



## Donor 6562

### Genetic Testing Summary

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

Last Updated: 03/01/24

Donor Reported Ancestry: Mexican, Spanish, Cuban

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	Low MCV and MCH	Carrier of Alpha Thalassemia
Expanded Genetic Disease Carrier Screening Panel attached- 502 diseases by gene sequencing.  Personalized residual risk by gene is in the attached report.	Carrier: Alpha-Thalassemia (HBA1/HBA2) silent carrier aa/-a  Carrier: Mucopolysaccharidosis Type IIIB (NAGLU)  Negative for other genes sequenced.	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 6562  
 Date of Birth: [REDACTED]  
 Sema4 ID: [REDACTED]  
 Client ID: [REDACTED]  
 Indication: Carrier Screening

**Specimen Information**

Specimen Type: Blood  
 Date Collected: 12/07/2022  
 Date Received: 12/08/2022  
 Final Report: 01/03/2023

**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 Alpha-Thalassemia (AR)</b>            Associated gene(s): <i>HBA1/HBA2</i>            Variant(s) Detected: One copy of the alpha 3,7 deletion</p> <p><b>Carrier of Mucopolysaccharidosis Type IIIB (AR)</b>            Associated gene(s): <i>NAGLU</i>            Variant(s) Detected: c.1693C&gt;T, p.R565W, 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.
- As genetic technologies may improve and variant classifications may change over time, it is recommended to obtain a new carrier screening test or reanalysis when a new pregnancy is being considered.

Interpretation of positive results

**Alpha-Thalassemia (AR)**

**Results and Interpretation**

*HBA1* Copy Number: 2  
*HBA2* Copy Number: 1  
 One copy of the alpha 3,7 deletion detected  
*HBA1/HBA2* Sequencing: Negative  
**Gene(s) analyzed:** *HBA1* (NM\_000558.4) and *HBA2* (NM\_000517.4)  
**Inheritance:** Autosomal Recessive

This patient carries a heterozygous alpha 3.7 deletion, resulting in the loss of one copy of the alpha-globin gene and is therefore a silent carrier of alpha-thalassemia (aa/-a). No pathogenic or likely pathogenic variants were identified by sequence analysis.

Typically, individuals have four functional alpha-globin genes: 2 copies of *HBA1* and 2 copies of *HBA2*, whose expression is regulated by a cis-acting regulatory element HS-40. Alpha-thalassemia carriers have three (silent carrier) or two (carrier of the alpha-thalassemia trait) functional alpha-globin genes with or without a mild phenotype.

#### What is Alpha-Thalassemia?

Alpha-thalassemia is an autosomal recessive condition that affects the red blood cells. It can affect people of any ethnicity, but is more common in people who can trace their ancestry to Southeast Asia, India, equatorial Africa, the Mediterranean, or the Arabian Peninsula. There are two major forms of alpha-thalassemia:

- Hemoglobin Bart syndrome is caused by a loss of all 4 alpha-globin genes (--/--). It is very severe, and fetuses are either stillborn or die shortly after birth.
- Alpha-thalassemia (also called HbH disease) is caused by a loss of 3 alpha-globin genes (-a/--). This disease results in anemia, an enlarged spleen, and mild jaundice. Most individuals are mildly disabled by this condition. Some people with more severe disease require frequent blood transfusions.

The type of disease as well as the severity of symptoms can be predicted based on the genetic variants detected. Carriers may have mild anemia.

#### Mucopolysaccharidosis Type IIIB (AR)

##### Results and Interpretation


A heterozygous (one copy) pathogenic missense variant, c.1693C>T, p.R565W, was detected in the *NAGLU* gene (NM\_000263.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for mucopolysaccharidosis type IIIB. Therefore, this individual is expected to be at least a carrier for mucopolysaccharidosis type IIIB. Heterozygous carriers are not expected to exhibit symptoms of this disease.

#### What is Mucopolysaccharidosis Type IIIB?

Mucopolysaccharidosis type IIIB, also known as Sanfilippo syndrome type B, is a pan-ethnic, autosomal recessive disease caused by pathogenic variants in the gene *NAGLU*. This disease is characterized by severe behavioral disturbances, including hyperactivity, sleep disturbances and destructive behavior. The age of onset is usually around 3 to 4 years of age. Other features include intellectual disability, enlarged liver and spleen, stiffness of the joints, hearing loss and seizures. No treatment is known. Life expectancy is generally reported to be into adolescence or early adulthood, but may be variable. No clear genotype-phenotype correlation is known.

## 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.



Preti Jain, Ph.D., FACMG, DABMGG, Director - Molecular Genetics

## 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>				
Alpha-Thalassemia	HBA1/HBA2	AR	Silent Carrier	HBA1 Copy Number: 2 HBA2 Copy Number: 1 One copy of the alpha 3,7 deletion detected HBA1/HBA2 Sequencing: Negative
Mucopolysaccharidosis Type IIIB	NAGLU	AR	Carrier	c.1693C>T, p.R565W, Pathogenic, Heterozygous (one copy)
<b>Negative</b>				
2-Methylbutyrylglycinuria	ACADSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	HSD3B2	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related)	MCCC1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)	MCCC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
3-Methylglutaconic Aciduria, Type III	OPA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,300
3-Phosphoglycerate Dehydrogenase Deficiency	PHGDH	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
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
WNT10A-Related Ectodermal Dysplasia	WNT10A	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
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 150
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 35,000
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 420,000
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 10,000
Aicardi-Goutieres Syndrome (TREX1-Related)	TREX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Albinism, Oculocutaneous, Type III	TYRP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
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 Intellectual Disability Syndrome	ATRX	XL	Reduced Risk	Personalized Residual Risk: 1 in 48,000

