Donor 6519

Genetic Testing Summary

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

Last Updated: 09/22/22

Donor Reported Ancestry: Lithuanian, Ukrainian, Austrian Jewish Ancestry: Yes

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.	Negative for genes sequenced. Carrier: Canavan Disease (ASPA) Carrier: Gaucher Disease (GBA) Carrier: Mucolipidosis IV (MCOLN1) 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 6519
Date of Birth: [redacted]
Sema4 ID: [redacted]
Client ID: [redacted]
Indication: Carrier Screening

Specimen Information
Specimen Type: Blood
Date Collected: 01/07/2022
Date Received: 01/08/2022
Final Report: 01/20/2022

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

Expanded Carrier Screen (502 genes)

with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
Carrier of Canavan Disease (AR) Associated gene(s): *ASPA* Variant(s) Detected: c.854A>C, p.E285A, Pathogenic, Heterozygous (one copy) **Carrier of Gaucher Disease (AR)** Associated gene(s): *GBA* Variant(s) Detected: c.1226A>G, p.N409S, Pathogenic, Heterozygous (one copy) **Carrier of Mucolipidosis IV (AR)** Associated gene(s): *MCOLN1* Variant(s) Detected: c.-1016_788del6434, Pathogenic, Heterozygous (one copy)	**Negative for all other genes tested** To view a full list of genes and diseases tested please see Table 1 in this report

AR=Autosomal recessive; XL=X-linked

Recommendations

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

Interpretation of positive results

Canavan Disease (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.854A>C, p.E285A, was detected in the *ASPA* gene (NM_000049.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Canavan disease. Therefore, this individual is expected to be at least a carrier for Canavan disease. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Canavan Disease?

Canavan disease is an autosomal recessive disorder caused by pathogenic variants in the gene *ASPA* and is most commonly observed among those of Ashkenazi Jewish descent and European ancestry. The neonatal/infantile form of Canavan disease is severe and characterized by enlarged head circumference, developmental delay, hypotonia, and failure to thrive. The progression of the disease leads to severe muscle weakness and inability to sit without support and to eat independently. Life expectancy is usually shortened to mid-teen years. The milder form of Canavan disease is characterized by mild developmental delays that may be unrecognized throughout life. Several specific variants have been associated with the infantile and later-onset forms of the disease, and therefore the severity of the disease may be predicted based on the genotype in some patients. Individuals with one mild variant and one severe variant usually present with the milder form of Canavan disease.

Gaucher Disease (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.1226A>G, p.N409S, was detected in the *GBA* gene (NM_001005741.2). Affected individuals with this variant tend to have a milder form of the disease. Individuals with at least one copy of the p.N409S variant do not develop primary neurologic disease. When present in the homozygous form, the disease phenotype may vary from asymptomatic to severe, although usually tends to be milder than the disease resulting from other genotypes. When this variant is present in trans with a pathogenic variant, it is considered to be causative for Gaucher disease. Therefore, this individual is expected to be at least a carrier for Gaucher disease. Heterozygous carriers are not expected to exhibit symptoms of this disease, but have an increased risk of developing Parkinson's disease. This risk is approximately five times higher than the general population in heterozygous carriers and 10-20 times higher than the general population in homozygous carriers (PMID: 31010158).

What is Gaucher Disease?

Gaucher disease is an autosomal recessive disease caused by pathogenic variants in the gene *GBA* . While it is found in populations worldwide, it is most prevalent in individuals of Ashkenazi Jewish descent. Gaucher disease has variable clinical features and can be divided into the following subtypes.

- Type 1 is characterized by bone disease and the lack of neurological involvement. The bone disease can vary in severity from asymptomatic to destruction of bone tissue and painful "bone crises". Patients often have anemia and abnormal blood cell counts and may have lung disease. Some patients may be asymptomatic.
- Type 2 is a severe form that begins in infancy and usually results in death by the age of 2 years. It is characterized by severe neurologic deterioration, seizures, anemia, poor feeding and failure to thrive.
- The perinatal-lethal form is a more severe subtype of type 2, where accumulation of fluid in the fetus results in death in utero, or in the first several days of life. Some patients do not have the excess fluid, but die within three months.
- Type 3 is characterized by neurologic deterioration, as with type 2, but onset may be anywhere from childhood to adulthood, and progresses more slowly. Patients develop seizures and declining intelligence. Patients also experience the bone disease and anemia seen in type I.
- The cardiovascular form is a subtype of type 3 that is characterized by calcification of the heart valves during adolescence. Patients may also have problems controlling their eye movements. The cardiac manifestations are usually fatal.

