: 11/05/2021<br>Received: 11/06/2021 / 23:06 EST<br>Reported: 11/16/2021 / 23:16 EST | Client #: 48041578<br>GENOMICS, SEMA4 |




**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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Quest Diagnostics

**Report Status: Final**

**6747, DONOR**

| Patient Information | Specimen Information | Client Information |
|---|---|---|
| **6747, DONOR**<br><br>**DOB:** [redacted] **AGE:** [redacted]<br>Gender: M<br>Phone: NG<br>Patient ID: [redacted] | Specimen: [redacted]<br>Requisition: [redacted]<br>Lab Ref #: [redacted]<br><br>Collected: 11/05/2021<br>Received: 11/06/2021 / 22:24 EST<br>Reported: 11/09/2021 / 12:57 EST | Client #: 48041578 NYNJMAIL<br>GENOMICS, SEMA4<br>SEMA4<br>62 SOUTHFIELD AVE<br>STAMFORD, CT 06902-7229 |

Ward: FFAXCB

| Test Name | In Range | Out Of Range | Reference Range | Lab |
|---|---|---|---|---|
| HEMOGLOBINOPATHY EVALUATION | | | | |
| RED BLOOD CELL COUNT | 5.44 | | 4.20-5.80 Million/uL | Z99 |
| HEMOGLOBIN | 15.9 | | 13.2-17.1 g/dL | |
| HEMATOCRIT | 46.6 | | 38.5-50.0 % | |
| MCV | 85.7 | | 80.0-100.0 fL | |
| MCH | 29.2 | | 27.0-33.0 pg | |
| RDW | 12.9 | | 11.0-15.0 % | |
| HEMOGLOBIN A | 97.4 | | >96.0 % | Z99 |
| HEMOGLOBIN F | <1.0 | | <2.0 % | |
| HEMOGLOBIN A2 (QUANT) | 2.6 | | 2.2-3.2 % | |
| INTERPRETATION | * | | | |
| Normal phenotype. | | | | |

**PERFORMING SITE:**

Z99 QUEST DIAGNOSTICS CLIFTON, 1 INSIGHTS DRIVE, CLIFTON, NJ 07012-2355 Laboratory Director: SHELLA K MONGIA,MD, CLIA: 31D0696246



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[redacted]

Patient Information:
**6747, Donor**
**DOB:** [redacted]
Sex: M
MR#: 6747
Patient#: [redacted]

Accession:
[redacted]
Test#: [redacted]
Order#: [redacted]
Ext Test#: [redacted]
Ext Order#: [redacted]
Specimen Type: DNA
Collected: Apr 06,2023
Received Date: Apr 18,2023
Authorized Date: Apr 20,2023

Physician:
**Seitz, Suzanne**
ATTN: Seitz, Suzanne
Fairfax Cryobank
3015 Williams Drive
Fairfax, VA 22031
Phone:
Fax:

Laboratory:
**Fulgent Genetics**
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Dr. Hanlin (Harry) Gao
Report Date: **Apr 26,2023**

Final Report

## TEST PERFORMED

**POLG Single Gene**
(1 Gene Panel: *POLG*; gene sequencing with deletion and duplication analysis)

## RESULTS:

**No clinically significant sequence or copy-number variants were identified in the submitted specimen.**

**A negative result does not rule out the possibility of a genetic predisposition nor does it rule out any pathogenic mutations of the sort not queried by this test or in areas not reliably assessed by this test.**

## INTERPRETATION:

**Notes and Recommendations:**

- As requested, this report only includes variants classified as Pathogenic, Likely Pathogenic, or Risk Allele at the time of analysis. If detected, this report does not include variants classified as of uncertain significance.
- Gene specific notes and limitations may be present. See below.
- These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.
- 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)
- Guide to Interpreting Genomic Reports: A Genomics Toolkit (CSER Consortium; February 2017) (https://www.genome.gov/For-Health-Professionals/Provider-Genomics-Education-Resources#hep)

## GENES TESTED:

**POLG Single Gene**
1 genes tested (100.00% at >20x).

*POLG*

**Gene Specific Notes and Limitations**

No gene specific limitations apply to the genes on the tested panel.