Alport Syndrome (COL4A3-Related)	COL4A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Alport Syndrome (COL4A4-Related)	COL4A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Alport Syndrome (COL4A5-Related)	COL4A5	XL	Reduced Risk	Personalized Residual Risk: 1 in 150,000
Alstrom Syndrome	ALMS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Andermann Syndrome	SLC12A6	AR	Reduced Risk	Personalized Residual Risk: 1 in 76,000
Antley-Bixler Syndrome (POR-Related)	POR	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Argininemia	ARG1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Argininosuccinic Aciduria	ASL	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Aromatase Deficiency	CYP19A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Arthrogryposis, Intellectual Disability, and Seizures	SLC35A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 454,000
Asparagine Synthetase Deficiency	ASNS	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Aspartylglycosaminuria	AGA	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Ataxia With Isolated Vitamin E Deficiency	TTPA	AR	Reduced Risk	Personalized Residual Risk: 1 in 61,000
Ataxia-Telangiectasia	ATM	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Ataxia-Telangiectasia-Like Disorder 1	MRE11	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	SACS	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Bardet-Biedl Syndrome (ARL6-Related)	ARL6	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000
Bardet-Biedl Syndrome (BBS10-Related)	BBS10	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Bardet-Biedl Syndrome (BBS12-Related)	BBS12	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,900
Bardet-Biedl Syndrome (BBS1-Related)	BBS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Bardet-Biedl Syndrome (BBS2-Related)	BBS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Bardet-Biedl Syndrome (BBS4-Related)	BBS4	AR	Reduced Risk	Personalized Residual Risk: 1 in 22,000
Bare Lymphocyte Syndrome, Type II	CIITA	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Barth Syndrome	TAZ	XL	Reduced Risk	Personalized Residual Risk: 1 in 183,000
Bartter Syndrome, Type 3	CLCNKB	AR	Reduced Risk	Personalized Residual Risk: 1 in 350
Bartter Syndrome, Type 4A	BSND	AR	Reduced Risk	Personalized Residual Risk: 1 in 91,000
Bernard-Soulier Syndrome, Type A1	GP1BA	AR	Reduced Risk	Personalized Residual Risk: 1 in 42,000
Bernard-Soulier Syndrome, Type C	GP9	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Beta-Globin-Related Hemoglobinopathies	HBB	AR	Reduced Risk	Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies): 1 in 2,000 Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant): 1 in 23,000 Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant): 1 in 42,000
Beta-Ketothiolase Deficiency	ACAT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Beta-Mannosidosis	MANBA	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,100
BH4-Deficient Hyperphenylalaninemia C	QDPR	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
BH4-Deficient Hyperphenylalaninemia D	PCBD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,000
Bilateral Frontoparietal Polymicrogyria	GPR56	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Biotinidase Deficiency	BTBD	AR	Reduced Risk	Personalized Residual Risk: 1 in 500
Bloom Syndrome	BLM	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
Canavan Disease	ASPA	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Carbamoylphosphate Synthetase I Deficiency	CPS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Carnitine Acylcarnitine Translocase Deficiency	SLC25A20	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Carnitine Palmitoyltransferase IA Deficiency	CPT1A	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Carnitine Palmitoyltransferase II Deficiency	CPT2	AR	Reduced Risk	Personalized Residual Risk: 1 in 670
Carpenter Syndrome	RAB23	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Cartilage-Hair Hypoplasia	RMRP	AR	Reduced Risk	Personalized Residual Risk: 1 in 960



Catecholaminergic Polymorphic Ventricular Tachycardia	CASQ2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,900
Central Hypothyroidism and Testicular Enlargement	IGSF1	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 781,000
Cerebral Creatine Deficiency Syndrome 1	SLC6A8	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 208,000
Cerebral Creatine Deficiency Syndrome 2	GAMT	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
Cerebral Creatine Deficiency Syndrome 3	GATM	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,900
Cerebral Dysgenesis, Neuropathy, Ichthyosis, and Palmoplantar Keratoderma Syndrome	SNAP29	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 210,000
Cerebrotendinous Xanthomatosis	CYP27A1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,900
Charcot-Marie-Tooth Disease, Type 4D	NDRG1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 730,000
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	PRPS1	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 114,000
Charcot-Marie-Tooth Disease, X-Linked	GJB1	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Chediak-Higashi Syndrome	LYST	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,100
Chondrodysplasia Punctata	ARSE	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 862,000
Choreoacanthocytosis	VPS13A	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,500
Choroideremia	CHM	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 125,000
Chronic Granulomatous Disease (CYBA-Related)	CYBA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Chronic Granulomatous Disease (CYBB-Related)	CYBB	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 294,000
Citrin Deficiency	SLC25A13	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Citrullinemia, Type 1	ASS1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,500
Cockayne Syndrome, Type A	ERCC8	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,900
Cockayne Syndrome, Type B and other ERCC6-Related Disorders	ERCC6	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,100
Cohen Syndrome	VPS13B	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,400
Combined Factor V and VIII Deficiency	LMAN1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 102,000
Combined Malonic and Methylmalonic Aciduria	ACSF3	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
Combined Oxidative Phosphorylation Deficiency 1	GFM1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Combined Oxidative Phosphorylation Deficiency 3	TSM	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 27,000
Combined Pituitary Hormone Deficiency 1	POU1F1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,900
Combined Pituitary Hormone Deficiency 2	PROP1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,800
Combined Pituitary Hormone Deficiency 3	LHX3	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 140,000
Combined SAP Deficiency	PSAP	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 44,000
Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1	GUCY2D	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency	CYP11B1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 520
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	CYP17A1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	CYP21A2	AR	Reduced Risk	CYP21A2 copy number: 2 CYP21A2 sequencing: Negative <b>Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)):</b> 1 in 200 <b>Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)):</b> 1 in 1,300
Congenital Adrenal Hypoplasia (NR0B1-Related)	NR0B1	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 353,000
Congenital Adrenal Insufficiency (CYP11A1-Related)	CYP11A1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,100
Congenital Amegakaryocytic Thrombocytopenia	MPL	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,100
Congenital Bile Acid Synthesis Defect (AKR1D1-Related)	AKR1D1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,900
Congenital Bile Acid Synthesis Defect (HSD3B7-Related)	HSD3B7	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,900

