



## Donor 6797

### Genetic Testing Summary

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

Last Updated: 01/18/23

Donor Reported Ancestry: Japanese, Polish, Hungarian, German, Czech, Russian

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: Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome (NPHS2)</p> <p>Carrier: Retinitis Pigmentosa 25 (EYS)</p> <p>Carrier: Wolman Disease / Cholesteryl Ester Storage Disease (LIPA)</p> <p>Negative for other genes sequenced</p>	Partner testing recommended before using this donor.

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

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

**Patient Information**

Name: Donor 6797  
 Date of Birth: [REDACTED]  
 Sema4 ID: [REDACTED]  
 Client ID: [REDACTED]  
 Indication: Carrier Screening

**Specimen Information**

Specimen Type: Blood  
 Date Collected: 07/08/2022  
 Date Received: 07/09/2022  
 Final Report: 07/22/2022

**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><b>Carrier of Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome (AR)</b>            Associated gene(s): <i>NPHS2</i>            Variant(s) Detected: c.686G&gt;A, p.R229Q, Pathogenic, Heterozygous (one copy)</p> <p><b>Carrier of Retinitis Pigmentosa 25 (AR)</b>            Associated gene(s): <i>EYS</i>            Variant(s) Detected: c.2528G&gt;A, p.G843E, Pathogenic, Heterozygous (one copy)</p> <p><b>Carrier of Wolman Disease / Cholesteryl Ester Storage Disease (AR)</b>            Associated gene(s): <i>LIPA</i>            Variant(s) Detected: c.894G&gt;A, p.Q298=, Pathogenic, Heterozygous (one copy)</p>	<p><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. Please note that residual risks for X-linked diseases (including full repeat expansions for Fragile X syndrome) may not be accurate for males and the actual residual risk is likely to be lower.

## Interpretation of positive results

### Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome (AR)

#### Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.686G>A, p.R229Q, was detected in the *NPHS2* gene (NM\_014625.3). Please note that this is a mild variant that is only expected to cause disease when found in trans with one of a specific set of variants that occurs in exons 7 or 8. Please see the disease interpretation below for additional information. Homozygotes are not expected to be affected, unless this variant is part of a more complex allele. When this variant is present in trans with a pathogenic variant, it is considered to be causative for an *NPHS2*-related disorder. Therefore, this individual is expected to be at least a carrier for an *NPHS2*-related disorder. Heterozygous carriers are not expected to exhibit symptoms of this disease.

#### What is Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome?

Pathogenic variants in the *NPHS2* gene cause two autosomal recessive, pan-ethnic disorders: steroid-resistant nephrotic syndrome and focal segmental glomerulosclerosis.

- Steroid-resistant nephrotic syndrome (SRNS) is a severe disorder with onset usually occurring during childhood. Patients lose protein in their urine, which results in progressive kidney failure. Death will occur without a kidney transplant, usually by adolescence; however, many patients are cured after kidney transplant.
- Focal segmental glomerulosclerosis (FSGS) is a type of scarring of the kidney, and is usually diagnosed in the patient's second or third decade of life. FSGS is more slowly progressing than SRNS and usually leads to end-stage renal disease by the ages of 10-50.

Mutations in *NPHS2* have been demonstrated to have a complex genotype-phenotype correlation. A common pathogenic variant, p.R229Q, causes FSGS when found in trans with a number of specific variants, including p.A284V, p.A288T, p.R291W, p.A297V, p.E310K, p.E310V, p.L327F, p.Q328R, and p.F344LfsX4. While all of the variants that are disease-causing when in trans with R229Q are located in exons 7 and 8, not all pathogenic variants in exons 7 and 8 cause disease when in trans with R229Q. Examples of variants in exons 7 and 8 that do not cause disease when in trans with R229Q are p.R286TfsX17, p.V290M, and p.A317LfsX31. Additionally, p.R229Q is not disease-causing in the homozygous state (PMID: 24509478 and 29660491).

### Retinitis Pigmentosa 25 (AR)

#### Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.2528G>A, p.G843E, was detected in the *EYS* gene (NM\_001142800.1). When this variant is present in trans with a pathogenic variant, it is considered to be causative for retinitis pigmentosa 25. Therefore, this individual is expected to be at least a carrier for retinitis pigmentosa 25. Heterozygous carriers are not expected to exhibit symptoms of this disease.

#### What is Retinitis Pigmentosa 25?

Retinitis pigmentosa 25 is an autosomal recessive disorder caused by pathogenic variants in the gene *EYS*. While it has been reported in populations worldwide, it is more prevalent in Spain and Sephardic Jewish populations from Morocco. Retinitis pigmentosa begins with the onset of night blindness in childhood, and progresses to tunnel vision and blindness in adulthood. Age of onset and severity of vision loss may vary between patients. Life expectancy is not reduced. No genotype-phenotype correlation has been reported.

### Wolman Disease / Cholesteryl Ester Storage Disease (AR)

#### Results and Interpretation

A heterozygous (one copy) pathogenic synonymous variant, c.894G>A, p.Q298=, was detected in the *LIPA* gene (NM\_000235.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for lysosomal acid lipase deficiency. Therefore, this individual is expected to be at least a carrier for lysosomal acid lipase deficiency. Heterozygous carriers are not expected to exhibit symptoms of this disease.

#### What is Wolman Disease / Cholesteryl Ester Storage Disease?

Lysosomal acid lipase deficiency consists of two disorders known as Wolman disease and cholesterol ester storage disease. Both diseases are caused by pathogenic variants in the gene *LIPA* and are inherited in an autosomal recessive manner. While reported in multiple ethnicities, it is most prevalent in Sephardic Jewish individuals from Iran due to the presence of a founder mutation.