Some pathogenic variants are associated with a specific type of Gaucher disease. However, there is significant variability in the phenotypes, even between identical twins. Therefore, it is not always possible to predict the severity of disease based on genotype.

Mucolipidosis IV (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic deletion, c.-1016_788del6434, was detected in the *MCOLN1* gene (NM_020533.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for mucolipidosis IV. Therefore, this individual is expected to be at least a carrier for mucolipidosis IV. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Mucolipidosis IV?

Mucolipidosis IV is an autosomal recessive disorder caused by pathogenic variants in the gene *MCOLN1* . It is predominantly diagnosed in individuals of Ashkenazi Jewish descent, although it has also been reported in patients of other ethnicities. The typical form of the disease is

characterized by a severe motor delay (which halts at the level of a 1 or 2 year old) and vision loss as a result of retinal degeneration and corneal clouding. Most patients do not learn to speak or walk, but may learn some sign language or be able to sit independently. Patients are intellectually disabled and have difficulty controlling their movements. Approximately 15% of patients experience deterioration of neurological symptoms over time, but the neurologic deficits do not change in the remainder of patients. About 5% of patients have a milder, atypical form characterized by progressive ataxia and eye abnormalities, and they may learn to walk. Most patients live into adulthood, although life expectancy is shorter than normal. Specific variants have been associated with typical or atypical disease, and therefore it may be possible to predict the severity of disease based on the genotype. The pathogenic variant common in the Ashkenazi Jewish population is associated with the more severe form.

Test description

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

Alice K Tanner

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

Genes and diseases tested

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

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

	Disease	Gene	Inheritance Pattern	Status	Detailed Summary
⊕	**Positive**				
	Canavan Disease	*ASPA*	AR	Carrier	c.854A>C, p.E285A, Pathogenic, Heterozygous (one copy)
	Gaucher Disease	*GBA*	AR	Carrier	c.1226A>G, p.N409S, Pathogenic, Heterozygous (one copy)
	Mucolipidosis IV	*MCOLN1*	AR	Carrier	c.-1016_788del6434, Pathogenic, Heterozygous (one copy)
⊖	**Negative**				
	2-Methylbutyrylglycinuria	*ACADSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 84,000
	3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	*HSD3B2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 164,000
	3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC1*-Related)	*MCCC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,500
	3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC2*-Related)	*MCCC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 27,000
	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 30,000
	6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	*PTS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 156,000
	***CD59*-Mediated Hemolytic Anemia**	*CD59*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 513,000
	Abetalipoproteinemia	*MTTP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,800
	Achalasia-Addisonianism-Alacrimia Syndrome	*AAAS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,200
	Achromatopsia (*CNGA3*-Related)	*CNGA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 440
	Achromatopsia (*CNGB3*-related)	*CNGB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,600
	Acrodermatitis Enteropathica	*SLC39A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
	Acute Infantile Liver Failure	*TRMU*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 46,000
	Acyl-CoA Oxidase I Deficiency	*ACOX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 59,000
	Adams-Oliver Syndrome 4	*EOGT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 43,000
	Adenosine Deaminase Deficiency	*ADA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,300
	Adrenocorticotropic Hormone Deficiency	*TBX19*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
	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 348,000
	Aicardi-Goutieres Syndrome (*RNASEH2C*-Related)	*RNASEH2C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
	Aicardi-Goutieres Syndrome (*SAMHD1*-Related)	*SAMHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
	Aicardi-Goutieres Syndrome (*TREX1*-Related)	*TREX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 164,000
	Albinism, Oculocutaneous, Type III	*TYRP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
	Alkaptonuria	*HGD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
	Alpha-Mannosidosis	*MAN2B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,000

