



## Donor 6390

### Genetic Testing Summary

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

Last Updated: 01/29/2025

Donor Reported Ancestry: Chinese

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
Expanded Genetic Disease Carrier Screening Panel attached- 502 diseases by gene sequencing.  Personalized residual risk by gene is on attached report.	<p>Carrier: Albinism, Oculocutaneous, Type III (TYRP1)</p> <p>Carrier: Phenylalanine Hydroxylase Deficiency (PAH)</p> <p>Carrier: Thyroid Dyshormonogenesis 6 (DUOX2)</p> <p>Negative for other genes sequenced</p>	Partner testing recommended before using this donor.
<b>Special Testing</b>		
MCPH1	Negative by gene sequence and del/dup	

\*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: 6390 Donor  
 Date of Birth: [REDACTED]  
 Sema4 ID: [REDACTED]  
 Client ID: [REDACTED]  
 Indication: Carrier Screening

**Specimen Information**

Specimen Type: Blood  
 Date Collected: 02/15/2022  
 Date Received: 02/16/2022  
 Final Report: 03/04/2022

**Referring Provider**

[REDACTED]  
 Fairfax Cryobank, Inc.  
 [REDACTED]  
 [REDACTED]

## Expanded Carrier Screen (502 genes) with Personalized Residual Risk

### SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
<p style="text-align: center;"><b>Carrier of Albinism, Oculocutaneous, Type III (AR)</b>            Associated gene(s): <i>TYRP1</i>            Variant(s) Detected: c.1014_1017dupAGTT, p.G340SfsX5, Likely Pathogenic, Heterozygous (one copy)</p> <p style="text-align: center;"><b>Carrier of Phenylalanine Hydroxylase Deficiency (AR)</b>            Associated gene(s): <i>PAH</i>            Variant(s) Detected: c.1197A&gt;T, p. V399=, Pathogenic, Heterozygous (one copy)</p> <p style="text-align: center;"><b>Carrier of Thyroid Dyshormonogenesis 6 (AR)</b>            Associated gene(s): <i>DUOX2</i>            Variant(s) Detected: c.364C&gt;A, p.P122T, Likely Pathogenic, Heterozygous (one copy)</p>	<p style="text-align: center;"><b>Negative for all other genes tested</b>            To view a full list of genes and diseases tested please see Table 1 in this report</p>

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

**Albinism, Oculocutaneous, Type III (AR)**

**Results and Interpretation**

A heterozygous (one copy) likely pathogenic frameshift variant, c.1014\_1017dupAGTT, p.G340SfsX5, was detected in the *TYRP1* gene (NM\_000550.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for albinism, oculocutaneous, type III. Therefore, this individual is expected to be at least a carrier for albinism, oculocutaneous, type III. Heterozygous carriers are not expected to exhibit symptoms of this disease.

### What is Albinism, Oculocutaneous, Type III?

Albinism, oculocutaneous, type III (OCA-3) is an autosomal recessive disorder caused by pathogenic variants in the gene *TYRP1*. This disorder is found to be more prevalent in individuals of African descent and causes rufous oculocutaneous albinism. The disease is characterized by the presence of lighter-colored skin and hair (albinism), reduced vision, nystagmus, and photophobia. Long-term sun exposure greatly increases the risk of skin damage and skin cancer. Individuals with OCA-3 tend to have skin that is reddish-brown in color, hair may be red in color, and hazel or brown eyes. In comparison to other types, OCA-3 is associated with milder vision abnormalities. No clear genotype-phenotype correlation has been established.

### Phenylalanine Hydroxylase Deficiency (AR)

#### Results and Interpretation

A heterozygous (one copy) pathogenic synonymous variant, c.1197A>T, p. V399=, was detected in the *PAH* gene (NM\_000277.1). When this variant is present in trans with a pathogenic variant, it is considered to be causative for phenylalanine hydroxylase deficiency. Therefore, this individual is expected to be at least a carrier for phenylalanine hydroxylase deficiency. Heterozygous carriers are not expected to exhibit symptoms of this disease.

### What is Phenylalanine Hydroxylase Deficiency?

Phenylalanine hydroxylase deficiency is an autosomal recessive disorder caused by pathogenic variants in the gene *PAH*. While it is found in many different ethnicities, it is particularly prevalent in Sephardic Jewish, Sicilian, Irish, and Turkish individuals, as well as Caucasians. Pathogenic *PAH* variants result in loss of function of the phenylalanine hydroxylase enzyme, which breaks down the amino acid phenylalanine. The most severe form of the disease is called phenylketonuria. If untreated, buildup of phenylalanine will result in irreversible brain damage and severe intellectual disability. Treatment involves the removal of phenylalanine from the diet. Even with strict adherence to the treatment, some neurologic deficiencies have been noticed in long-term survivors. Psychological problems, including anxiety, depression, phobias and panic attacks may occur in adults who do not comply well to their treatment. Some patients have a milder form of hyperphenylalaninemia and may tolerate higher levels of phenylalanine in their diet. Depending on the genotype, patients may be responsive to BH4, which can direct their treatment. However, it is not always possible to predict the severity of the disease based on genotype.

### Thyroid Dyshormonogenesis 6 (AR)

#### Results and Interpretation

A heterozygous (one copy) likely pathogenic missense variant, c.364C>A, p.P122T, was detected in the *DUOX2* gene (NM\_014080.4). When this variant is present in trans with a pathogenic variant, it is considered to be causative for thyroid dyshormonogenesis 6. Therefore, this individual is expected to be at least a carrier for thyroid dyshormonogenesis 6. Heterozygous carriers may exhibit clinical symptoms, mainly transient hypothyroidism in infancy.

### What is Thyroid Dyshormonogenesis 6?

Thyroid dyshormonogenesis 6 is an autosomal recessive disorder caused by pathogenic variants in the gene *DUOX2*. Affected individuals manifest hypothyroidism and goiter, and if left untreated, may develop intellectual disability and experience slow growth. Affected infants may be asymptomatic or may present with lethargy, sleepiness, feeding difficulty, and constipation. While life expectancy for this disorder is normal, patients may have neurocognitive impairment. Heterozygous pathogenic variants in this gene have also been associated with a mild and transient autosomal dominant form of hypothyroidism in infancy.

## 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](http://go.sema4.com/residualrisk). Only variants determined to be pathogenic or likely pathogenic are reported in this carrier screening test.

A handwritten signature in black ink that reads "Christie Buchovecky".