- Cholesterol ester storage disease is the more common form. In this disease, blood cells known as macrophages become filled with cholesteryl esters, which cause increased levels of cholesterol in the blood and progressive liver disease. Buildup of cholesterol in the arteries may also occur. This disease can present early and lead to death in childhood or adolescence due to cirrhosis of the liver, or it may have a late onset with survival into adulthood.
- Wolman disease begins in infancy and has a more severe phenotype than cholesterol ester storage disease. Death occurs in infancy due to multi-organ failure caused by cholesterol infiltration and buildup.
- Pathogenic *LIPA* variants that result in a protein with some residual function are more likely to result in cholesterol ester storage disease rather than Wolman disease. Depending on the specific variants identified, it may be possible to predict whether a patient will develop Wolman disease or cholesterol ester storage disease.

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

*Hongli Zhan*

**Hongli Zhan, Ph.D., Director**

Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D

## Genes and diseases tested

The personalized residual risks listed below are specific to this individual. The complete residual risk table is available at [go.sema4.com/residualrisk](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>				
Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome	NPHS2	AR	Carrier	c.686G>A, p.R229Q, Pathogenic, Heterozygous (one copy)
Retinitis Pigmentosa 25	EYS	AR	Carrier	c.2528G>A, p.G843E, Pathogenic, Heterozygous (one copy)
Wolman Disease / Cholesteryl Ester Storage Disease	LIPA	AR	Carrier	c.894G>A, p.Q298-, Pathogenic, Heterozygous (one copy)
<b>Negative</b>				
2-Methylbutyrylglycinuria	ACADSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 410
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	HSD3B2	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related)	MCCC1	AR	Reduced Risk	Personalized Residual Risk: 1 in 930
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)	MCCC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 500
3-Methylglutaconic Aciduria, Type III	OPA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000
3-Phosphoglycerate Dehydrogenase Deficiency	PHGDH	AR	Reduced Risk	Personalized Residual Risk: 1 in 63,000
6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	PTS	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
CD59-Mediated Hemolytic Anemia	CD59	AR	Reduced Risk	Personalized Residual Risk: 1 in 415,000
Abetalipoproteinemia	MTTP	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Achalasia-Addisonianism-Alacrimia Syndrome	AAAS	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,500
Achromatopsia (CNGA3-Related)	CNGA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 320
Achromatopsia (CNGB3-related)	CNGB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,600
Acrodermatitis Enteropathica	SLC39A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Acute Infantile Liver Failure	TRMU	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,400
Acyl-CoA Oxidase I Deficiency	ACOX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 39,000
Adams-Oliver Syndrome 4	EOGT	AR	Reduced Risk	Personalized Residual Risk: 1 in 44,000
Adenosine Deaminase Deficiency	ADA	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,100
Adrenocorticotrophic Hormone Deficiency	TBX19	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,500
Adrenoleukodystrophy, X-Linked	ABCD1	XL	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Agammaglobulinemia	BTK	XL	Reduced Risk	Personalized Residual Risk: 1 in 250,000
Agenesis of the Corpus Callosum	FRMD4A	AR	Reduced Risk	Personalized Residual Risk: 1 in 348,000
Aicardi-Goutieres Syndrome (RNASEH2C-Related)	RNASEH2C	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Aicardi-Goutieres Syndrome (SAMHD1-Related)	SAMHD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Aicardi-Goutieres Syndrome (TREX1-Related)	TREX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Albinism, Oculocutaneous, Type III	TYRP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 430
Alkaptonuria	HGD	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Alpha-Mannosidosis	MAN2B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,200



Alpha-Thalassemia	HBA1/HBA2	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: 1 in 380</b>
Alpha-Thalassemia Intellectual Disability Syndrome	ATRX	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 48,000</b>
Alport Syndrome (COL4A3-Related)	COL4A3	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,700</b>
Alport Syndrome (COL4A4-Related)	COL4A4	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 510</b>
Alport Syndrome (COL4A5-Related)	COL4A5	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 150,000</b>
Alstrom Syndrome	ALMS1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,100</b>
Andermann Syndrome	SLC12A6	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 151,000</b>
Antley-Bixler Syndrome (POR-Related)	POR	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 650</b>
Argininemia	ARG1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,900</b>
Argininosuccinic Aciduria	ASL	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,200</b>
Aromatase Deficiency	CYP19A1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,200</b>
Arthrogryposis, Intellectual Disability, and Seizures	SLC35A3	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 240,000</b>
Asparagine Synthetase Deficiency	ASNS	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 178,000</b>
Aspartylglycosaminuria	AGA	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 13,000</b>
Ataxia With Isolated Vitamin E Deficiency	TTPA	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 20,000</b>
Ataxia-Telangiectasia	ATM	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 540</b>
Ataxia-Telangiectasia-Like Disorder 1	MRE11	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,500</b>
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	SACS	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
BH4-Deficient Hyperphenylalaninemia C	QDPR	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,100</b>
BH4-Deficient Hyperphenylalaninemia D	PCBD1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 8,000</b>
Bardet-Biedl Syndrome (ARL6-Related)	ARL6	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,300</b>
Bardet-Biedl Syndrome (BBS10-Related)	BBS10	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
Bardet-Biedl Syndrome (BBS12-Related)	BBS12	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 9,900</b>
Bardet-Biedl Syndrome (BBS1-Related)	BBS1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,400</b>
Bardet-Biedl Syndrome (BBS2-Related)	BBS2	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,200</b>
Bardet-Biedl Syndrome (BBS4-Related)	BBS4	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 22,000</b>
Bare Lymphocyte Syndrome, Type II	CIITA	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 35,000</b>
Barth Syndrome	TAZ	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 183,000</b>
Bartter Syndrome, Type 3	CLCNKB	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 710</b>
Bartter Syndrome, Type 4A	BSND	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 69,000</b>
Bernard-Soulier Syndrome, Type A1	GP1BA	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 42,000</b>
Bernard-Soulier Syndrome, Type C	GP9	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
Beta-Globin-Related Hemoglobinopathies	HBB	AR	Reduced Risk	<b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies): 1 in 1,200</b> <b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant): 1 in 11,000</b> <b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant): 1 in 42,000</b>
Beta-Ketothiolase Deficiency	ACAT1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,800</b>
Beta-Mannosidosis	MANBA	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 9,100</b>
Bilateral Frontoparietal Polymicrogyria	GPR56	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 143,000</b>
Biotinidase Deficiency	BTBD	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 500</b>
Bloom Syndrome	BLM	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,400</b>
Canavan Disease	ASPA	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,000</b>
Carbamoylphosphate Synthetase I Deficiency	CPS1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 690</b>