## METHODS:

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[redacted]

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, 100.00% and 100.00% 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 identified by NGS are confirmed by an orthogonal method (qPCR or MLPA), unless exceeding an internally specified and validated quality score, beyond which deletions and duplications are considered real without further confirmation. New York patients: diagnostic findings are confirmed by Sanger, MLPA, or qPCR; exception SNV variants in genes for which confirmation of NGS results has been performed >=10 times may not be confirmed if identified with high quality by NGS. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

## LIMITATIONS:

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to this individual's phenotype, and negative results do not rule out a genetic cause for the indication for testing. 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 designed and validated for detection of germline variants only. It 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 (eg. trinucleotide or hexanucleotide repeat expansion). 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 are two or more contiguous exons in size; 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.

## SIGNATURE:

**Zhenbin Chen, Ph.D., CGMBS, FACMG** on **4/26/2023 04:34 PM PDT**
Electronically signed

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[redacted]

## DISCLAIMER:

This test was developed and its performance characteristics determined by**Fulgent Genetics**. 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 **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.

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[redacted]

Patient Information:
**6747, Donor**
**DOB:** [redacted]
Sex: M
MR#: 6747
Patient#: [redacted]

Partner Information:
**Not Tested**

Physician:
**Seitz, Suzanne**
ATTN: Seitz, Suzanne
Fairfax Cryobank
3015 Williams Drive
Fairfax, VA 22031

Laboratory:
**Fulgent Genetics**
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Dr. Hanlin (Harry) Gao
Report Date: **Dec 24,2023**

Accession:
[redacted]
Test#: [redacted]
Specimen Type: DNA
Collected: Apr 06,2023

Accession:
**N/A**

## FINAL RESULTS

No carrier mutations identified

## TEST PERFORMED

**Custom Beacon Carrier Screening Panel**

(2 Gene Panel: *AMN and MRE11*; gene sequencing with deletion and duplication analysis)

## INTERPRETATION:

**Notes and Recommendations:**

- No carrier mutations were identified in the submitted specimen. A negative result does not rule out the possibility of a genetic predisposition nor does it rule out any pathogenic mutations in areas not assessed by this test or in regions that were covered at a level too low to reliably assess. Also, it does not rule out mutations that are of the sort not queried by this test; see Methods and Limitations for more information.
- This carrier screening test does not screen for all possible genetic conditions, nor for all possible mutations in every gene tested. Individuals with negative test results may still have up to a 3-4% risk to have a child with a birth defect due to genetic and/or environmental factors.
- 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.
- This report does not include variants of uncertain significance.
- 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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## GENES TESTED:

### Custom Beacon Carrier Screening Panel - 2 Genes

This analysis was run using the Custom Beacon Carrier Screening Panel gene list. 2 genes were tested with 100.0% of targets sequenced at >20x coverage. For more gene specific information and assistance with residual risk calculation, see the SUPPLEMENTAL TABLE.

*AMN, MRE11*

## 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, 100.00% and 100.00% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). All genes listed were evaluated for large deletions and/or duplications. However, single exon deletions or duplications will not be detected in this assay, nor will copy number alterations in regions of genes with significant pseudogenes. Putative deletions or duplications are analyzed using Fulgent Germline proprietary pipeline for this specimen. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

## LIMITATIONS:

**General Limitations**

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to future pregnancies, and negative results do not rule out the genetic risk to a pregnancy. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions other than specified genes. DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution

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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**

No gene specific limitations apply to the genes on the tested panel.

## SIGNATURE:

**Dr. Harry Gao, DABMG, FACMG** on **12/24/2023 3:58 PM PST**
Electronically signed

## DISCLAIMER:

This test was developed and its performance characteristics determined by **Fulgent Genetics**. 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 **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.