**Christie Buchovecky, Ph.D., Assistant Director, Reproductive Genomic**

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](https://go.sema4.com/residualrisk)

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

Disease	Gene	Inheritance Pattern	Status	Detailed Summary
<b>Positive</b>				
Albinism, Oculocutaneous, Type III	<i>TYRP1</i>	AR	Carrier	c.1014_1017dupAGTT, p.G340SfsX5, Likely Pathogenic, Heterozygous (one copy)
Phenylalanine Hydroxylase Deficiency	<i>PAH</i>	AR	Carrier	c.1197A>T, p. V399=, Pathogenic, Heterozygous (one copy)
Thyroid Dysmorphogenesis 6	<i>DUOX2</i>	AR	Carrier	c.364C>A, p.P122T, Likely Pathogenic, Heterozygous (one copy)
<b>Negative</b>				
2-Methylbutyrylglycinuria	<i>ACADSB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 410
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	<i>HSD3B2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 181,000
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related)	<i>MCCC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 930
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)	<i>MCCC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 500
3-Methylglutaconic Aciduria, Type III	<i>OPA3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 29,000
3-Phosphoglycerate Dehydrogenase Deficiency	<i>PHGDH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 123,000
6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	<i>PTS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,800
CD59-Mediated Hemolytic Anemia	<i>CD59</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 513,000
Abetalipoproteinemia	<i>MTTP</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,500
Achalasia-Addisonianism-Alacrimia Syndrome	<i>AAAS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
Achromatopsia (CNGA3-Related)	<i>CNGA3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 320
Achromatopsia (CNGB3-related)	<i>CNGB3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 21,000
Acrodermatitis Enteropathica	<i>SLC39A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 62,000
Acute Infantile Liver Failure	<i>TRMU</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 55,000
Acyl-CoA Oxidase I Deficiency	<i>ACOX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 59,000
Adams-Oliver Syndrome 4	<i>EOGT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 59,000
Adenosine Deaminase Deficiency	<i>ADA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 127,000
Adrenocorticotrophic Hormone Deficiency	<i>TBX19</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,500
Adrenoleukodystrophy, X-Linked	<i>ABCD1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 19,000
Agammaglobulinemia	<i>BTK</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 250,000
Agenesis of the Corpus Callosum	<i>FRMD4A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 348,000
Aicardi-Goutieres Syndrome (RNASEH2C-Related)	<i>RNASEH2C</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Aicardi-Goutieres Syndrome (SAMHD1-Related)	<i>SAMHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Aicardi-Goutieres Syndrome (TREX1-Related)	<i>TREX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
Alkaptonuria	<i>HGD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,200
Alpha-Mannosidosis	<i>MAN2B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,000
Alpha-Thalassemia	<i>HBA1/HBA2</i>	AR	Reduced Risk	HBA1 Copy Number: 2 HBA2 Copy Number: 2 No pathogenic copy number variants detected HBA1/HBA2 Sequencing: Negative <b>Personalized Residual Risk:</b> 1 in 380

Alpha-Thalassemia Intellectual Disability Syndrome	<i>ATRX</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 48,000
Alport Syndrome ( <i>COL4A3</i> -Related)	<i>COL4A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,700
Alport Syndrome ( <i>COL4A4</i> -Related)	<i>COL4A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 510
Alport Syndrome ( <i>COL4A5</i> -Related)	<i>COL4A5</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 150,000
Alstrom Syndrome	<i>ALMS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,100
Andermann Syndrome	<i>SLC12A6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 287,000
Antley-Bixler Syndrome ( <i>POR</i> -Related)	<i>POR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 650
Argininemia	<i>ARG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,900
Argininosuccinic Aciduria	<i>ASL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,000
Aromatase Deficiency	<i>CYP19A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Arthrogryposis, Intellectual Disability, and Seizures	<i>SLC35A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 240,000
Asparagine Synthetase Deficiency	<i>ASNS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 178,000
Aspartylglycosaminuria	<i>AGA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
Ataxia With Isolated Vitamin E Deficiency	<i>TTPA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 20,000
Ataxia-Telangiectasia	<i>ATM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 540
Ataxia-Telangiectasia-Like Disorder 1	<i>MRE11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,700
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	<i>SACS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
BH4-Deficient Hyperphenylalaninemia C	<i>QDPR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
BH4-Deficient Hyperphenylalaninemia D	<i>PCBD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Bardet-Biedl Syndrome ( <i>ARL6</i> -Related)	<i>ARL6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
Bardet-Biedl Syndrome ( <i>BBS10</i> -Related)	<i>BBS10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
Bardet-Biedl Syndrome ( <i>BBS12</i> -Related)	<i>BBS12</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 287,000
Bardet-Biedl Syndrome ( <i>BBS1</i> -Related)	<i>BBS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
Bardet-Biedl Syndrome ( <i>BBS2</i> -Related)	<i>BBS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,400
Bardet-Biedl Syndrome ( <i>BBS4</i> -Related)	<i>BBS4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 287,000
Bare Lymphocyte Syndrome, Type II	<i>CIITA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 129,000
Barth Syndrome	<i>TAZ</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 183,000
Bartter Syndrome, Type 3	<i>CLCNKB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 710
Bartter Syndrome, Type 4A	<i>BSND</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 69,000
Bernard-Soulier Syndrome, Type A1	<i>GP1BA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
Bernard-Soulier Syndrome, Type C	<i>GP9</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Beta-Globin-Related Hemoglobinopathies	<i>HBB</i>	AR	Reduced Risk	<b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies):</b> 1 in 1,200 <b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant):</b> 1 in 11,000 <b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant):</b> 1 in 42,000
Beta-Ketothiolase Deficiency	<i>ACAT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
Beta-Mannosidosis	<i>MANBA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 57,000
Bilateral Frontoparietal Polymicrogyria	<i>GPR56</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 143,000
Biotinidase Deficiency	<i>BTD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
Bloom Syndrome	<i>BLM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 34,000
Canavan Disease	<i>ASPA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,200
Carbamoylphosphate Synthetase I Deficiency	<i>CPS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 690
Carnitine Acylcarnitine Translocase Deficiency	<i>SLC25A20</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,500
Carnitine Palmitoyltransferase IA Deficiency	<i>CPT1A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 143,000
Carnitine Palmitoyltransferase II Deficiency	<i>CPT2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 930
Carpenter Syndrome	<i>RAB23</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 28,000