Carnitine Acylcarnitine Translocase Deficiency	<i>SLC25A20</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,100
Carnitine Palmitoyltransferase IA Deficiency	<i>CPT1A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 24,000
Carnitine Palmitoyltransferase II Deficiency	<i>CPT2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 670
Carpenter Syndrome	<i>RAB23</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
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 5,900
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 2,100
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 7,100
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 2,500
Cockayne Syndrome, Type A	<i>ERCC8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,900
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 6,400
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 2,400
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 2,800
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 44,000
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 520
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</p> <p>Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)): 1 in 200</p> <p>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 6,100

<b>Congenital Amegakaryocytic Thrombocytopenia</b>	<i>MPL</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,100</b>
<b>Congenital Bile Acid Synthesis Defect (AKR1D1-Related)</b>	<i>AKR1D1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,900</b>
<b>Congenital Bile Acid Synthesis Defect (HSD3B7-Related)</b>	<i>HSD3B7</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,700</b>
<b>Congenital Disorder of Deglycosylation</b>	<i>NGLY1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,000</b>
<b>Congenital Disorder of Glycosylation, Type Ia</b>	<i>PMM2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 540</b>
<b>Congenital Disorder of Glycosylation, Type Ib</b>	<i>MPI</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
<b>Congenital Disorder of Glycosylation, Type Ic</b>	<i>ALG6</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,300</b>
<b>Congenital Disorder of Glycosylation, Type Im</b>	<i>DOLK</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 134,000</b>
<b>Congenital Dyserythropoietic Anemia Type 2</b>	<i>SEC23B</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,000</b>
<b>Congenital Dyserythropoietic Anemia, Type Ia</b>	<i>CDAN1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 470</b>
<b>Congenital Ichthyosis 4A and 4B</b>	<i>ABCA12</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,500</b>
<b>Congenital Insensitivity to Pain with Anhidrosis</b>	<i>NTRK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,000</b>
<b>Congenital Muscular Dystrophy (LAMA2-Related)</b>	<i>LAMA2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 640</b>
<b>Congenital Myasthenic Syndrome (CHAT-Related)</b>	<i>CHAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,500</b>
<b>Congenital Myasthenic Syndrome (CHRNE-Related)</b>	<i>CHRNE</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,100</b>
<b>Congenital Myasthenic Syndrome (DOK7-Related)</b>	<i>DOK7</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 470</b>
<b>Congenital Myasthenic Syndrome (RAPSN-Related)</b>	<i>RAPSN</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,900</b>
<b>Congenital Neutropenia (HAX1-Related)</b>	<i>HAX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 82,000</b>
<b>Congenital Neutropenia (VPS45-Related)</b>	<i>VPS45</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 110,000</b>
<b>Congenital Nongoitrous Hypothyroidism 1</b>	<i>TSHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 230</b>
<b>Congenital Nongoitrous Hypothyroidism 4</b>	<i>TSHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 118,000</b>
<b>Congenital Secretory Chloride Diarrhea 1</b>	<i>SLC26A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,400</b>
<b>Corneal Dystrophy and Perceptive Deafness</b>	<i>SLC4A11</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,200</b>
<b>Corticosterone Methyloxidase Deficiency</b>	<i>CYP11B2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,500</b>
<b>Cystic Fibrosis</b>	<i>CFTR</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 440</b>
<b>Cystinosis</b>	<i>CTNS</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,100</b>
<b>Cystinuria (SLC3A1-Related)</b>	<i>SLC3A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 530</b>
<b>Cytochrome C Oxidase Deficiency / Leigh Syndrome (COX15-Related)</b>	<i>COX15</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,300</b>
<b>D-Bifunctional Protein Deficiency</b>	<i>HSD17B4</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,700</b>
<b>Deafness, Autosomal Recessive 3</b>	<i>MYO15A</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 100</b>
<b>Deafness, Autosomal Recessive 59</b>	<i>PJVK</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 57,000</b>
<b>Deafness, Autosomal Recessive 7</b>	<i>TMC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
<b>Deafness, Autosomal Recessive 76</b>	<i>SYNE4</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 43,000</b>
<b>Deafness, Autosomal Recessive 77</b>	<i>LOXHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,800</b>
<b>Deafness, Autosomal Recessive 8/10</b>	<i>TMPPRS3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 330</b>
<b>Deafness, Autosomal Recessive 9</b>	<i>OTOF</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 370</b>
<b>Desbuquois Dysplasia 1</b>	<i>CANT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,800</b>
<b>Desmosterolosis</b>	<i>DHCR24</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 27,000</b>
<b>Diaphanospondylodysostosis</b>	<i>BMPER</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 18,000</b>
<b>Distal Renal Tubular Acidosis and other SLC4A1-related Disorders</b>	<i>SLC4A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 910</b>
<b>Duchenne Muscular Dystrophy / Becker Muscular Dystrophy</b>	<i>DMD</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 10,000</b>
<b>Dyskeratosis Congenita (DKC1-related)</b>	<i>DKC1</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 9,259,000</b>
<b>Dyskeratosis Congenita (RTEL1-Related)</b>	<i>RTEL1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,900</b>
<b>Dystrophic Epidermolysis Bullosa</b>	<i>COL7A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 900</b>