<b>Congenital Disorder of Deglycosylation</b>	<i>NGLY1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,400
<b>Congenital Disorder of Glycosylation, Type Ia</b>	<i>PMM2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 540
<b>Congenital Disorder of Glycosylation, Type Ib</b>	<i>MPI</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,600
<b>Congenital Disorder of Glycosylation, Type Ic</b>	<i>ALG6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
<b>Congenital Disorder of Glycosylation, Type Im</b>	<i>DOLK</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 134,000
<b>Congenital Dyserythropoietic Anemia Type 2</b>	<i>SEC23B</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,000
<b>Congenital Dyserythropoietic Anemia, Type Ia</b>	<i>CDAN1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 470
<b>Congenital Ichthyosis 4A and 4B</b>	<i>ABCA12</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,100
<b>Congenital Insensitivity to Pain with Anhidrosis</b>	<i>NTRK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,700
<b>Congenital Muscular Dystrophy (LAMA2-Related)</b>	<i>LAMA2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 640
<b>Congenital Myasthenic Syndrome (CHAT-Related)</b>	<i>CHAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,100
<b>Congenital Myasthenic Syndrome (CHRNE-Related)</b>	<i>CHRNE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
<b>Congenital Myasthenic Syndrome (DOK7-Related)</b>	<i>DOK7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
<b>Congenital Myasthenic Syndrome (RAPSN-Related)</b>	<i>RAPSN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,900
<b>Congenital Neutropenia (HAX1-Related)</b>	<i>HAX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 82,000
<b>Congenital Neutropenia (VPS45-Related)</b>	<i>VPS45</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 163,000
<b>Congenital Nongoitrous Hypothyroidism 1</b>	<i>TSHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,000
<b>Congenital Nongoitrous Hypothyroidism 4</b>	<i>TSHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 118,000
<b>Congenital Secretory Chloride Diarrhea 1</b>	<i>SLC26A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
<b>Corneal Dystrophy and Perceptive Deafness</b>	<i>SLC4A11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
<b>Corticosterone Methyloxidase Deficiency</b>	<i>CYP11B2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
<b>Cystic Fibrosis</b>	<i>CFTR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 440
<b>Cystinosis</b>	<i>CTNS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,700
<b>Cystinuria (SLC3A1-Related)</b>	<i>SLC3A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 590
<b>Cytochrome C Oxidase Deficiency / Leigh Syndrome (COX15-Related)</b>	<i>COX15</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,300
<b>D-Bifunctional Protein Deficiency</b>	<i>HSD17B4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
<b>Deafness, Autosomal Recessive 3</b>	<i>MYO15A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 240
<b>Deafness, Autosomal Recessive 59</b>	<i>PJVK</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
<b>Deafness, Autosomal Recessive 7</b>	<i>TMC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
<b>Deafness, Autosomal Recessive 76</b>	<i>SYNE4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 43,000
<b>Deafness, Autosomal Recessive 77</b>	<i>LOXHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,700
<b>Deafness, Autosomal Recessive 8/10</b>	<i>TMPPRS3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 510
<b>Deafness, Autosomal Recessive 9</b>	<i>OTOF</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 630
<b>Desbuquois Dysplasia 1</b>	<i>CANT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,700
<b>Desmosterolosis</b>	<i>DHCR24</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 27,000
<b>Diaphanospondylodysostosis</b>	<i>BMPER</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 18,000
<b>Distal Renal Tubular Acidosis and other SLC4A1-related Disorders</b>	<i>SLC4A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,000
<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 9,800
<b>Dystrophic Epidermolysis Bullosa</b>	<i>COL7A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 900
<b>Ehlers-Danlos Syndrome, Type VI</b>	<i>PLOD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 20,000
<b>Ehlers-Danlos Syndrome, Type VIIC</b>	<i>ADAMTS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 243,000
<b>Ellis-Van Creveld Syndrome (EVC2-Related)</b>	<i>EVC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,300
<b>Ellis-van Creveld Syndrome (EVC-Related)</b>	<i>EVC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,200
<b>Emery-Dreifuss Myopathy 1</b>	<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 450
Factor XI Deficiency	<i>F11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
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 280
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	<i>HADH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,000
Familial Hyperinsulinism (ABCC8-Related)	<i>ABCC8</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 450
Familial Hyperinsulinism (KCNJ11-Related)	<i>KCNJ11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,300
Familial Hyperphosphatemic Tumor Calcinosi	<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 28,000
Fanconi-Bickel Syndrome	<i>SLC2A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
Fragile X Syndrome	<i>FMR1</i>	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. <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 1,600
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 2,000
Galactokinase Deficiency	<i>GALK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Galactose Epimerase Deficiency	<i>GALE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,600
Galactosemia	<i>GALT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,200
Galactosialidosis	<i>CTSA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7900
Gaucher Disease	<i>GBA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
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 290
Glanzmann Thrombasthenia (ITGA2B-Related)	<i>ITGA2B</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Glanzmann Thrombasthenia (ITGB3-Related)	<i>ITGB3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
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 4,700
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 1,700
Glutathione Synthetase Deficiency	<i>GSS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,500
Glycine Encephalopathy (AMT-Related)	<i>AMT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 920
Glycine Encephalopathy (GLDC-Related)	<i>GLDC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 760
Glycogen Storage Disease, Type 0	<i>GYS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Glycogen Storage Disease, Type Ia	<i>G6PC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,100
Glycogen Storage Disease, Type Ib	<i>SLC37A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,300
Glycogen Storage Disease, Type II	<i>GAA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 520
Glycogen Storage Disease, Type III	<i>AGL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,600



Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	<i>GBE1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
Glycogen Storage Disease, Type IXb	<i>PHKB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 700
Glycogen Storage Disease, Type V	<i>PYGM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Glycogen Storage Disease, Type VI	<i>PYGL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
Glycogen Storage Disease, Type VII	<i>PFKM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
GM3 Synthase Deficiency	<i>ST3GAL5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
GRACILE Syndrome and Other <i>BCS1L</i> -Related Disorders	<i>BCS1L</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,900
Gray Platelet Syndrome	<i>NBEAL2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,800
Growth Hormone Deficiency, Type IB	<i>GHRHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,900
Hemochromatosis, Type 2A	<i>HFE2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,300
Hemochromatosis, Type 3	<i>TFR2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Hereditary Fructose Intolerance	<i>ALDOB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
Hereditary Spastic Paraparesis 49	<i>TECPR2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 116,000
Hermansky-Pudlak Syndrome, Type 1	<i>HPS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,500
Hermansky-Pudlak Syndrome, Type 3	<i>HPS3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 49,000
Hermansky-Pudlak Syndrome, Type 4	<i>HPS4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 35,000
Hermansky-Pudlak Syndrome, Type 6	<i>HPS6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,400
HMG-CoA Lyase Deficiency	<i>HMGCL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Hmg-CoA Synthase 2 Deficiency	<i>HMGCS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,000
Holocarboxylase Synthetase Deficiency	<i>HLCS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,500
Homocystinuria ( <i>CBS</i> -Related)	<i>CBS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
Homocystinuria due to <i>MTHFR</i> Deficiency	<i>MTHFR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Homocystinuria, cblE Type	<i>MTRR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,600
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	<i>MTR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
Hydrocephalus	<i>L1CAM</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
Hydroletharus Syndrome	<i>HYLS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 52,000
Hyper-Igm Syndrome	<i>CD40LG</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,167,000
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	<i>SLC25A15</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,700
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	<i>SARS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 23,000
Hypohidrotic Ectodermal Dysplasia 1	<i>EDA</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 22,000
Hypomagnesemia 1	<i>TRPM6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Hypomyelinating Leukodystrophy 3	<i>AIMP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 341,000
Hypomyelinating Leukodystrophy 12	<i>VPS11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 72,000
Hypophosphatasia	<i>ALPL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 790
Hypophosphatemic Rickets with Hypercalciuria	<i>SLC34A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Hypotrichosis 8 / Autosomal Recessive Woolly Hair 1	<i>LPAR6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 27,000
Immunodeficiency 18	<i>CD3E</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 73,000
Immunodeficiency 19	<i>CD3D</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 16,000
Inclusion Body Myopathy 2	<i>GNE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,000
Infantile Cerebral and Cerebellar Atrophy	<i>MED17</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 129,000
Infantile Neuroaxonal Dystrophy 1 and other <i>PLA2G6</i> -Related Disorders	<i>PLA2G6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 690
Intellectual Disability, Autosomal Recessive 3	<i>CC2D1A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 92,000
Intrahepatic Cholestasis	<i>ATP8B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
Isovaleric Acidemia	<i>IVD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,000
Joubert Syndrome 2	<i>TMEM216</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 152,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronphthisis 1	<i>NPHP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 21,000

Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	<i>RPGRIPL1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 13,000</b>
Junctional Epidermolysis Bullosa ( <i>COL17A1</i> -Related)	<i>COL17A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,200</b>
Junctional Epidermolysis Bullosa ( <i>ITGA6</i> -Related)	<i>ITGA6</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 125,000</b>
Junctional Epidermolysis Bullosa ( <i>ITGB4</i> -Related)	<i>ITGB4</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,400</b>
Junctional Epidermolysis Bullosa ( <i>LAMA3</i> -Related)	<i>LAMA3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 21,000</b>
Junctional Epidermolysis Bullosa ( <i>LAMB3</i> -Related)	<i>LAMB3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,900</b>
Junctional Epidermolysis Bullosa ( <i>LAMC2</i> -Related)	<i>LAMC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 77,000</b>
Kohlschutter-Tonz Syndrome	<i>ROGDI</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,300</b>
Krabbe Disease	<i>GALC</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 860</b>
Lamellar Ichthyosis, Type 1	<i>TGM1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,500</b>
Laron Dwarfism	<i>GHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,700</b>
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	<i>CEP290</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
Leber Congenital Amaurosis 13	<i>RDH12</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,600</b>
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	<i>TULP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,800</b>
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	<i>RPE65</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,400</b>
Leber Congenital Amaurosis 4	<i>AIP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
Leber Congenital Amaurosis 5	<i>LCA5</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,200</b>
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	<i>CRB1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 990</b>
Leigh Syndrome ( <i>NDUFS7</i> -Related)	<i>NDUFS7</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 26,000</b>
Leigh Syndrome ( <i>SURF1</i> -Related)	<i>SURF1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,400</b>
Leigh Syndrome, French-Canadian Type	<i>LRPPRC</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 32,000</b>
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogyposis with Anterior Horn Cell Disease	<i>GLE1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,800</b>
Lethal Congenital Contracture Syndrome 2	<i>ERBB3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 36,000</b>
Lethal Congenital Contracture Syndrome 3	<i>PIP5K1C</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 151,000</b>
Leukoencephalopathy with Vanishing White Matter	<i>EIF2B5</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,300</b>
Limb-Girdle Muscular Dystrophy, Type 2A	<i>CAPN3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 960</b>
Limb-Girdle Muscular Dystrophy, Type 2B	<i>DYSF</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
Limb-Girdle Muscular Dystrophy, Type 2C	<i>SGCG</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,900</b>
Limb-Girdle Muscular Dystrophy, Type 2D	<i>SGCA</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,500</b>
Limb-Girdle Muscular Dystrophy, Type 2E	<i>SGCB</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 31,000</b>
Limb-Girdle Muscular Dystrophy, Type 2F	<i>SGCD</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 52,000</b>
Limb-Girdle Muscular Dystrophy, Type 2H	<i>TRIM32</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 10,000</b>
Limb-Girdle Muscular Dystrophy, Type 2I	<i>FKRP</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 550</b>
Limb-Girdle Muscular Dystrophy, Type 2L	<i>ANO5</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 660</b>
Lipoamide Dehydrogenase Deficiency	<i>DLD</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,300</b>
Lipoid Adrenal Hyperplasia	<i>STAR</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,600</b>
Lipoprotein Lipase Deficiency	<i>LPL</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,000</b>
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	<i>HADHA</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,900</b>
Lowe Syndrome	<i>OCRL</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,375,000</b>
Lysinuric Protein Intolerance	<i>SLC7A7</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,000</b>
Malonyl-CoA Decarboxylase Deficiency	<i>MLYCD</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,800</b>
Maple Syrup Urine Disease, Type 1a	<i>BCKDHA</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,100</b>