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[redacted]

Supplemental Table

| Gene | Condition | Inheritance | Ethnicity | Carrier Rate | Detection Rate | Post-test Carrier Probability* | Residual Risk* |
|---|---|---|---|---|---|---|---|
| *AMN* | Megaloblastic anemia 1 | AR | General Population | <1 in 500 | 99% | 1 in 49,901 | <1 in 10 million |
| *MRE11* | Ataxia-Telangiectasia-Like Disorder 1 | AR | General Population | <1 in 500 | 99% | 1 in 49,901 | <1 in 10 million |

* For genes that have tested negative

Abbreviations: AR, autosomal recessive; XL, X-linked

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[redacted]

Patient Information:
**6747, Donor**
**DOB:** [redacted]
Sex: M
MR#: 6747
Patient#: [redacted]

Partner Information:
**Not Tested**

Physician:
**Seitz, Suzanne**
ATTN: Seitz, Suzanne
Fairfax Cryobank
3015 Williams Drive
Fairfax, VA 22031

Laboratory:
**Fulgent Therapeutics, LLC**
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Dr. Hanlin (Harry) Gao
Report Date: **Feb 29,2024**

Accession:
[redacted]
Test#: [redacted]
Specimen Type: DNA
Collected: Apr 06,2023

Accession:
**N/A**

## FINAL RESULTS

No carrier mutations identified

## TEST PERFORMED

**Custom Beacon Carrier Screening Panel**

(3 Gene Panel: *CC2D2A, NAGA, and SERPINA1*; gene sequencing with deletion and duplication analysis)

## INTERPRETATION:

**Notes and Recommendations:**

- No carrier mutations were identified in the submitted specimen. A negative result does not rule out the possibility of a genetic predisposition nor does it rule out any pathogenic mutations in areas not assessed by this test or in regions that were covered at a level too low to reliably assess. Also, it does not rule out mutations that are of the sort not queried by this test; see Methods and Limitations for more information. A negative result reduces, but does not eliminate, the chance to be a carrier for any condition included in this screen. Please see the supplemental table for details.
- This carrier screening test does not screen for all possible genetic conditions, nor for all possible mutations in every gene tested. This report does not include variants of uncertain significance; only variants classified as pathogenic or likely pathogenic at the time of testing, and considered relevant for reproductive carrier screening, are reported. Please see the gene specific notes for details. Please note that the classification of variants can change over time.
- Patients may wish to discuss any carrier results with blood relatives, as there is an increased chance that they are also carriers. These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.
- X-linked genes are not routinely analyzed for male carrier screening tests. Gene specific notes and limitations may be present. See below.
- Genetic counseling is recommended. Available genetic counselors and additional resources can be found at the National Society of Genetic Counselors (NSGC; https://www.nsgc.org)

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[redacted]

## GENES TESTED:

### Custom Beacon Carrier Screening Panel - 3 Genes

This analysis was run using the Custom Beacon Carrier Screening Panel gene list. 3 genes were tested with 100.0% of targets sequenced at >20x coverage. For more gene-specific information and assistance with residual risk calculation, see the SUPPLEMENTAL TABLE.

*CC2D2A, NAGA, SERPINA1*

## 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, 100.00% and 100.00% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). All genes listed were evaluated for large deletions and/or duplications. However, single exon deletions or duplications will not be detected in this assay, nor will copy number alterations in regions of genes with significant pseudogenes. Putative deletions or duplications are analyzed using Fulgent Germline proprietary pipeline for this specimen. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

## LIMITATIONS:

**General Limitations**

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to future pregnancies, and negative results do not rule out the genetic risk to a pregnancy. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions other than specified genes. DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution

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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**

*SERPINA1:* If detected the variant NM_000295.5:c.863A>T (p.Glu288Val) will not be reported as this variant is associated with low disease penetrance and is not associated with severe early onset disease.

## SIGNATURE:

**Yan Meng, Ph.D., CGMB, FACMG** on **2/29/2024**
Laboratory Director, Fulgent

## DISCLAIMER:

This test was developed and its performance characteristics determined by **Fulgent Therapeutics, LLC**. 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 **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.