Ehlers-Danlos Syndrome, Type VI	<i>PLOD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,700
Ehlers-Danlos Syndrome, Type VIIC	<i>ADAMTS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 63,000
Ellis-Van Creveld Syndrome ( <i>EVC2</i> -Related)	<i>EVC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,100
Ellis-van Creveld Syndrome ( <i>EVC</i> -Related)	<i>EVC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,200
Emery-Dreifuss Myopathy 1	<i>EMD</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 833,000
Enhanced S-Cone Syndrome	<i>NR2E3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
Ethylmalonic Encephalopathy	<i>ETHE1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,400
Fabry Disease	<i>GLA</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,700
Factor IX Deficiency	<i>F9</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,100
Factor VII Deficiency	<i>F7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 300
Factor XI Deficiency	<i>F11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 440
Familial Autosomal Recessive Hypercholesterolemia	<i>LDLRAP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 136,000
Familial Dysautonomia	<i>IKBKAP</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 51,000
Familial Hypercholesterolemia	<i>LDLR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 260
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	<i>HADH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,000
Familial Hyperinsulinism ( <i>ABCC8</i> -Related)	<i>ABCC8</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 240
Familial Hyperinsulinism ( <i>KCNJ11</i> -Related)	<i>KCNJ11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
Familial Hyperphosphatemic Tumoral Calcinosis	<i>GALNT3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
Familial Mediterranean Fever	<i>MEFV</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Fanconi Anemia, Group A	<i>FANCA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Fanconi Anemia, Group C	<i>FANCC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Fanconi Anemia, Group G	<i>FANCG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Fanconi-Bickel Syndrome	<i>SLC2A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,000
Fragile X Syndrome	<i>FMR1</i>	XL	Reduced Risk	<i>FMR1</i> CGG repeat sizes: Not Performed <i>FMR1</i> 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. <b>Personalized Residual Risk:</b> 1 in 19,000
Fructose-1,6-Bisphosphatase Deficiency	<i>FBP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,600
Fucosidosis	<i>FUCA1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,200
Fumarase Deficiency	<i>FH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,500
Fundus Albipunctatus	<i>RDH5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 810
GRACILE Syndrome and Other <i>BCS1L</i> -Related Disorders	<i>BCS1L</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,900
Galactokinase Deficiency	<i>GALK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
Galactose Epimerase Deficiency	<i>GALE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 850
Galactosemia	<i>GALT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 390
Galactosialidosis	<i>CTSA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,900
Gaucher Disease	<i>GBA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Generalized Thyrotropin-Releasing Hormone Resistance	<i>TRHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 104,000
Geroderma Osteodysplasticum	<i>GORAB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 70,000
Gitelman Syndrome	<i>SLC12A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 230
Glanzmann Thrombasthenia ( <i>ITGA2B</i> -Related)	<i>ITGA2B</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Glanzmann Thrombasthenia ( <i>ITGB3</i> -Related)	<i>ITGB3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Glutaric Acidemia, Type I	<i>GCDH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Glutaric Acidemia, Type IIa	<i>ETFA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
Glutaric Acidemia, Type IIb	<i>ETFB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,900
Glutaric Acidemia, Type IIc	<i>ETFDH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 260
Glutathione Synthetase Deficiency	<i>GSS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,500