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 **Personalized Residual Risk:** 1 in 490
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 23,000
Alport Syndrome (*COL4A4*-Related)	*COL4A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
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 4,400
Andermann Syndrome	*SLC12A6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 164,000
Antley-Bixler Syndrome (*POR*-Related)	*POR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,100
Argininemia	*ARG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Argininosuccinic Aciduria	*ASL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 56,000
Aromatase Deficiency	*CYP19A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,800
Arthrogryposis, Intellectual Disability, and Seizures	*SLC35A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 37,000
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 51,000
Ataxia-Telangiectasia	*ATM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,900
Ataxia-Telangiectasia-Like Disorder 1	*MRE11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,200
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	*SACS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,500
BH4-Deficient Hyperphenylalaninemia C	*QDPR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,000
BH4-Deficient Hyperphenylalaninemia D	*PCBD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 42,000
Bardet-Biedl Syndrome (*ARL6*-Related)	*ARL6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Bardet-Biedl Syndrome (*BBS10*-Related)	*BBS10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 30,000
Bardet-Biedl Syndrome (*BBS12*-Related)	*BBS12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Bardet-Biedl Syndrome (*BBS1*-Related)	*BBS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Bardet-Biedl Syndrome (*BBS2*-Related)	*BBS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Bardet-Biedl Syndrome (*BBS4*-Related)	*BBS4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Bare Lymphocyte Syndrome, Type II	*CIITA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 65,000
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 164,000
Bernard-Soulier Syndrome, Type A1	*GP1BA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 66,000
Bernard-Soulier Syndrome, Type C	*GP9*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Beta-Globin-Related Hemoglobinopathies	*HBB*	AR	Reduced Risk	**Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies):** 1 in 2,700 **Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant):** 1 in 11,000 **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 6,900
Beta-Mannosidosis	*MANBA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Bilateral Frontoparietal Polymicrogyria	*GPR56*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 62,000
Biotinidase Deficiency	*BTD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Bloom Syndrome	*BLM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Carbamoylphosphate Synthetase I Deficiency	*CPS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Carnitine Acylcarnitine Translocase Deficiency	*SLC25A20*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600

Carnitine Palmitoyltransferase IA Deficiency	*CPT1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 49,000
Carnitine Palmitoyltransferase II Deficiency	*CPT2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Carpenter Syndrome	*RAB23*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Cartilage-Hair Hypoplasia	*RMRP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,700
Catecholaminergic Polymorphic Ventricular Tachycardia	*CASQ2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Central Hypothyroidism and Testicular Enlargement	*IGSF1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 781,000
Cerebral Creatine Deficiency Syndrome 1	*SLC6A8*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 208,000
Cerebral Creatine Deficiency Syndrome 2	*GAMT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 70,000
Cerebral Creatine Deficiency Syndrome 3	*GATM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Cerebral Dysgenesis, Neuropathy, Ichthyosis, and Palmoplantar Keratoderma Syndrome	*SNAP29*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 383,000
Cerebrotendinous Xanthomatosis	*CYP27A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 33,000
Charcot-Marie-Tooth Disease, Type 4D	*NDRG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 693,000
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	*PRPS1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 114,000
Charcot-Marie-Tooth Disease, X-Linked	*GJB1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Chediak-Higashi Syndrome	*LYST*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Chondrodysplasia Punctata	*ARSE*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 862,000
Choreoacanthocytosis	*VPS13A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 31,000
Choroideremia	*CHM*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 125,000
Chronic Granulomatous Disease (*CYBA*-Related)	*CYBA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Chronic Granulomatous Disease (*CYBB*-Related)	*CYBB*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 294,000
Citrin Deficiency	*SLC25A13*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 27,000
Citrullinemia, Type 1	*ASS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 167,000
Cockayne Syndrome, Type A	*ERCC8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Cockayne Syndrome, Type B and other *ERCC6*-Related Disorders	*ERCC6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,200
Cohen Syndrome	*VPS13B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Combined Factor V and VIII Deficiency	*LMAN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 70,000
Combined Malonic and Methylmalonic Aciduria	*ACSF3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,800
Combined Oxidative Phosphorylation Deficiency 1	*GFM1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Combined Oxidative Phosphorylation Deficiency 3	*TSFM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
Combined Pituitary Hormone Deficiency 1	*POU1F1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
Combined Pituitary Hormone Deficiency 2	*PROP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,300
Combined Pituitary Hormone Deficiency 3	*LHX3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 197,000
Combined SAP Deficiency	*PSAP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 78,000
Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1	*GUCY2D*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency	*CYP11B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 510
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	*CYP17A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	*CYP21A2*	AR	Reduced Risk	*CYP21A2* copy number: 2 *CYP21A2* sequencing: Negative **Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)):** 1 in 120 **Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)):** 1 in 780
Congenital Adrenal Hypoplasia (*NR0B1*-Related)	*NR0B1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 353,000
Congenital Adrenal Insufficiency (*CYP11A1*-Related)	*CYP11A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 50,000