Cartilage-Hair Hypoplasia	<i>RMRP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 450
Catecholaminergic Polymorphic Ventricular Tachycardia	<i>CASQ2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 63,000
Central Hypothyroidism and Testicular Enlargement	<i>IGSF1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 781,000
Cerebral Creatine Deficiency Syndrome 1	<i>SLC6A8</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 208,000
Cerebral Creatine Deficiency Syndrome 2	<i>GAMT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Cerebral Creatine Deficiency Syndrome 3	<i>GATM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Cerebral Dysgenesis, Neuropathy, Ichthyosis, and Palmoplantar Keratoderma Syndrome	<i>SNAP29</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 383,000
Cerebrotendinous Xanthomatosis	<i>CYP27A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 750
Charcot-Marie-Tooth Disease, Type 4D	<i>NDRG1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 225,000
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	<i>PRPS1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 114,000
Charcot-Marie-Tooth Disease, X-Linked	<i>GJB1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Chediak-Higashi Syndrome	<i>LYST</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 129,000
Chondrodysplasia Punctata	<i>ARSE</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 862,000
Choreoacanthocytosis	<i>VPS13A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,700
Choroideremia	<i>CHM</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 125,000
Chronic Granulomatous Disease (CYBA-Related)	<i>CYBA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Chronic Granulomatous Disease (CYBB-Related)	<i>CYBB</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 294,000
Citrin Deficiency	<i>SLC25A13</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
Citrullinemia, Type 1	<i>ASS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 81,000
Cockayne Syndrome, Type A	<i>ERCC8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 32,000
Cockayne Syndrome, Type B and other ERCC6-Related Disorders	<i>ERCC6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Cohen Syndrome	<i>VPS13B</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Combined Factor V and VIII Deficiency	<i>LMAN1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 68,000
Combined Malonic and Methylmalonic Aciduria	<i>ACSF3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 23,000
Combined Oxidative Phosphorylation Deficiency 1	<i>GFM1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,100
Combined Oxidative Phosphorylation Deficiency 3	<i>TSMF</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Combined Pituitary Hormone Deficiency 1	<i>POU1F1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Combined Pituitary Hormone Deficiency 2	<i>PROP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Combined Pituitary Hormone Deficiency 3	<i>LHX3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 121,000
Combined SAP Deficiency	<i>PSAP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 78,000
Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1	<i>GUCY2D</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 720
Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency	<i>CYP11B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	<i>CYP17A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 840
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	<i>CYP21A2</i>	AR	Reduced Risk	<p><i>CYP21A2</i> copy number: 2  <i>CYP21A2</i> sequencing: Negative            Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)): 1 in 300            Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)): 1 in 1,200</p>
Congenital Adrenal Hypoplasia (NR0B1-Related)	<i>NR0B1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 353,000
Congenital Adrenal Insufficiency (CYP11A1-Related)	<i>CYP11A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 128,000
Congenital Amegakaryocytic Thrombocytopenia	<i>MPL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 68,000
Congenital Bile Acid Synthesis Defect (AKR1D1-Related)	<i>AKR1D1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 63,000

<b>Congenital Bile Acid Synthesis Defect (HSD3B7-Related)</b>	<i>HSD3B7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,700
<b>Congenital Disorder of Deglycosylation</b>	<i>NGLY1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,000
<b>Congenital Disorder of Glycosylation, Type Ia</b>	<i>PMM2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 550
<b>Congenital Disorder of Glycosylation, Type Ib</b>	<i>MPI</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
<b>Congenital Disorder of Glycosylation, Type Ic</b>	<i>ALG6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,300
<b>Congenital Disorder of Glycosylation, Type Im</b>	<i>DOLK</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 216,000
<b>Congenital Dyserythropoietic Anemia Type 2</b>	<i>SEC23B</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,700
<b>Congenital Dyserythropoietic Anemia, Type Ia</b>	<i>CDAN1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 640
<b>Congenital Ichthyosis 4A and 4B</b>	<i>ABCA12</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
<b>Congenital Insensitivity to Pain with Anhidrosis</b>	<i>NTRK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,000
<b>Congenital Muscular Dystrophy (LAMA2-Related)</b>	<i>LAMA2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 690
<b>Congenital Myasthenic Syndrome (CHAT-Related)</b>	<i>CHAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
<b>Congenital Myasthenic Syndrome (CHRNE-Related)</b>	<i>CHRNE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 30,000
<b>Congenital Myasthenic Syndrome (DOK7-Related)</b>	<i>DOK7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 470
<b>Congenital Myasthenic Syndrome (RAPSN-Related)</b>	<i>RAPSN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 47,000
<b>Congenital Neutropenia (HAX1-Related)</b>	<i>HAX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 126,000
<b>Congenital Neutropenia (VPS45-Related)</b>	<i>VPS45</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 110,000
<b>Congenital Nongoitrous Hypothyroidism 1</b>	<i>TSHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 230
<b>Congenital Nongoitrous Hypothyroidism 4</b>	<i>TSHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 227,000
<b>Congenital Secretory Chloride Diarrhea 1</b>	<i>SLC26A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
<b>Corneal Dystrophy and Perceptive Deafness</b>	<i>SLC4A11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,200
<b>Corticosterone Methyloxidase Deficiency</b>	<i>CYP11B2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,700
<b>Cystic Fibrosis</b>	<i>CFTR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
<b>Cystinosis</b>	<i>CTNS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,100
<b>Cystinuria (SLC3A1-Related)</b>	<i>SLC3A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 530
<b>Cytochrome C Oxidase Deficiency / Leigh Syndrome (COX15-Related)</b>	<i>COX15</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 182,000
<b>D-Bifunctional Protein Deficiency</b>	<i>HSD17B4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
<b>Deafness, Autosomal Recessive 3</b>	<i>MYO15A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 100
<b>Deafness, Autosomal Recessive 59</b>	<i>PJVK</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 73,000
<b>Deafness, Autosomal Recessive 7</b>	<i>TMC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
<b>Deafness, Autosomal Recessive 76</b>	<i>SYNE4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 121,000
<b>Deafness, Autosomal Recessive 77</b>	<i>LOXHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,800
<b>Deafness, Autosomal Recessive 8/10</b>	<i>TMPRSS3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 330
<b>Deafness, Autosomal Recessive 9</b>	<i>OTOF</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 370
<b>Desbuquois Dysplasia 1</b>	<i>CANT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7800
<b>Desmoterolosis</b>	<i>DHCR24</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 28,000
<b>Diaphanospondylodysostosis</b>	<i>BMPER</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 144,000
<b>Distal Renal Tubular Acidosis and other SLC4A1-related Disorders</b>	<i>SLC4A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 910
<b>Duchenne Muscular Dystrophy / Becker Muscular Dystrophy</b>	<i>DMD</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
<b>Dyskeratosis Congenita (DKC1-related)</b>	<i>DKC1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,259,000
<b>Dyskeratosis Congenita (RTEL1-Related)</b>	<i>RTEL1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,900
<b>Dystrophic Epidermolysis Bullosa</b>	<i>COL7A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
<b>Ehlers-Danlos Syndrome, Type VI</b>	<i>PLOD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,700
<b>Ehlers-Danlos Syndrome, Type VIIC</b>	<i>ADAMTS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 63,000
<b>Ellis-Van Creveld Syndrome (EVC2-Related)</b>	<i>EVC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,100