Glycine Encephalopathy (AMT-Related)	AMT	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,700
Glycine Encephalopathy (GLDC-Related)	GLDC	AR	Reduced Risk	Personalized Residual Risk: 1 in 240
Glycogen Storage Disease, Type 0	GYS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Glycogen Storage Disease, Type II	GAA	AR	Reduced Risk	Personalized Residual Risk: 1 in 280
Glycogen Storage Disease, Type III	AGL	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,600
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	GBE1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Glycogen Storage Disease, Type IXb	PHKB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Glycogen Storage Disease, Type Ia	G6PC	AR	Reduced Risk	Personalized Residual Risk: 1 in 410
Glycogen Storage Disease, Type Ib	SLC37A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,900
Glycogen Storage Disease, Type V	PYGM	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Glycogen Storage Disease, Type VI	PYGL	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Glycogen Storage Disease, Type VII	PFKM	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Gray Platelet Syndrome	NBEAL2	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,800
Growth Hormone Deficiency, Type IB	GHRHR	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,900
HMG-CoA Lyase Deficiency	HMGCL	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Hemochromatosis, Type 2A	HFE2	AR	Reduced Risk	Personalized Residual Risk: 1 in 740
Hemochromatosis, Type 3	TFR2	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Hereditary Fructose Intolerance	ALDOB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Hereditary Spastic Paraparesis 49	TECPR2	AR	Reduced Risk	Personalized Residual Risk: 1 in 116,000
Hermansky-Pudlak Syndrome, Type 1	HPS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Hermansky-Pudlak Syndrome, Type 3	HPS3	AR	Reduced Risk	Personalized Residual Risk: 1 in 22,000
Hermansky-Pudlak Syndrome, Type 4	HPS4	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Hermansky-Pudlak Syndrome, Type 6	HPS6	AR	Reduced Risk	Personalized Residual Risk: 1 in 680
Hmg-CoA Synthase 2 Deficiency	HMGCS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Holocarboxylase Synthetase Deficiency	HLCS	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Homocystinuria (CBS-Related)	CBS	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Homocystinuria due to MTHFR Deficiency	MTHFR	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Homocystinuria, cblE Type	MTRR	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,600
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	MTR	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Hydrocephalus	L1CAM	XL	Reduced Risk	Personalized Residual Risk: 1 in 40,000
Hydroletharus Syndrome	HYLS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 52,000
Hyper-Igm Syndrome	CD40LG	XL	Reduced Risk	Personalized Residual Risk: 1 in 1,167,000
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	SLC25A15	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,700
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	SARS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 23,000
Hypohidrotic Ectodermal Dysplasia 1	EDA	XL	Reduced Risk	Personalized Residual Risk: 1 in 22,000
Hypomagnesemia 1	TRPM6	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Hypomyelinating Leukodystrophy 3	AIMP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 273,000
Hypomyelinating Leukodystrophy 12	VPS11	AR	Reduced Risk	Personalized Residual Risk: 1 in 72,000
Hypoparathyroidism-Retardation-Dysmorphic Syndrome	TBCE	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Hypophosphatasia	ALPL	AR	Reduced Risk	Personalized Residual Risk: 1 in 790
Hypophosphatemic Rickets with Hypercalciuria	SLC34A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Hypotrichosis 8 / Autosomal Recessive Woolly Hair 1	LPAR6	AR	Reduced Risk	Personalized Residual Risk: 1 in 17,000
Immunodeficiency 18	CD3E	AR	Reduced Risk	Personalized Residual Risk: 1 in 73,000
Immunodeficiency 19	CD3D	AR	Reduced Risk	Personalized Residual Risk: 1 in 46,000
Inclusion Body Myopathy 2	GNE	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Infantile Cerebral and Cerebellar Atrophy	MED17	AR	Reduced Risk	Personalized Residual Risk: 1 in 129,000



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	<b>Personalized Residual Risk: 1 in 2,000</b>
Joubert Syndrome 2	TMEM216	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 133,000</b>
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	NPHP1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,000</b>
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	RPGRIP1L	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
Junctional Epidermolysis Bullosa (COL17A1-Related)	COL17A1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,200</b>
Junctional Epidermolysis Bullosa (ITGA6-Related)	ITGA6	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 125,000</b>
Junctional Epidermolysis Bullosa (ITGB4-Related)	ITGB4	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,400</b>
Junctional Epidermolysis Bullosa (LAMA3-Related)	LAMA3	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 21,000</b>
Junctional Epidermolysis Bullosa (LAMB3-Related)	LAMB3	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,900</b>
Junctional Epidermolysis Bullosa (LAMC2-Related)	LAMC2	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 28,000</b>
Kohlschutter-Tonz Syndrome	ROGDI	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,300</b>
Krabbe Disease	GALC	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 340</b>
Lamellar Ichthyosis, Type 1	TGM1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,500</b>
Laron Dwarfism	GHR	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	CEP290	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
Leber Congenital Amaurosis 13	RDH12	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,500</b>
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	TULP1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,600</b>
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	RPE65	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
Leber Congenital Amaurosis 4	AIPL1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
Leber Congenital Amaurosis 5	LCA5	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,200</b>
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	CRB1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 960</b>
Leigh Syndrome (NDUFS7-Related)	NDUFS7	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 26,000</b>
Leigh Syndrome (SURF1-Related)	SURF1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,000</b>
Leigh Syndrome, French-Canadian Type	LRPPRC	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 22,000</b>
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogyposis with Anterior Horn Cell Disease	GLE1	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,900</b>
Lethal Congenital Contracture Syndrome 2	ERBB3	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 52,000</b>
Lethal Congenital Contracture Syndrome 3	PIP5K1C	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 304,000</b>
Leukoencephalopathy with Vanishing White Matter	EIF2B5	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,300</b>
Limb-Girdle Muscular Dystrophy, Type 2A	CAPN3	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 960</b>
Limb-Girdle Muscular Dystrophy, Type 2B	DYSF	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
Limb-Girdle Muscular Dystrophy, Type 2C	SGCG	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,900</b>
Limb-Girdle Muscular Dystrophy, Type 2D	SGCA	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,500</b>
Limb-Girdle Muscular Dystrophy, Type 2E	SGCB	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 31,000</b>
Limb-Girdle Muscular Dystrophy, Type 2F	SGCD	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 36,000</b>
Limb-Girdle Muscular Dystrophy, Type 2H	TRIM32	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 10,000</b>
Limb-Girdle Muscular Dystrophy, Type 2I	FKRP	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 460</b>
Limb-Girdle Muscular Dystrophy, Type 2L	ANO5	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 660</b>
Lipoamide Dehydrogenase Deficiency	DLD	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 14,000</b>

Lipoid Adrenal Hyperplasia	STAR	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,600
Lipoprotein Lipase Deficiency	LPL	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 800
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	HADHA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,500
Lowe 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 3,000
MEDNIK Syndrome	AP1S1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 211,000
Malonyl-CoA Decarboxylase Deficiency	MLYCD	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,800
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 1,100
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 1,700
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 4,300
Megaloblastic Anemia 1	AMN	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,300
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 1,000
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 15,000
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 6,600
Methylmalonyl-CoA Epimerase Deficiency	MCEE	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 98,000
Microphthalmia / Anophthalmia	VSX2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
Mitochondrial Complex I Deficiency (ACAD9-Related)	ACAD9	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Mitochondrial Complex I Deficiency (NDUFA11-Related)	NDUFA11	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 414,000
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 870
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 42,000
Mitochondrial Complex IV Deficiency (COX6B1-related)	COX6B1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,116,000
Mitochondrial Complex IV Deficiency (APOPT1-Related)	APOPT1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,200
Mitochondrial Complex IV Deficiency (PET100-Related)	PET100	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 469,000
Mitochondrial Complex IV Deficiency (SCO1-related)	SCO1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
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 4,900