Maple Syrup Urine Disease, Type 1b	<i>BCKDHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Maple Syrup Urine Disease, Type 2	<i>DBT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,600
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	<i>MKS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,700
Medium Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
MEDNIK Syndrome	<i>AP1S1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 211,000
Megalencephalic Leukoencephalopathy with Subcortical Cysts	<i>MLC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
Megaloblastic Anemia 1	<i>AMN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,300
Menkes Disease	<i>ATP7A</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
Metachromatic Leukodystrophy	<i>ARSA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,000
Methionine Adenosyltransferase I/III Deficiency	<i>MAT1A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
Methylmalonic Acidemia (MMAA-Related)	<i>MMAA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Methylmalonic Acidemia (MMAB-Related)	<i>MMAB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
Methylmalonic Acidemia (MUT-Related)	<i>MUT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	<i>MMACHC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,800
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	<i>MMADHC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 219,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	<i>LMBRD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
Methylmalonyl-CoA Epimerase Deficiency	<i>MCEE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 98,000
Microphthalmia / Anophthalmia	<i>VSX2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
Mitochondrial Complex I Deficiency (ACAD9-Related)	<i>ACAD9</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Mitochondrial Complex I Deficiency (NDUFA11-Related)	<i>NDUFA11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 414,000
Mitochondrial Complex I Deficiency (NDUFAF5-Related)	<i>NDUFAF5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,800
Mitochondrial Complex I Deficiency (NDUFS6-Related)	<i>NDUFS6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 353,000
Mitochondrial Complex I Deficiency (NDUFV1-Related)	<i>NDUFV1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 870
Mitochondrial Complex I Deficiency / Leigh Syndrome (FOXRED1-Related)	<i>FOXRED1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,900
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFAF2-Related)	<i>NDUFAF2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 168,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFS4-Related)	<i>NDUFS4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 41,000
Mitochondrial Complex IV Deficiency (COX20-related)	<i>COX20</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 42,000
Mitochondrial Complex IV Deficiency (COX6B1-related)	<i>COX6B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,116,000
Mitochondrial Complex IV Deficiency (APOPT1-Related)	<i>APOPT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,200
Mitochondrial Complex IV Deficiency (PET100-Related)	<i>PET100</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 469,000
Mitochondrial Complex IV Deficiency (SCO1-related)	<i>SCO1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Mitochondrial Complex IV Deficiency / Leigh Syndrome (COX10-Related)	<i>COX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,400
Mitochondrial DNA Depletion Syndrome 2	<i>TK2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,900
Mitochondrial DNA Depletion Syndrome 3	<i>DGUOK</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,200
Mitochondrial DNA Depletion Syndrome 4A and 4B and other POLG-Related Disorders	<i>POLG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 320
Mitochondrial DNA Depletion Syndrome 5	<i>SUCLA2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 45,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	<i>MPV17</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	<i>PUS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 449,000



Mitochondrial Trifunctional Protein Deficiency (HADHB-Related)	HADHB	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,000
Molybdenum Cofactor Deficiency A	MOCS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Mucopolipidosis II / IIIA	GNPTAB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Mucopolipidosis III Gamma	GNPTG	AR	Reduced Risk	Personalized Residual Risk: 1 in 68,000
Mucopolipidosis IV	MCOLN1	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,100
Mucopolysaccharidosis Type I	IDUA	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Mucopolysaccharidosis Type II	IDS	XL	Reduced Risk	Personalized Residual Risk: 1 in 76,000
Mucopolysaccharidosis Type IIIA	SGSH	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Mucopolysaccharidosis Type IIIC	HGSNAT	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Mucopolysaccharidosis Type IIID	GNS	AR	Reduced Risk	Personalized Residual Risk: 1 in 137,000
Mucopolysaccharidosis Type IVa	GALNS	AR	Reduced Risk	Personalized Residual Risk: 1 in 690
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	GLB1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Mucopolysaccharidosis type IX	HYAL1	AR	Reduced Risk	Personalized Residual Risk: 1 in 149,000
Mucopolysaccharidosis type VI	ARSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Mucopolysaccharidosis VII	GUSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Mulibrey Nanism	TRIM37	AR	Reduced Risk	Personalized Residual Risk: 1 in 31,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	PIGN	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Multiple Pterygium Syndrome	CHRNA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,900
Multiple Sulfatase Deficiency	SUMF1	AR	Reduced Risk	Personalized Residual Risk: 1 in 69,000
Muscle-Eye-Brain Disease and Other POMGNT1-Related Congenital Muscular Dystrophy-Dystroglycanopathies	POMGNT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Myoneurogastrointestinal Encephalopathy	TYMP	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Myotubular Myopathy 1	MTM1	XL	Reduced Risk	Personalized Residual Risk: 1 in 192,000
N-Acetylglutamate Synthase Deficiency	NAGS	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Nemaline Myopathy 2	NEB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Nephrogenic Diabetes insipidus (AVPR2-related) / Nephrogenic Syndrome of Inappropriate Antidiuresis	AVPR2	XL	Reduced Risk	Personalized Residual Risk: 1 in 471,000
Nephrogenic Diabetes Insipidus, Type II	AQP2	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Nephronophthisis 2	INVS	AR	Reduced Risk	Personalized Residual Risk: 1 in 56,000
Nephrotic Syndrome (NPHS1-Related) / Congenital Finnish Nephrosis	NPHS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 920
Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome	NPHS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 780
Neurodegeneration due to Cerebral Folate Transport Deficiency	FOLR1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	PLAA	AR	Reduced Risk	Personalized Residual Risk: 1 in 229,000
Neuronal Ceroid-Lipofuscinosis (CLN3-Related)	CLN3	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Neuronal Ceroid-Lipofuscinosis (CLN5-Related)	CLN5	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Neuronal Ceroid-Lipofuscinosis (CLN6-Related)	CLN6	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,600
Neuronal Ceroid-Lipofuscinosis (CLN8-Related)	CLN8	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
Neuronal Ceroid-Lipofuscinosis (MFSD8-Related)	MFSD8	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,200
Neuronal Ceroid-Lipofuscinosis (PPT1-Related)	PPT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Neuronal Ceroid-Lipofuscinosis (TPP1-Related)	TPP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,300
Niemann-Pick Disease (SMPD1-Related)	SMPD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Niemann-Pick Disease, Type C (NPC1-Related)	NPC1	AR	Reduced Risk	Personalized Residual Risk: 1 in 690
Niemann-Pick Disease, Type C (NPC2-Related)	NPC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600
Nijmegen Breakage Syndrome	NBN	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Non-Syndromic Hearing Loss (GJB2-Related)	GJB2	AR	Reduced Risk	Personalized Residual Risk: 1 in 600