Ellis-van Creveld Syndrome (EVC-Related)	EVC	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
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 1,700
Ethylmalonic Encephalopathy	ETHE1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600
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 VII Deficiency	F7	AR	Reduced Risk	Personalized Residual Risk: 1 in 300
Factor XI Deficiency	F11	AR	Reduced Risk	Personalized Residual Risk: 1 in 440
Familial Autosomal Recessive Hypercholesterolemia	LDLRAP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 171,000
Familial Dysautonomia	IKBKAP	AR	Reduced Risk	Personalized Residual Risk: 1 in 78,000
Familial Hypercholesterolemia	LDLR	AR	Reduced Risk	Personalized Residual Risk: 1 in 260
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	HADH	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,000
Familial Hyperinsulinism (ABCC8-Related)	ABCC8	AR	Reduced Risk	Personalized Residual Risk: 1 in 240
Familial Hyperinsulinism (KCNJ11-Related)	KCNJ11	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Familial Hyperphosphatemic Tumor Calcinosi	GALNT3	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,100
Familial Mediterranean Fever	MEFV	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Fanconi Anemia, Group A	FANCA	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Fanconi Anemia, Group C	FANCC	AR	Reduced Risk	Personalized Residual Risk: 1 in 34,000
Fanconi Anemia, Group G	FANCG	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Fanconi-Bickel Syndrome	SLC2A2	AR	Reduced Risk	Personalized Residual Risk: 1 in 295,000
Fragile X Syndrome	FMR1	XL	Reduced Risk	FMR1 CGG repeat sizes: Not Performed FMR1 Sequencing: Negative 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. Personalized Residual Risk: 1 in 222,000
Fructose-1,6-Bisphosphatase Deficiency	FBP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Fucosidosis	FUCA1	AR	Reduced Risk	Personalized Residual Risk: 1 in 49,000
Fumarase Deficiency	FH	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Fundus Albipunctatus	RDH5	AR	Reduced Risk	Personalized Residual Risk: 1 in 810
GRACILE Syndrome and Other BCS1L-Related Disorders	BCS1L	AR	Reduced Risk	Personalized Residual Risk: 1 in 82,000
Galactokinase Deficiency	GALK1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Galactose Epimerase Deficiency	GALE	AR	Reduced Risk	Personalized Residual Risk: 1 in 850
Galactosemia	GALT	AR	Reduced Risk	Personalized Residual Risk: 1 in 390
Galactosialidosis	CTSA	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Gaucher Disease	GBA	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Generalized Thyrotropin-Releasing Hormone Resistance	TRHR	AR	Reduced Risk	Personalized Residual Risk: 1 in 296,000
Geroderma Osteodysplasticum	GORAB	AR	Reduced Risk	Personalized Residual Risk: 1 in 76,000
Gitelman Syndrome	SLC12A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 230
Glanzmann Thrombasthenia (ITGA2B-Related)	ITGA2B	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Glanzmann Thrombasthenia (ITGB3-Related)	ITGB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Glutaric Acidemia, Type I	GCDH	AR	Reduced Risk	Personalized Residual Risk: 1 in 20,000
Glutaric Acidemia, Type IIa	ETFA	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Glutaric Acidemia, Type IIb	ETFB	AR	Reduced Risk	Personalized Residual Risk: 1 in 7800
Glutaric Acidemia, Type IIc	ETFDH	AR	Reduced Risk	Personalized Residual Risk: 1 in 260
Glutathione Synthetase Deficiency	GSS	AR	Reduced Risk	Personalized Residual Risk: 1 in 48,000
Glycine Encephalopathy (AMT-Related)	AMT	AR	Reduced Risk	Personalized Residual Risk: 1 in 144,000
Glycine Encephalopathy (GLDC-Related)	GLDC	AR	Reduced Risk	Personalized Residual Risk: 1 in 240
Glycogen Storage Disease, Type 0	GYS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000

Glycogen Storage Disease, Type II	GAA	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 280</b>
Glycogen Storage Disease, Type III	AGL	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 55,000</b>
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	GBE1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 64,000</b>
Glycogen Storage Disease, Type IXb	PHKB	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,600</b>
Glycogen Storage Disease, Type Ia	G6PC	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 410</b>
Glycogen Storage Disease, Type Ib	SLC37A4	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,900</b>
Glycogen Storage Disease, Type V	PYGM	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,400</b>
Glycogen Storage Disease, Type VI	PYGL	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
Glycogen Storage Disease, Type VII	PFKM	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,900</b>
Gray Platelet Syndrome	NBEAL2	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,400</b>
Growth Hormone Deficiency, Type IB	GHRHR	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 104,000</b>
HMG-CoA Lyase Deficiency	HMGCL	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 113,000</b>
Hemochromatosis, Type 2A	HFE2	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 740</b>
Hemochromatosis, Type 3	TFR2	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 275,000</b>
Hereditary Fructose Intolerance	ALDOB	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 35,000</b>
Hereditary Spastic Paraparesis 49	TECPR2	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 166,000</b>
Hermansky-Pudlak Syndrome, Type 1	HPS1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 286,000</b>
Hermansky-Pudlak Syndrome, Type 3	HPS3	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 22,000</b>
Hermansky-Pudlak Syndrome, Type 4	HPS4	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 287,000</b>
Hermansky-Pudlak Syndrome, Type 6	HPS6	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 680</b>
Hmg-CoA Synthase 2 Deficiency	HMGCS2	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,000</b>
Holocarboxylase Synthetase Deficiency	HLCS	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,900</b>
Homocystinuria (CBS-Related)	CBS	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,200</b>
Homocystinuria due to MTHFR Deficiency	MTHFR	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,000</b>
Homocystinuria, cblE Type	MTRR	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 16,000</b>
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	MTR	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 35,000</b>
Hydrocephalus	L1CAM	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 40,000</b>
Hydrolethals Syndrome	HYLS1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 296,000</b>
Hyper-Igm Syndrome	CD40LG	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,167,000</b>
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	SLC25A15	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 30,000</b>
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	SARS2	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 220,000</b>
Hypohidrotic Ectodermal Dysplasia 1	EDA	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 22,000</b>
Hypomagnesemia 1	TRPM6	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 86,000</b>
Hypomyelinating Leukodystrophy 3	AIMP1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 273,000</b>
Hypomyelinating Leukodystrophy 12	VPS11	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 94,000</b>
Hypoparathyroidism-Retardation-Dysmorphic Syndrome	TBCE	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 66,000</b>
Hypophosphatasia	ALPL	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,200</b>
Hypophosphatemic Rickets with Hypercalciuria	SLC34A3	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,000</b>
Hypotrichosis 8 / Autosomal Recessive Woolly Hair 1	LPAR6	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 17,000</b>
Immunodeficiency 18	CD3E	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 120,000</b>
Immunodeficiency 19	CD3D	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 69,000</b>
Inclusion Body Myopathy 2	GNE	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,600</b>
Infantile Cerebral and Cerebellar Atrophy	MED17	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 130,000</b>
Infantile Neuroaxonal Dystrophy 1 and other PLA2G6-Related Disorders	PLA2G6	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 380</b>
Intellectual Disability, Autosomal Recessive 3	CC2D1A	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 108,000</b>
Intrahepatic Cholestasis	ATP8B1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 580</b>