Mitochondrial DNA Depletion Syndrome 3	<i>DGUOK</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,200
Mitochondrial DNA Depletion Syndrome 4A and 4B and other <i>POLG</i> -Related Disorders	<i>POLG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 180
Mitochondrial DNA Depletion Syndrome 5	<i>SUCLA2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 78,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	<i>MPV17</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	<i>PUS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 333,000
Mitochondrial Trifunctional Protein Deficiency ( <i>HADHB</i> -Related)	<i>HADHB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Molybdenum Cofactor Deficiency A	<i>MOCS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,700
Mucopolipidosis II / IIIA	<i>GNPTAB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Mucopolipidosis III Gamma	<i>GNPTG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 68,000
Mucopolipidosis IV	<i>MCOLN1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,500
Mucopolysaccharidosis Type I	<i>IDUA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 630
Mucopolysaccharidosis Type II	<i>IDS</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 76,000
Mucopolysaccharidosis Type IIIA	<i>SGSH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 700
Mucopolysaccharidosis Type IIIB	<i>NAGLU</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 900
Mucopolysaccharidosis Type IIIC	<i>HGSNAT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Mucopolysaccharidosis Type IIID	<i>GNS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 137,000
Mucopolysaccharidosis Type IVa	<i>GALNS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 440
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	<i>GLB1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Mucopolysaccharidosis VII	<i>GUSB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Mucopolysaccharidosis type IX	<i>HYAL1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 63,000
Mucopolysaccharidosis type VI	<i>ARSB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Mulibrey Nanism	<i>TRIM37</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 31,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	<i>PIGN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Multiple Pterygium Syndrome	<i>CHRNA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Multiple Sulfatase Deficiency	<i>SUMF1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 69,000
Muscle-Eye-Brain Disease and Other <i>POMGNT1</i> -Related Congenital Muscular Dystrophy-Dysglycanopathies	<i>POMGNT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Myoneurogastrointestinal Encephalopathy	<i>TYMP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Myotubular Myopathy 1	<i>MTM1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 192,000
N-Acetylglutamate Synthase Deficiency	<i>NAGS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Nemaline Myopathy 2	<i>NEB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 300
Nephrogenic Diabetes Insipidus, Type II	<i>AQP2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Nephrogenic Diabetes insipidus ( <i>AVPR2</i> -related)/ Nephrogenic Syndrome of Inappropriate Antidiuresis	<i>AVPR2</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 471,000
Nephronophthisis 2	<i>INVS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 24,000
Nephrotic Syndrome ( <i>NPHS1</i> -Related) / Congenital Finnish Nephrosis	<i>NPHS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 920
Neurodegeneration due to Cerebral Folate Transport Deficiency	<i>FOLR1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	<i>PLAA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 217,000
Neuronal Ceroid-Lipofuscinosis ( <i>CLN3</i> -Related)	<i>CLN3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,200
Neuronal Ceroid-Lipofuscinosis ( <i>CLN5</i> -Related)	<i>CLN5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Neuronal Ceroid-Lipofuscinosis ( <i>CLN6</i> -Related)	<i>CLN6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,600
Neuronal Ceroid-Lipofuscinosis ( <i>CLN8</i> -Related)	<i>CLN8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
Neuronal Ceroid-Lipofuscinosis ( <i>MFSD8</i> -Related)	<i>MFSD8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,200
Neuronal Ceroid-Lipofuscinosis ( <i>PPT1</i> -Related)	<i>PPT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300