Oculocutaneous Albinism, Type IA / IB	<i>TYR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 240
Oculocutaneous Albinism, Type IV	<i>SLC45A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 830
Omenn Syndrome ( <i>RAG2</i> -Related)	<i>RAG2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 17,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	<i>DCLRE1C</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,500
Omenn Syndrome and other <i>RAG1</i> -Related Disorders	<i>RAG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 850
Ornithine Aminotransferase Deficiency	<i>OAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
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 9,500
Osteopetrosis 1	<i>TCIRG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,700
Osteopetrosis 8	<i>SNX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 16,000
Otospondylomegapiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	<i>COL11A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Papillon-Lefevre Syndrome	<i>CTSC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Pendred Syndrome	<i>SLC26A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 390
Peroxisome Biogenesis Disorder 3A and 3B	<i>PEX12</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 30,000
Peroxisome Biogenesis Disorder 7A and 7B	<i>PEX26</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,300
Phenylalanine Hydroxylase Deficiency	<i>PAH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 340
Polycystic Kidney Disease, Autosomal Recessive	<i>PKHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 450
Polyglandular Autoimmune Syndrome, Type 1	<i>AIRE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,300
Pontocerebellar Hypoplasia, Type 1A	<i>VRK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 25,000
Pontocerebellar Hypoplasia, Type 1B	<i>EXOSC3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
Pontocerebellar Hypoplasia, Type 2A and Type 4	<i>TSEN54</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,700
Pontocerebellar Hypoplasia, Type 2E	<i>VPS53</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 139,000
Pontocerebellar Hypoplasia, Type 6	<i>RARS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,600
Primary Carnitine Deficiency	<i>SLC22A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
Primary Ciliary Dyskinesia ( <i>CCDC103</i> -Related)	<i>CCDC103</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 27,000
Primary Ciliary Dyskinesia ( <i>CCDC151</i> -Related)	<i>CCDC151</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 59,000
Primary Ciliary Dyskinesia ( <i>CCDC39</i> -Related)	<i>CCDC39</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Primary Ciliary Dyskinesia ( <i>DNAH5</i> -Related)	<i>DNAH5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
Primary Ciliary Dyskinesia ( <i>DNAI1</i> -Related)	<i>DNAI1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Primary Ciliary Dyskinesia ( <i>DNAI2</i> -Related)	<i>DNAI2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 76,000
Primary Ciliary Dyskinesia ( <i>RSPH9</i> -Related)	<i>RSPH9</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Primary Coenzyme Q10 Deficiency 7	<i>COQ4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,300
Primary Congenital Glaucoma 3A	<i>CYP11B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 880
Primary Hyperoxaluria, Type 1	<i>AGXT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
Primary Hyperoxaluria, Type 2	<i>GRHPR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Primary Hyperoxaluria, Type 3	<i>HOGA1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
Progressive Cerebello-Cerebral Atrophy	<i>SEPSECS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
Progressive Familial Intrahepatic Cholestasis, Type 2	<i>ABCB11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 950
Progressive Myoclonic Epilepsy, Type 1B	<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 5,100
Propionic Acidemia ( <i>PCCA</i> -Related)	<i>PCCA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Propionic Acidemia ( <i>PCCB</i> -Related)	<i>PCCB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,200
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 2,000
Pyridoxamine 5'-Phosphate Oxidase Deficiency	<i>PNPO</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
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 15,000
Renal Tubular Acidosis and Deafness	<i>ATP6V1B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
Retinitis Pigmentosa 25	<i>EYS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Retinitis Pigmentosa 26	<i>CERKL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
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 601,000
Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16	<i>C8ORF37</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 50,000
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 139,000
Salla Disease	<i>SLC17A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,300
Sandhoff Disease	<i>HEXB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Sanjad-Sakati Syndrome	<i>TBCE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,100
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 1,700
Segawa Syndrome	<i>TH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,100
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 8,500
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 108,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 660
Shwachman-Diamond Syndrome	<i>SBDS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,700
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 5,500
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 46,000
Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly	<i>SLC1A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 80,000
Spherocytosis, Type 5	<i>EPB42</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,200
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
Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S	<i>IGHMBP2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Spinocerebellar Ataxia with Axonal Neuropathy 3	<i>COA7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,400
Spondylocostal Dysostosis 1	<i>DLL3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,200
Spondylometaphyseal Dysplasia ( <i>DDR2</i> -Related)	<i>DDR2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 236,000
Spondylothoracic Dysostosis	<i>MESP2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 233,000