Isovaleric Acidemia	IVD	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Joubert Syndrome 2	TMEM216	AR	Reduced Risk	Personalized Residual Risk: 1 in 133,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	NPHP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	RPGRIPL	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Junctional Epidermolysis Bullosa (COL17A1-Related)	COL17A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Junctional Epidermolysis Bullosa (ITGA6-Related)	ITGA6	AR	Reduced Risk	Personalized Residual Risk: 1 in 287,000
Junctional Epidermolysis Bullosa (ITGB4-Related)	ITGB4	AR	Reduced Risk	Personalized Residual Risk: 1 in 26,000
Junctional Epidermolysis Bullosa (LAMA3-Related)	LAMA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 49,000
Junctional Epidermolysis Bullosa (LAMB3-Related)	LAMB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,600
Junctional Epidermolysis Bullosa (LAMC2-Related)	LAMC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 28,000
Kohlschutter-Tonz Syndrome	ROGDI	AR	Reduced Risk	Personalized Residual Risk: 1 in 287,000
Krabbe Disease	GALC	AR	Reduced Risk	Personalized Residual Risk: 1 in 340
Lamellar Ichthyosis, Type 1	TGM1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600
Laron Dwarfism	GHR	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
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 88,000
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	TULP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	RPE65	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Leber Congenital Amaurosis 4	AIPL1	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,100
Leber Congenital Amaurosis 5	LCA5	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	CRB1	AR	Reduced Risk	Personalized Residual Risk: 1 in 960
Leigh Syndrome (NDUFS7-Related)	NDUFS7	AR	Reduced Risk	Personalized Residual Risk: 1 in 38,000
Leigh Syndrome (SURF1-Related)	SURF1	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Leigh Syndrome, French-Canadian Type	LRPPRC	AR	Reduced Risk	Personalized Residual Risk: 1 in 22,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogyposis with Anterior Horn Cell Disease	GLE1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Lethal Congenital Contracture Syndrome 2	ERBB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 52,000
Lethal Congenital Contracture Syndrome 3	PIP5K1C	AR	Reduced Risk	Personalized Residual Risk: 1 in 304,000
Leukoencephalopathy with Vanishing White Matter	EIF2B5	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,200
Limb-Girdle Muscular Dystrophy, Type 2A	CAPN3	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Limb-Girdle Muscular Dystrophy, Type 2B	DYSF	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Limb-Girdle Muscular Dystrophy, Type 2C	SGCG	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,000
Limb-Girdle Muscular Dystrophy, Type 2D	SGCA	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
Limb-Girdle Muscular Dystrophy, Type 2E	SGCB	AR	Reduced Risk	Personalized Residual Risk: 1 in 72,000
Limb-Girdle Muscular Dystrophy, Type 2F	SGCD	AR	Reduced Risk	Personalized Residual Risk: 1 in 36,000
Limb-Girdle Muscular Dystrophy, Type 2H	TRIM32	AR	Reduced Risk	Personalized Residual Risk: 1 in 123,000
Limb-Girdle Muscular Dystrophy, Type 2I	FKRP	AR	Reduced Risk	Personalized Residual Risk: 1 in 460
Limb-Girdle Muscular Dystrophy, Type 2L	ANO5	AR	Reduced Risk	Personalized Residual Risk: 1 in 920
Lipoamide Dehydrogenase Deficiency	DLD	AR	Reduced Risk	Personalized Residual Risk: 1 in 225,000
Lipoid Adrenal Hyperplasia	STAR	AR	Reduced Risk	Personalized Residual Risk: 1 in 36,000
Lipoprotein Lipase Deficiency	LPL	AR	Reduced Risk	Personalized Residual Risk: 1 in 800
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	HADHA	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,500

Lowre Syndrome	OCRL	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,375,000
Lysinuric Protein Intolerance	SLC7A7	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 72,000
MEDNIK Syndrome	AP1S1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 294,000
Malonyl-CoA Decarboxylase Deficiency	MLYCD	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
Maple Syrup Urine Disease, Type 1a	BCKDHA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,000
Maple Syrup Urine Disease, Type 1b	BCKDHB	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
Maple Syrup Urine Disease, Type 2	DBT	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 790
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	MKS1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 28,000
Medium Chain Acyl-CoA Dehydrogenase Deficiency	ACADM	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
Megalencephalic Leukoencephalopathy with Subcortical Cysts	MLC1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 171,000
Megaloblastic Anemia 1	AMN	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Menkes Disease	ATP7A	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
Metachromatic Leukodystrophy	ARSA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,600
Methionine Adenosyltransferase I/III Deficiency	MAT1A	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,700
Methylmalonic Acidemia (MMAA-Related)	MMAA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 216,000
Methylmalonic Acidemia (MMAB-Related)	MMAB	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,700
Methylmalonic Acidemia (MUT-Related)	MUT	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 830
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	MMACHC	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	MMADHC	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	LMBRD1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 43,000
Methylmalonyl-CoA Epimerase Deficiency	MCEE	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 168,000
Microphthalmia / Anophthalmia	VSX2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 83,000
Mitochondrial Complex I Deficiency (ACAD9-Related)	ACAD9	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,100
Mitochondrial Complex I Deficiency (NDUFA11-Related)	NDUFA11	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 548,000
Mitochondrial Complex I Deficiency (NDUFAF5-Related)	NDUFAF5	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 770
Mitochondrial Complex I Deficiency (NDUFS6-Related)	NDUFS6	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 211,000
Mitochondrial Complex I Deficiency (NDUFV1-Related)	NDUFV1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,100
Mitochondrial Complex I Deficiency / Leigh Syndrome (FOXRED1-Related)	FOXRED1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,900
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFAF2-Related)	NDUFAF2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 114,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFS4-Related)	NDUFS4	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 31,000
Mitochondrial Complex IV Deficiency (COX20-related)	COX20	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 68,000
Mitochondrial Complex IV Deficiency (COX6B1-related)	COX6B1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,231,000
Mitochondrial Complex IV Deficiency (APOPT1-Related)	APOPT1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 22,000
Mitochondrial Complex IV Deficiency (PET100-Related)	PET100	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 546,000
Mitochondrial Complex IV Deficiency (SCO1-related)	SCO1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 74,000
Mitochondrial Complex IV Deficiency / Leigh Syndrome (COX10-Related)	COX10	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,900
Mitochondrial DNA Depletion Syndrome 2	TK2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,700
Mitochondrial DNA Depletion Syndrome 3	DGUOK	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,500
Mitochondrial DNA Depletion Syndrome 4A and 4B and other POLG-Related Disorders	POLG	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 180
Mitochondrial DNA Depletion Syndrome 5	SUCLA2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 152,000

Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	MPV17	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	PUS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 333,000
Mitochondrial Trifunctional Protein Deficiency (HADHB-Related)	HADHB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Molybdenum Cofactor Deficiency A	MOCS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 215,000
Mucopolipidosis II / IIIA	GNPTAB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Mucopolipidosis III Gamma	GNPTG	AR	Reduced Risk	Personalized Residual Risk: 1 in 213,000
Mucopolipidosis IV	MCOLN1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,500
Mucopolysaccharidosis Type I	IDUA	AR	Reduced Risk	Personalized Residual Risk: 1 in 630
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 700
Mucopolysaccharidosis Type IIIB	NAGLU	AR	Reduced Risk	Personalized Residual Risk: 1 in 900
Mucopolysaccharidosis Type IIIC	HGSNAT	AR	Reduced Risk	Personalized Residual Risk: 1 in 42,000
Mucopolysaccharidosis Type IIID	GNS	AR	Reduced Risk	Personalized Residual Risk: 1 in 201,000
Mucopolysaccharidosis Type IVa	GALNS	AR	Reduced Risk	Personalized Residual Risk: 1 in 440
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	GLB1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Mucopolysaccharidosis VII	GUSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Mucopolysaccharidosis type IX	HYAL1	AR	Reduced Risk	Personalized Residual Risk: 1 in 63,000
Mucopolysaccharidosis type VI	ARSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 144,000
Mulibrey Nanism	TRIM37	AR	Reduced Risk	Personalized Residual Risk: 1 in 36,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	PIGN	AR	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Multiple Pterygium Syndrome	CHRNA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Multiple Sulfatase Deficiency	SUMF1	AR	Reduced Risk	Personalized Residual Risk: 1 in 144,000
Muscle-Eye-Brain Disease and Other POMGNT1-Related Congenital Muscular Dystrophy-Dystroglycanopathies	POMGNT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,100
Myoneurogastrointestinal Encephalopathy	TYMP	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
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 5,700
Nemaline Myopathy 2	NEB	AR	Reduced Risk	Personalized Residual Risk: 1 in 300
Nephrogenic Diabetes Insipidus, Type II	AQP2	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,700
Nephrogenic Diabetes insipidus (AVPR2-related) / Nephrogenic Syndrome of Inappropriate Antidiuresis	AVPR2	XL	Reduced Risk	Personalized Residual Risk: 1 in 471,000
Nephronophthisis 2	INVS	AR	Reduced Risk	Personalized Residual Risk: 1 in 24,000
Nephrotic Syndrome (NPHS1-Related) / Congenital Finnish Nephrosis	NPHS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 980
Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome	NPHS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Neurodegeneration due to Cerebral Folate Transport Deficiency	FOLR1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	PLAA	AR	Reduced Risk	Personalized Residual Risk: 1 in 217,000
Neuronal Ceroid-Lipofuscinosis (CLN3-Related)	CLN3	AR	Reduced Risk	Personalized Residual Risk: 1 in 59,000
Neuronal Ceroid-Lipofuscinosis (CLN5-Related)	CLN5	AR	Reduced Risk	Personalized Residual Risk: 1 in 75,000
Neuronal Ceroid-Lipofuscinosis (CLN6-Related)	CLN6	AR	Reduced Risk	Personalized Residual Risk: 1 in 91,000
Neuronal Ceroid-Lipofuscinosis (CLN8-Related)	CLN8	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Neuronal Ceroid-Lipofuscinosis (MFSD8-Related)	MFSD8	AR	Reduced Risk	Personalized Residual Risk: 1 in 87,000
Neuronal Ceroid-Lipofuscinosis (PPT1-Related)	PPT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Neuronal Ceroid-Lipofuscinosis (TPP1-Related)	TPP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,000
Niemann-Pick Disease (SMPD1-Related)	SMPD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300

Niemann-Pick Disease, Type C ( <i>NPC1</i> -Related)	<i>NPC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,600
Niemann-Pick Disease, Type C ( <i>NPC2</i> -Related)	<i>NPC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Nijmegen Breakage Syndrome	<i>NBN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 214,000
Non-Syndromic Hearing Loss ( <i>GJB2</i> -Related)	<i>GJB2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 280
Oculocutaneous Albinism, Type IA / IB	<i>TYR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 220
Oculocutaneous Albinism, Type IV	<i>SLC45A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 980
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	<i>WNT10A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 900
Omenn Syndrome ( <i>RAG2</i> -Related)	<i>RAG2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 32,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	<i>DCLRE1C</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 48,000
Omenn Syndrome and other <i>RAG1</i> -Related Disorders	<i>RAG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 180
Ornithine Aminotransferase Deficiency	<i>OAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,900
Ornithine Transcarbamylase Deficiency	<i>OTC</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 103,000
Osteogenesis Imperfecta, Type XI	<i>FKBP10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,100
Osteopetrosis 1	<i>TCRG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,700
Osteopetrosis 8	<i>SNX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 215,000
Otospondylomegapiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	<i>COL11A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,800
Papillon-Lefevre Syndrome	<i>CTSC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,400
Pendred Syndrome	<i>SLC26A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 72
Peroxisome Biogenesis Disorder 3A and 3B	<i>PEX12</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 225,000
Peroxisome Biogenesis Disorder 7A and 7B	<i>PEX26</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 23,000
Polycystic Kidney Disease, Autosomal Recessive	<i>PKHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 350
Polyglandular Autoimmune Syndrome, Type 1	<i>AIRE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
Pontocerebellar Hypoplasia, Type 1A	<i>VRK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 215,000
Pontocerebellar Hypoplasia, Type 1B	<i>EXOSC3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 54,000
Pontocerebellar Hypoplasia, Type 2A and Type 4	<i>TSEN54</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,800
Pontocerebellar Hypoplasia, Type 2E	<i>VPS53</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 146,000
Pontocerebellar Hypoplasia, Type 6	<i>RARS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 52,000
Primary Carnitine Deficiency	<i>SLC22A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 600
Primary Ciliary Dyskinesia ( <i>CCDC103</i> -Related)	<i>CCDC103</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 33,000
Primary Ciliary Dyskinesia ( <i>CCDC151</i> -Related)	<i>CCDC151</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 215,000
Primary Ciliary Dyskinesia ( <i>CCDC39</i> -Related)	<i>CCDC39</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 84,000
Primary Ciliary Dyskinesia ( <i>DNAH5</i> -Related)	<i>DNAH5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 19,000
Primary Ciliary Dyskinesia ( <i>DNAI1</i> -Related)	<i>DNAI1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,300
Primary Ciliary Dyskinesia ( <i>DNAI2</i> -Related)	<i>DNAI2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 144,000
Primary Ciliary Dyskinesia ( <i>RSPH9</i> -Related)	<i>RSPH9</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 73,000
Primary Coenzyme Q10 Deficiency 7	<i>COQ4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 31,000
Primary Congenital Glaucoma 3A	<i>CYP1B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 130
Primary Hyperoxaluria, Type 1	<i>AGXT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
Primary Hyperoxaluria, Type 2	<i>GRHPR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 68,000
Primary Hyperoxaluria, Type 3	<i>HOGA1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Progressive Cerebello-Cerebral Atrophy	<i>SEPSECS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 247,000
Progressive Familial Intrahepatic Cholestasis, Type 2	<i>ABCB11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 390
Progressive Myoclonic Epilepsy, Type 1B	<i>PRICKLE1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 136,000
Progressive Pseudorheumatoid Dysplasia	<i>WISP3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 287,000
Prolidase Deficiency	<i>PEPD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,900
Propionic Acidemia ( <i>PCCA</i> -Related)	<i>PCCA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,600