<b>Neuronal Ceroid-Lipofuscinosis (TPP1-Related)</b>	<i>TPP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,000
<b>Niemann-Pick Disease (SMPD1-Related)</b>	<i>SMPD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
<b>Niemann-Pick Disease, Type C (NPC1-Related)</b>	<i>NPC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 690
<b>Niemann-Pick Disease, Type C (NPC2-Related)</b>	<i>NPC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
<b>Nijmegen Breakage Syndrome</b>	<i>NBN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
<b>Non-Syndromic Hearing Loss (GJB2-Related)</b>	<i>GJB2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 280
<b>Oculocutaneous Albinism, Type IA / IB</b>	<i>TYR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 220
<b>Oculocutaneous Albinism, Type IV</b>	<i>SLC45A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 830
<b>Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome</b>	<i>WNT10A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 900
<b>Omenn Syndrome (RAG2-Related)</b>	<i>RAG2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 17,000
<b>Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type</b>	<i>DCLRE1C</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,500
<b>Omenn Syndrome and other RAG1-Related Disorders</b>	<i>RAG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 180
<b>Ornithine Aminotransferase Deficiency</b>	<i>OAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,400
<b>Ornithine Transcarbamylase Deficiency</b>	<i>OTC</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 103,000
<b>Osteogenesis Imperfecta, Type XI</b>	<i>FKBP10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,100
<b>Osteopetrosis 1</b>	<i>TCIRG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,700
<b>Osteopetrosis 8</b>	<i>SNX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 16,000
<b>Otospondylomegapiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2</b>	<i>COL11A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
<b>Papillon-Lefevre Syndrome</b>	<i>CTSC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
<b>Pendred Syndrome</b>	<i>SLC26A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 72
<b>Peroxisome Biogenesis Disorder 3A and 3B</b>	<i>PEX12</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 30,000
<b>Peroxisome Biogenesis Disorder 7A and 7B</b>	<i>PEX26</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 23,000
<b>Phenylalanine Hydroxylase Deficiency</b>	<i>PAH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 150
<b>Polycystic Kidney Disease, Autosomal Recessive</b>	<i>PKHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 350
<b>Polyglandular Autoimmune Syndrome, Type 1</b>	<i>AIRE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
<b>Pontocerebellar Hypoplasia, Type 1A</b>	<i>VRK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 25,000
<b>Pontocerebellar Hypoplasia, Type 1B</b>	<i>EXOSC3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
<b>Pontocerebellar Hypoplasia, Type 2A and Type 4</b>	<i>TSEN54</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,700
<b>Pontocerebellar Hypoplasia, Type 2E</b>	<i>VPS53</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 139,000
<b>Pontocerebellar Hypoplasia, Type 6</b>	<i>RARS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,600
<b>Primary Carnitine Deficiency</b>	<i>SLC22A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 600
<b>Primary Ciliary Dyskinesia (CCDC103-Related)</b>	<i>CCDC103</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 27,000
<b>Primary Ciliary Dyskinesia (CCDC151-Related)</b>	<i>CCDC151</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 59,000
<b>Primary Ciliary Dyskinesia (CCDC39-Related)</b>	<i>CCDC39</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
<b>Primary Ciliary Dyskinesia (DNAH5-Related)</b>	<i>DNAH5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
<b>Primary Ciliary Dyskinesia (DNAI1-Related)</b>	<i>DNAI1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
<b>Primary Ciliary Dyskinesia (DNAI2-Related)</b>	<i>DNAI2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 76,000
<b>Primary Ciliary Dyskinesia (RSPH9-Related)</b>	<i>RSPH9</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 73,000
<b>Primary Coenzyme Q10 Deficiency 7</b>	<i>COQ4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
<b>Primary Congenital Glaucoma 3A</b>	<i>CYP1B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 130
<b>Primary Hyperoxaluria, Type 1</b>	<i>AGXT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
<b>Primary Hyperoxaluria, Type 2</b>	<i>GRHPR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
<b>Primary Hyperoxaluria, Type 3</b>	<i>HOGA1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
<b>Progressive Cerebello-Cerebral Atrophy</b>	<i>SEPSECS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,400
<b>Progressive Familial Intrahepatic Cholestasis, Type 2</b>	<i>ABCB11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 390
<b>Progressive Myoclonic Epilepsy, Type 1B</b>	<i>PRICKLE1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 98,000

Progressive Pseudorheumatoid Dysplasia	<i>WISP3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,600
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
Propionic Acidemia ( <i>PCCB</i> -Related)	<i>PCCB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 920
Pulmonary Surfactant Dysfunction	<i>ABCA3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Pycnodysostosis	<i>CTSK</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,100
Pyridoxamine 5'-Phosphate Oxidase Deficiency	<i>PNPO</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
Pyridoxine-Dependent Epilepsy	<i>ALDH7A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Pyruvate Carboxylase Deficiency	<i>PC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,000
Pyruvate Dehydrogenase E1-Alpha Deficiency	<i>PDHA1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 139,000
Pyruvate Dehydrogenase E1-Beta Deficiency	<i>PDHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,300
Renal Tubular Acidosis and Deafness	<i>ATP6V1B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
Retinitis Pigmentosa 26	<i>CERKL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,000
Retinitis Pigmentosa 28	<i>FAM161A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 34,000
Retinitis Pigmentosa 36	<i>PRCD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 304,000
Retinitis Pigmentosa 59	<i>DHDDS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 201,000
Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16	<i>C8ORF37</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
Rh Deficiency Syndrome	<i>RHAG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 46,000
Rhizomelic Chondrodysplasia Punctata, Type 1	<i>PEX7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
Rhizomelic Chondrodysplasia Punctata, Type 3	<i>AGPS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 620,000
Roberts Syndrome	<i>ESCO2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 95,000
Salla Disease	<i>SLC17A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,400
Salt and Pepper Developmental Regression Syndrome	<i>ST3GAL5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 25,000
Sandhoff Disease	<i>HEXB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 680
Schimke Immunoosseous Dysplasia	<i>SMARCAL1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
Seckel Syndrome 5 / Microcephaly 9	<i>CEP152</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
Segawa Syndrome	<i>TH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,000
Sepiapterin Reductase Deficiency	<i>SPR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 35,000
Severe Combined Immunodeficiency ( <i>IL7R</i> -Related)	<i>IL7R</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 20,000
Severe Combined Immunodeficiency ( <i>JAK3</i> -Related)	<i>JAK3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
Severe Combined Immunodeficiency ( <i>PTPRC</i> -Related)	<i>PTPRC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,300
Severe Congenital Neutropenia 4	<i>G6PC3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
Severe Neonatal Hyperparathyroidism	<i>CASR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis	<i>POC1A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 98,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 340
Shwachman-Diamond Syndrome	<i>SBDS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Sialidosis, Type I and Type II	<i>NEU1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,000
Sjogren-Larsson Syndrome	<i>ALDH3A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
Smith-Lemli-Opitz Syndrome	<i>DHCR7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 750
Spastic Paraplegia 15	<i>ZFYVE26</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly	<i>SLC1A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 136,000
Spherocytosis, Type 5	<i>EPB42</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Spinal Muscular Atrophy	<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 1,107