Steel Syndrome	COL27A1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 93,000
Stuve-Wiedemann Syndrome	LIFR	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,000
Sulfate Transporter-Related Osteochondrodysplasia	SLC26A2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Tay-Sachs Disease	HEXA	AR	Reduced Risk	Tay-Sachs disease enzyme: Non-carrier White blood cells: Non-carrier <ul style="list-style-type: none"> <li>Hex A%: 65.0% (Non-carrier : 55.0 - 72.0%; Carrier: &lt;50%)</li> <li>Total hexosaminidase activity: 1816 nmol/hr/mg</li> </ul> Plasma: Non-carrier <ul style="list-style-type: none"> <li>Hex A%: 68.7 (Non-carrier : 58.0 - 72.0%; Carrier: &lt;54%)</li> <li>Total hexosaminidase activity: 762 nmol/hr/ml</li> </ul> HEXA Sequencing: Negative <b>Personalized Residual Risk:</b> 1 in 1,400
Thiamine-Responsive Megaloblastic Anemia Syndrome	SLC19A2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,200
Thyroid Dysmorphogenesis 1	SLC5A5	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
Thyroid Dysmorphogenesis 2A	TPO	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 910
Thyroid Dysmorphogenesis 3	TG	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 850
Thyroid Dysmorphogenesis 4	IYD	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Thyroid Dysmorphogenesis 5	DUOXA2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 29,000
Thyroid Dysmorphogenesis 6	DUOX2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 190
Trichohepatoenteric Syndrome 1	TTC37	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,700
Tyrosinemia, Type I	FAH	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
Tyrosinemia, Type II	TAT	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,800
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 1,000
Usher Syndrome, Type IC	USH1C	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
Usher Syndrome, Type ID	CDH23	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 690
Usher Syndrome, Type IF	PCDH15	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,000
Usher Syndrome, Type IIA	USH2A	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 290
Usher Syndrome, Type III	CLRN1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	ACADVL	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 920
Vitamin D-Dependent Rickets, Type I	CYP27B1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Vitamin D-Resistant Rickets, Type IIA	VDR	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 17,000
Walker-Warburg Syndrome and Other FKTN-Related Dystrophies	FKTN	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,200
Werner Syndrome	WRN	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,200
Wilson Disease	ATP7B	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 350
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 22,000
Wolman Disease / Cholesteryl Ester Storage Disease	LIPA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,200
Woodhouse-Sakati Syndrome	DCAF17	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 81,000
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 5,900
Xeroderma Pigmentosum, Group A	XPA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Xeroderma Pigmentosum, Group C	XPC	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 2,000
<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 1,600

AR=Autosomal recessive; XL=X-linked

## Test methods and comments

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

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

PCR amplification using Asuragen, Inc. AmpliX<sup>®</sup> *FMR1* PCR reagents followed by capillary electrophoresis for allele sizing was performed. Samples positive for *FMR1* premutations and full mutations greater than 90 CGG repeats in length were further analyzed by Southern blot analysis or methylation PCR to assess the size and methylation status of the *FMR1* CGG repeat. Additional testing to determine the status of AGG interruptions within the *FMR1* CGG repeat will be automatically performed for premutation alleles ranging from 55 to 90 repeats. These results, which may modify risk for expansion, will follow in a separate report.

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

Multiplex PCR amplification and single-base pair probe extension analyses using the Agena Bioscience iPlex Pro chemistry on a 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%)

Conventional MLPA and/or digitalMLPA<sup>®</sup> probe sets and reagents from MRC-Holland were used for copy number variations (CNVs) analysis of specific targets versus known control samples. digitalMLPA<sup>®</sup> is a semi-quantitative technique, based on the well-established conventional MLPA method, followed by Illumina based sequencing to determine read number for amplicon quantification. False positive or negative results may occur due to rare sequence variants in target regions detected by conventional MLPA or digitalMLPA<sup>®</sup> probes. Analytical sensitivity and specificity of both the conventional MLPA method and the digitalMLPA<sup>®</sup> method are greater than 99%.

For alpha thalassemia, the copy numbers of the *HBA1* and *HBA2* genes were analyzed. Alpha-globin gene deletions, duplications, 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 precisely specified without phase analysis. With the exception of duplications, 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. Depending on ethnicity, 6 - 29 % of carriers will not be identified by dosage sensitive methods as this testing cannot distinguish 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 identify intragenic mutation in *SMN1*. Please also note that 2% of individuals diagnosed with SMA have a causative *SMN1* variant that occurred de novo, 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).

In individuals with two copies of *SMN1* with Ashkenazi Jewish, East Asian, African American, Native American 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 6000 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; *F5* (NM\_000130.4) chr1:169,551,662-169,551,679 (partial exon 2); *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 not reported.

### Copy Number Variant (CNV) Analysis (Analytical Detection Rate >98% for CNVs of 3 exons and larger, >90% for CNVs of 2 exons)

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. Deletions and duplications near the lower limit of detection may not be detected due to run variability. Genomic regions with high homology or highly repetitive sequences are excluded from this analysis.

### Exon Array Comparative Genomic Hybridization (aCGH) (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 1,000,000 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 SYBR Green reagents on a LightCycler<sup>®</sup> 480 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. Please note that in rare cases, allele drop-out may occur, which has the potential to lead to false negative results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where multiple copies of *CYP21A2* are located on the same chromosome in tandem, only the last 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. A *CYP21A1P/CYP21A2* hybrid gene detected only by MLPA but not by long-range PCR will not be reported when the long-range PCR indicates the presence of two full *CYP21A2* gene copies (one on each chromosome), as the additional hybrid gene is nonfunctional. Classic 30-kb deletions are identified by MLPA and are also identified by the presence of multiple common pathogenic *CYP21A2* variants by long-range PCR. Since multiple pseudogene-derived variants are detected in all cases with the classic 30kb deletion, we cannot rule out the possibility that some variant(s) detected could be present in trans with the chimeric *CYP21A1P/CYP21A2* gene created by the 30kb deletion. 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>™</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.

Several genes have multiple residual risks associated to reflect the likelihood of the tested individual being a carrier for different diseases that are attributed to non-overlapping pathogenic variants in that gene. When calculating the couples' combined reproductive risk, the highest residual risk for each patient was selected.

#### 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 that it is not possible to perform Tay-Sachs disease enzyme analysis on saliva samples, buccal swabs, tissue samples, semen samples, or on samples received as extracted DNA.

This test was developed, and its performance characteristics determined by Sema4 Opco, Inc. It has not been cleared or approved by the US Food and Drug Administration. FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. 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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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

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Additional disease-specific references available upon request.