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Supplemental Table

| Gene | Condition | Inheritance | Ethnicity | Carrier Rate | Detection Rate | Post-test Carrier Probability* | Residual Risk* |
|---|---|---|---|---|---|---|---|
| *CC2D2A* | Joubert syndrome 9 | AR | General Population | 1 in 201 | 99% | 1 in 20,001 | 1 in 16,080,804 |
| *NAGA* | Schindler disease types 1 and 3 | AR | General Population | 1 in 94 | 99% | 1 in 9,301 | 1 in 3,497,176 |
| *SERPINA1* | Alpha-1 antitrypsin deficiency | AR | General Population | 1 in 33 | 95% | 1 in 641 | 1 in 84,612 |
| | | | Caucasian / European Population | 1 in 19 | 95% | 1 in 361 | 1 in 27,436 |

* For genes that have tested negative

Abbreviations: AR, autosomal recessive; XL, X-linked

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[redacted]

Patient Information:
**6747, Donor**
**DOB:** [redacted]
Sex: M
MR#: 6747
Patient#: [redacted]

Partner Information:
**Not Tested**

Physician:
**Seitz, Suzanne**
ATTN: Seitz, Suzanne
Fairfax Cryobank
3015 Williams Drive
Fairfax, VA 22031

Laboratory:
**Fulgent Therapeutics LLC**
CAP#: 8042697
CLIA#: 05D2043189
Laboratory Director:
Dr. Hanlin (Harry) Gao
Report Date: **Mar 31,2024**

Accession:
[redacted]
Test#: [redacted]
Specimen Type: DNA
Collected: Apr 06,2023

Accession:
**N/A**

## FINAL RESULTS

No carrier mutations identified

## TEST PERFORMED

### Custom Beacon Carrier Screening Panel

(2 Gene Panel: *GALNT3 and MYO15A*; gene sequencing with deletion and duplication analysis)

## INTERPRETATION:

**Notes and Recommendations:**

- No carrier mutations were identified in the submitted specimen. A negative result does not rule out the possibility of a genetic predisposition nor does it rule out any pathogenic mutations in areas not assessed by this test or in regions that were covered at a level too low to reliably assess. Also, it does not rule out mutations that are of the sort not queried by this test; see Methods and Limitations for more information. A negative result reduces, but does not eliminate, the chance to be a carrier for any condition included in this screen. Please see the supplemental table for details.
- This carrier screening test does not screen for all possible genetic conditions, nor for all possible mutations in every gene tested. This report does not include variants of uncertain significance; only variants classified as pathogenic or likely pathogenic at the time of testing, and considered relevant for reproductive carrier screening, are reported. Please see the gene specific notes for details. Please note that the classification of variants can change over time.
- Patients may wish to discuss any carrier results with blood relatives, as there is an increased chance that they are also carriers. These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.
- X-linked genes are not routinely analyzed for male carrier screening tests. Gene specific notes and limitations may be present. See below.
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## GENES TESTED:

### Custom Beacon Carrier Screening Panel - 2 Genes

This analysis was run using the Custom Beacon Carrier Screening Panel gene list. 2 genes were tested with 100.0% of targets sequenced at >20x coverage. For more gene-specific information and assistance with residual risk calculation, see the SUPPLEMENTAL TABLE.

*GALNT3, MYO15A*

## 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, 100.00% and 100.00% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). All genes listed were evaluated for large deletions and/or duplications. However, single exon deletions or duplications will not be detected in this assay, nor will copy number alterations in regions of genes with significant pseudogenes. Putative deletions or duplications are analyzed using Fulgent Germline proprietary pipeline for this specimen. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

## LIMITATIONS:

**General Limitations**

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to future pregnancies, and negative results do not rule out the genetic risk to a pregnancy. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions other than specified genes. DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution

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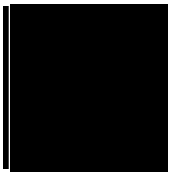

of pseudogene sequences or other highly-homologous sequences, sometimes these may still interfere with the technical ability of the assay to identify pathogenic alterations in both sequencing and deletion/duplication analyses. Deletion/duplication analysis can identify alterations of genomic regions 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**

No gene specific limitations apply to the genes on the tested panel.

## SIGNATURE:

**Dr. Harry Gao, DABMG, FACMG** on **3/31/2024**
Laboratory Director, Fulgent

## DISCLAIMER:

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