<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: 1 in 1,200</b>
<b>Spinocerebellar Ataxia with Axonal Neuropathy 3</b>	<i>COA7</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 12,000</b>
<b>Spondylocostal Dysostosis 1</b>	<i>DLL3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,200</b>
<b>Spondylometaepiphyseal Dysplasia (DDR2-Related)</b>	<i>DDR2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 220,000</b>
<b>Spondylothoracic Dysostosis</b>	<i>MESP2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 53,000</b>
<b>Steel Syndrome</b>	<i>COL27A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 93,000</b>
<b>Stuve-Wiedemann Syndrome</b>	<i>LIFR</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,000</b>
<b>Sulfate Transporter-Related Osteochondrodysplasia</b>	<i>SLC26A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,800</b>
<b>Tay-Sachs Disease</b>	<i>HEXA</i>	AR	Reduced Risk	Tay-Sachs disease enzyme: Non-carrier  White blood cells: Non-carrier  <ul style="list-style-type: none"> <li>Hex A%: 60.3% (Non-carrier : 55.0 - 72.0%; Carrier: &lt;50%)</li> <li>Total hexosaminidase activity: 1721 nmol/hr/mg</li> </ul> Plasma: Non-carrier  <ul style="list-style-type: none"> <li>Hex A%: 64.1 (Non-carrier : 58.0 - 72.0%; Carrier: &lt;54%)</li> <li>Total hexosaminidase activity: 455 nmol/hr/ml</li> </ul> HEXA Sequencing: Negative <b>Personalized Residual Risk: 1 in 1,400</b>
<b>Thiamine-Responsive Megaloblastic Anemia Syndrome</b>	<i>SLC19A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 11,000</b>
<b>Thyroid Dysmorphogenesis 1</b>	<i>SLC5A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,300</b>
<b>Thyroid Dysmorphogenesis 2A</b>	<i>TPO</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 350</b>
<b>Thyroid Dysmorphogenesis 3</b>	<i>TG</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 130</b>
<b>Thyroid Dysmorphogenesis 4</b>	<i>IYD</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,800</b>
<b>Thyroid Dysmorphogenesis 5</b>	<i>DUOXA2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,300</b>
<b>Thyroid Dysmorphogenesis 6</b>	<i>DUOX2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 32</b>
<b>Trichohepatoenteric Syndrome 1</b>	<i>TTC37</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 11,000</b>
<b>Tyrosinemia, Type I</b>	<i>FAH</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,900</b>
<b>Tyrosinemia, Type II</b>	<i>TAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,200</b>
<b>Tyrosinemia, Type III</b>	<i>HPD</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 15,000</b>
<b>Usher Syndrome, Type IB</b>	<i>MYO7A</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 180</b>
<b>Usher Syndrome, Type IC</b>	<i>USH1C</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 400</b>
<b>Usher Syndrome, Type ID</b>	<i>CDH23</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 880</b>
<b>Usher Syndrome, Type IF</b>	<i>PCDH15</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
<b>Usher Syndrome, Type IIA</b>	<i>USH2A</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 54</b>
<b>Usher Syndrome, Type III</b>	<i>CLRN1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,300</b>
<b>Very Long Chain Acyl-CoA Dehydrogenase Deficiency</b>	<i>ACADVL</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 380</b>
<b>Vitamin D-Dependent Rickets, Type I</b>	<i>CYP27B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,600</b>
<b>Vitamin D-Resistant Rickets, Type IIA</b>	<i>VDR</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 17,000</b>
<b>Walker-Warburg Syndrome and Other FKTN-Related Dystrophies</b>	<i>FKTN</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 390</b>
<b>Werner Syndrome</b>	<i>WRN</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,000</b>
<b>Wilson Disease</b>	<i>ATP7B</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 150</b>
<b>Wiskott-Aldrich Syndrome (WAS-Related)</b>	<i>WAS</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,203,000</b>
<b>Wolcott-Rallison Syndrome</b>	<i>EIF2AK3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 22,000</b>
<b>Woodhouse-Sakati Syndrome</b>	<i>DCAF17</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 59,000</b>



<b>X-Linked Juvenile Retinoschisis</b>	<i>RS1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
<b>X-Linked Severe Combined Immunodeficiency</b>	<i>IL2RG</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 250,000
<b>Xeroderma Pigmentosum (POLH-Related)</b>	<i>POLH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
<b>Xeroderma Pigmentosum, Group A</b>	<i>XPA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
<b>Xeroderma Pigmentosum, Group C</b>	<i>XPC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
<b>Xeroderma Pigmentosum, Group G</b>	<i>ERCC5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,000
<b>Zellweger Syndrome Spectrum (PEX10-Related)</b>	<i>PEX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,300
<b>Zellweger Syndrome Spectrum (PEX1-Related)</b>	<i>PEX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 740
<b>Zellweger Syndrome Spectrum (PEX2-Related)</b>	<i>PEX2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 77,000
<b>Zellweger Syndrome Spectrum (PEX6-Related)</b>	<i>PEX6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500

AR=Autosomal recessive; XL=X-linked

## Test methods and comments

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

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

PCR amplification using Asuragen, Inc. AmplideX<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 silent carrier.

MLPA for Gaucher disease (*GBA*), cystic fibrosis (*CFTR*), and non-syndromic hearing loss (*GJB2/GJB6*) will only be performed if indicated for confirmation of detected CNVs. If *GBA* analysis was performed, the copy numbers of exons 1, 3, 4, and 6 - 10 of the *GBA* gene (of 11 exons total) were analyzed. If *CFTR* analysis was performed, the copy numbers of all 27 *CFTR* exons were analyzed. If *GJB2/GJB6* analysis was performed, the copy number of the two *GJB2* exons were analyzed, as well as the presence or absence of the two upstream deletions of the *GJB2* regulatory region, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854).

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

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

Agilent SureSelect™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%)

Th 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 ≥98%)**

Hexosaminidase activity and Hex A% activity were measured by a standard heat-inactivation, fluorometric method using artificial 4-MU-β-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.

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Additional disease-specific references available upon request.