Patient Information	Specimen Information	Client Information
<b>6562, DONOR</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] Gender: M Phone: [REDACTED] Patient ID: [REDACTED]	Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED]  Collected: 12/07/2022 Received: 12/08/2022 / 21:08 EST Reported: 12/20/2022 / 16:54 EST	Client #: 48041578     NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229

Ward:     FFAXCB
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**Cytogenetic Report**

**CHROMOSOME ANALYSIS, BLOOD - 14596** **Lab: EZ**

**CHROMOSOME ANALYSIS, BLOOD**

Order ID: [REDACTED]  
 Specimen Type: Blood  
 Clinical Indication: Donor of other specified organs or

**RESULT:**  
 NORMAL MALE KARYOTYPE

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

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

**NOMENCLATURE:**  
 46,XY

**ASSAY INFORMATION:**

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

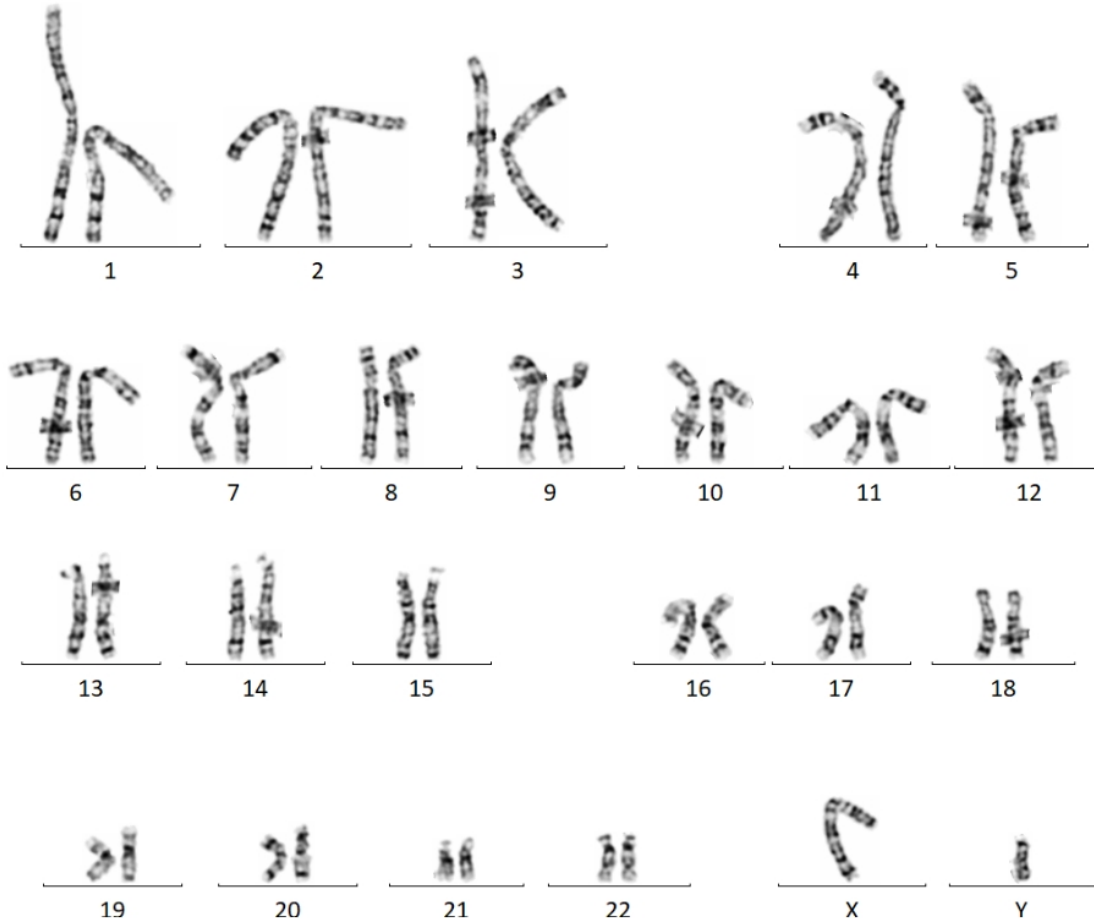
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

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

Electronic Signature:     12/20/2022 3:59 PM



Patient Information	Specimen Information	Client Information
<b>6562, DONOR</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] <b>Gender:</b> M <b>Patient ID:</b> [REDACTED]	<b>Specimen:</b> [REDACTED] <b>Collected:</b> 12/07/2022 <b>Received:</b> 12/08/2022 / 21:08 EST <b>Reported:</b> 12/20/2022 / 16:54 EST	<b>Client #:</b> 48041578 <b>GENOMICS, SEMA4</b>



**PERFORMING SITE:**

EZ QUEST DIAGNOSTICS/NICHOLS SJ, 33608 ORTEGA HWY, SAN JUAN CAPISTRANO, CA 92675-2042 Laboratory Director: IRINA MARAMICA, MD, PHD, MBA, CLIA: 05D0643352





Patient Information	Specimen Information	Client Information
<b>6562, DONOR</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] Gender: M Phone: [REDACTED] Patient ID: [REDACTED]	Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED]  Collected: 12/07/2022 Received: 12/08/2022 / 21:06 EST Reported: 12/09/2022 / 20:36 EST	Client #: 48041578     NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229

Ward:     FFXACB

Test Name	In Range	Out Of Range	Reference Range	Lab
HEMOGLOBINOPATHY EVALUATION				
RED BLOOD CELL COUNT	5.74		4.20-5.80 Million/uL	Z99
HEMOGLOBIN	15.1		13.2-17.1 g/dL	
HEMATOCRIT	45.6		38.5-50.0 %	
<b>MCV</b>		<b>79.4 L</b>	80.0-100.0 fL	
<b>MCH</b>		<b>26.3 L</b>	27.0-33.0 pg	
RDW	14.0		11.0-15.0 %	
HEMOGLOBIN A	97.5		>96.0 %	Z99
HEMOGLOBIN F	<1.0		<2.0 %	
HEMOGLOBIN A2 (QUANT)	2.5		2.2-3.2 %	
INTERPRETATION	*			

The red blood cell indices are suggestive of microcytosis and or hypochromia. Complete interpretation requires clinical correlation, review of family history and exclusion of possible etiologies for microcytosis and hypochromia, such as iron deficiency and alpha thalassemia.

**PERFORMING SITE:**

Z99    QUEST DIAGNOSTICS CLIFTON, 1 INSIGHTS DRIVE, CLIFTON, NJ 07012-2355 Laboratory Director: LEZA N GALLO, MD, CLIA: 31D0696246