<b>Propionic Acidemia (PCCB-Related)</b>	<i>PCCB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 920
<b>Pulmonary Surfactant Dysfunction</b>	<i>ABCA3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,300
<b>Pycnodysostosis</b>	<i>CTSK</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,200
<b>Pyridoxamine 5'-Phosphate Oxidase Deficiency</b>	<i>PNPO</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
<b>Pyridoxine-Dependent Epilepsy</b>	<i>ALDH7A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
<b>Pyruvate Carboxylase Deficiency</b>	<i>PC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 215,000
<b>Pyruvate Dehydrogenase E1-Alpha Deficiency</b>	<i>PDHA1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 139,000
<b>Pyruvate Dehydrogenase E1-Beta Deficiency</b>	<i>PDHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,300
<b>Renal Tubular Acidosis and Deafness</b>	<i>ATP6V1B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,800
<b>Retinitis Pigmentosa 25</b>	<i>EYS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 580
<b>Retinitis Pigmentosa 26</b>	<i>CERKL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,000
<b>Retinitis Pigmentosa 28</b>	<i>FAM161A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 145,000
<b>Retinitis Pigmentosa 36</b>	<i>PRCD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 422,000
<b>Retinitis Pigmentosa 59</b>	<i>DHDDS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 201,000
<b>Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16</b>	<i>C8ORF37</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
<b>Rh Deficiency Syndrome</b>	<i>RHAG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 94,000
<b>Rhizomelic Chondrodysplasia Punctata, Type 1</b>	<i>PEX7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 55,000
<b>Rhizomelic Chondrodysplasia Punctata, Type 3</b>	<i>AGPS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,024,000
<b>Roberts Syndrome</b>	<i>ESCO2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 95,000
<b>Salla Disease</b>	<i>SLC17A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
<b>Salt and Pepper Developmental Regression Syndrome</b>	<i>ST3GAL5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 108,000
<b>Sandhoff Disease</b>	<i>HEXB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 680
<b>Schimke Immunoosseous Dysplasia</b>	<i>SMARCAL1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 56,000
<b>Seckel Syndrome 5 / Microcephaly 9</b>	<i>CEP152</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
<b>Segawa Syndrome</b>	<i>TH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,000
<b>Sepiapterin Reductase Deficiency</b>	<i>SPR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 43,000
<b>Severe Combined Immunodeficiency (IL7R-Related)</b>	<i>IL7R</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 48,000
<b>Severe Combined Immunodeficiency (JAK3-Related)</b>	<i>JAK3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
<b>Severe Combined Immunodeficiency (PTPRC-Related)</b>	<i>PTPRC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,300
<b>Severe Congenital Neutropenia 4</b>	<i>G6PC3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 296,000
<b>Severe Neonatal Hyperparathyroidism</b>	<i>CASR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 216,000
<b>Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis</b>	<i>POC1A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 98,000
<b>Short-Chain Acyl-CoA Dehydrogenase Deficiency</b>	<i>ACADS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 340
<b>Shwachman-Diamond Syndrome</b>	<i>SBDS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
<b>Sialidosis, Type I and Type II</b>	<i>NEU1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,700
<b>Sjogren-Larsson Syndrome</b>	<i>ALDH3A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
<b>Smith-Lemli-Opitz Syndrome</b>	<i>DHCR7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
<b>Spastic Paraplegia 15</b>	<i>ZFYVE26</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
<b>Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly</b>	<i>SLC1A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 136,000
<b>Spherocytosis, Type 5</b>	<i>EPB42</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
<b>Spinal Muscular Atrophy</b>	<i>SMN1</i>	AR	Reduced Risk	SMN1 copy number: 2 SMN2 copy number: 2 c.3+80T>G: Negative SMN1 Sequencing: Negative <b>Personalized Residual Risk:</b> 1 in 1,115
<b>Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S</b>	<i>IGHMBP2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100

Spinocerebellar Ataxia with Axonal Neuropathy 3	COA7	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Spondylocostal Dysostosis 1	DLL3	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 156,000
Spondylometaphyseal Dysplasia (DDR2-Related)	DDR2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 220,000
Spondylothoracic Dysostosis	MESP2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 53,000
Steel Syndrome	COL27A1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 275,000
Stuve-Wiedemann Syndrome	LIFR	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
Sulfate Transporter-Related Osteochondrodysplasia	SLC26A2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,000
Tay-Sachs Disease	HEXA	AR	Reduced Risk	Tay-Sachs disease enzyme: Non-carrier White blood cells: Non-carrier • Hex A%: 59.6% (Non-carrier : 55.0 - 72.0%; Carrier: < 50.0%) • Total hexosaminidase activity: 1751 nmoL/hr/mg HEXA Sequencing: Negative <b>Personalized Residual Risk:</b> 1 in 2,700
Thiamine-Responsive Megaloblastic Anemia Syndrome	SLC19A2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 63,000
Thyroid Dysmorphogenesis 1	SLC5A5	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,300
Thyroid Dysmorphogenesis 2A	TPO	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 350
Thyroid Dysmorphogenesis 3	TG	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 130
Thyroid Dysmorphogenesis 4	IYD	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,900
Thyroid Dysmorphogenesis 5	DUOXA2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Trichohepatoenteric Syndrome 1	TTC37	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Tyrosinemia, Type I	FAH	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,900
Tyrosinemia, Type II	TAT	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,200
Tyrosinemia, Type III	HPD	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Usher Syndrome, Type IB	MYO7A	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 180
Usher Syndrome, Type IC	USH1C	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 400
Usher Syndrome, Type ID	CDH23	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 880
Usher Syndrome, Type IF	PCDH15	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Usher Syndrome, Type IIA	USH2A	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 54
Usher Syndrome, Type III	CLRN1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,800
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	ACADVL	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 380
Vitamin D-Dependent Rickets, Type I	CYP27B1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
Vitamin D-Resistant Rickets, Type IIA	VDR	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 21,000
Walker-Warburg Syndrome and Other FKTN-Related Dystrophies	FKTN	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 390
Werner Syndrome	WRN	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,000
Wilson Disease	ATP7B	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 150
Wiskott-Aldrich Syndrome (WAS-Related)	WAS	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,203,000
Wolcott-Rallison Syndrome	EIF2AK3	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 287,000
Wolman Disease / Cholesteryl Ester Storage Disease	LIPA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 32,000
Woodhouse-Sakati Syndrome	DCAF17	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 59,000
X-Linked Juvenile Retinoschisis	RS1	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
X-Linked Severe Combined Immunodeficiency	IL2RG	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 250,000
Xeroderma Pigmentosum (POLH-Related)	POLH	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
Xeroderma Pigmentosum, Group A	XPA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 170,000
Xeroderma Pigmentosum, Group C	XPC	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Xeroderma Pigmentosum, Group G	ERCC5	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,900

<b>Zellweger Syndrome Spectrum (PEX10-Related)</b>	<i>PEX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 218,000</b>
<b>Zellweger Syndrome Spectrum (PEX1-Related)</b>	<i>PEX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 740</b>
<b>Zellweger Syndrome Spectrum (PEX2-Related)</b>	<i>PEX2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 108,000</b>
<b>Zellweger Syndrome Spectrum (PEX6-Related)</b>	<i>PEX6</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,500</b>

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. AmpliX<sup>®</sup> *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<sup>®</sup> 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<sup>®</sup> 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 2+0 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.\*3+80T>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.\*3+80T>G is likely indicative of a silent (2+0) carrier. In individuals with two copies of *SMN1* with African American, Hispanic or Caucasian ancestry, the presence or absence of c.\*3+80T>G significantly increases or decreases, respectively, the likelihood of being a silent 2+0 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™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.

**Exceptions:** *ABCD1* (NM\_000033.3) exons 8 and 9; *ACADSB* (NM\_001609.3) chr10:124,810,695-124,810,707 (partial exon 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); *ALDH7A1* (NM\_001182.4) chr5:125,911,150-125,911,163 (partial exon 7) and chr5:125,896,807-125,896,821 (partial exon 10); *ALMS1* (NM\_015120.4) chr2:73,612,990-73,613,041 (partial exon 1); *APOPT1* (NM\_032374.4) chr14:104,040,437-104,040,455 (partial exon 3); *CDAN1* (NM\_138477.2) exon 2; *CEP152* (NM\_014985.3) chr15:49,061,146-49,061,165 (partial exon 14) and exon 22; *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); *COX10* (NM\_001303.3) exon 6; *CYP11B1* (NM\_000497.3) exons 3-7; *CYP11B2* (NM\_000498.3) exons 3-7; *DNAI2* (NM\_023036.4) chr17:72,308,136-72,308,147 (partial exon 12); *DOK7* (NM\_173660.4) chr4:3,465,131-3,465,161 (partial exon 1) and exon 2; *DUOX2* (NM\_014080.4) exons 6-8; *EIF2AK3* (NM\_004836.5) exon 8; *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; *GHR* (NM\_000163.4) exon 3; *GYS2* (NM\_021957.3) chr12:21,699,370-21,699,409 (partial exon 12); *HGSNAT* (NM\_152419.2) exon 1; *IDS* (NM\_000202.6) exon 3; *ITGB4* (NM\_000213.4) chr17:73,749,976-73,750,060 (partial exon 33); *JAK3* (NM\_000215.3) chr19:17,950,462-17,950,483 (partial exon 10); *LIFR* (NM\_002310.5) exon 19; *LMBRD1* (NM\_018368.3) chr6:70,459,226-70,459,257 (partial exon 5), chr6:70,447,828-70,447,836 (partial exon 7) and exon 12; *LYST* (NM\_000081.3) chr1:235,944,158-235,944,176 (partial exon 16) and chr1:235,875,350-235,875,362 (partial exon 43); *MLYCD* (NM\_012213.2) chr16:83,933,242-83,933,282 (partial exon 1); *MTR* (NM\_000254.2) chr1:237,024,418-237,024,439 (partial exon 20) and chr1:237,038,019-237,038,029 (partial exon 24); *NBEAL2* (NM\_015175.2) chr3:47,021,385-47,021,407 (partial exon 1); *NEB* (NM\_001271208.1) exons 82-105; *NPC1* (NM\_000271.4) chr18:21,123,519-21,123,538 (partial exon 14); *NPHP1* (NM\_000272.3) chr2:110,937,251-110,937,263 (partial exon 3); *OCRL* (NM\_000276.3) chrX:128,674,450-128,674,460 (partial exon 1); *PHKB* (NM\_000293.2) exon 1 and chr16:47,732,498-47,732,504 (partial exon 30); *PIGN* (NM\_176787.4) chr18:59,815,547-59,815,576 (partial exon 8); *PIP5K1C* (NM\_012398.2) exon 1 and chr19:3637602-3637616 (partial exon 17); *POU1F1* (NM\_000306.3) exon 5; *PTPRC* (NM\_002838.4) exons 11 and 23; *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; *ST3GAL5* (NM\_003896.3) exon 1; *SURF1* (NM\_003172.3) chr9:136,223,269-136,223,307 (partial exon 1); *TRPM6* (NM\_017662.4) chr9:77,362,800-77,362,811 (partial exon 31); *TSEN54* (NM\_207346.2) exon 1; *TYR* (NM\_000372.4) exon 5; *VWF* (NM\_000552.3) exons 24-26, chr12:6,125,675-6,125,684 (partial exon 30), chr12:6,121,244-6,121,265 (partial exon 33), and exon 34.

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  $\Delta\Delta C_t$  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 (cis/trans 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<sup>TM</sup>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<sup>th</sup> "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.

### Tay-Sachs Disease (TSD) Enzyme Analysis (Analytical Detection Rate $\geq$ 98%)

Hexosaminidase activity and Hex A% activity were measured by a standard heat-inactivation, fluorometric method using artificial 4-MU- $\beta$ -N-acetyl glucosaminide (4-MUG) substrate. This assay is highly sensitive and accurate in detecting Tay-Sachs carriers and individuals affected with TSD. Normal ranges of Hex A% activity are 55.0-72.0 for white blood cells and 58.0-72.0 for plasma. It is estimated that less than 0.5% of Tay-Sachs carriers have non-carrier levels of percent Hex A activity, and therefore may not be identified by this assay. In addition, this assay may detect individuals that are carriers of or are affected with Sandhoff disease. False positive results may occur if benign variants, such as pseudodeficiency alleles, interfere with the enzymatic assay. False negative results may occur if both *HEXA* and *HEXB* pathogenic or pseudodeficiency variants are present in the same individual.

Please note these tests were developed and their performance characteristics were determined by Sema4 Opco, 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.

## 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.

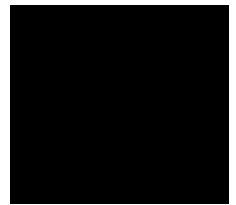
### Duchenne Muscular Dystrophy:

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:

**6390, Donor**

**DOB:** [REDACTED]

Sex: M

MR#: 6390

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. Amar Jariwala

Report Date: **Jan 25, 2025**

Accession:

[REDACTED]

Test#: [REDACTED]

Specimen Type: DNA

Collected: Not Provided

Accession:

**N/A**

## FINAL RESULTS



No carrier mutations identified

## TEST PERFORMED

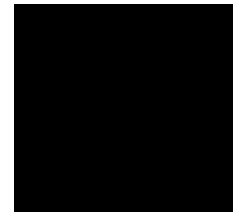
### Single Gene Carrier Screening: *MCPH1*

(1 Gene Panel: *MCPH1*; 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.
- 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>)



## GENES TESTED:

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### Custom Beacon Carrier Screening Panel - Gene

This analysis was run using the Custom Beacon Carrier Screening Panel gene list. 1 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.

*MCPH1*

## METHODS:

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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:

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### General Limitations

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



### Gene Specific Notes and Limitations

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

### SIGNATURE:

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A handwritten signature in black ink that reads "Harry Gao".

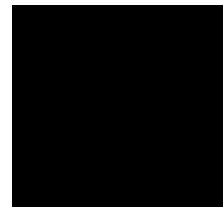
**Dr. Harry Gao, DABMG, FACMG** on 1/25/2025  
Laboratory Director, Fulgent

### DISCLAIMER:

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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](mailto: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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To view the supplemental table describing the carrier frequencies, detection rates, and residual risks associated with the genes tested on any Beacon panel, please visit the following link:

[Beacon Expanded Carrier Screening Supplemental Table](#)