Congenital Amegakaryocytic Thrombocytopenia	*MPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Congenital Bile Acid Synthesis Defect (*AKR1D1*-Related)	*AKR1D1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Congenital Bile Acid Synthesis Defect (*HSD3B7*-Related)	*HSD3B7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Congenital Disorder of Deglycosylation	*NGLY1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,700
Congenital Disorder of Glycosylation, Type Ia	*PMM2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,500
Congenital Disorder of Glycosylation, Type Ib	*MPI*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,900
Congenital Disorder of Glycosylation, Type Ic	*ALG6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,000
Congenital Disorder of Glycosylation, Type Im	*DOLK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 204,000
Congenital Dyserythropoietic Anemia Type 2	*SEC23B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 127,000
Congenital Dyserythropoietic Anemia, Type Ia	*CDAN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,500
Congenital Ichthyosis 4A and 4B	*ABCA12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Congenital Insensitivity to Pain with Anhidrosis	*NTRK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,600
Congenital Muscular Dystrophy (*LAMA2*-Related)	*LAMA2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Congenital Myasthenic Syndrome (*CHAT*-Related)	*CHAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Congenital Myasthenic Syndrome (*CHRNE*-Related)	*CHRNE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Congenital Myasthenic Syndrome (*DOK7*-Related)	*DOK7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Congenital Myasthenic Syndrome (*RAPSN*-Related)	*RAPSN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 25,000
Congenital Neutropenia (*HAX1*-Related)	*HAX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Congenital Neutropenia (*VPS45*-Related)	*VPS45*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 43,000
Congenital Nongoitrous Hypothyroidism 1	*TSHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Congenital Nongoitrous Hypothyroidism 4	*TSHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 227,000
Congenital Secretory Chloride Diarrhea 1	*SLC26A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Corneal Dystrophy and Perceptive Deafness	*SLC4A11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Corticosterone Methyloxidase Deficiency	*CYP11B2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Cystic Fibrosis	*CFTR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Cystinosis	*CTNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,200
Cystinuria (*SLC3A1*-Related)	*SLC3A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Cytochrome C Oxidase Deficiency / Leigh Syndrome (*COX15*-Related)	*COX15*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,300
D-Bifunctional Protein Deficiency	*HSD17B4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,900
Deafness, Autosomal Recessive 3	*MYO15A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 500
Deafness, Autosomal Recessive 59	*PJVK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 18,000
Deafness, Autosomal Recessive 7	*TMC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Deafness, Autosomal Recessive 76	*SYNE4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 65,000
Deafness, Autosomal Recessive 77	*LOXHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Deafness, Autosomal Recessive 8/10	*TMPRSS3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Deafness, Autosomal Recessive 9	*OTOF*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 660
Desbuquois Dysplasia 1	*CANT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 14,000
Desmosterolosis	*DHCR24*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
Diaphanospondylodysostosis	*BMPER*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 23,000
Distal Renal Tubular Acidosis and other *SLC4A1*-related Disorders	*SLC4A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Duchenne Muscular Dystrophy / Becker Muscular Dystrophy	*DMD*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Dyskeratosis Congenita (*DKC1*-related)	*DKC1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 9,259,000
Dyskeratosis Congenita (*RTEL1*-Related)	*RTEL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Dystrophic Epidermolysis Bullosa	*COL7A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,900

Ehlers-Danlos Syndrome, Type VI	*PLOD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Ehlers-Danlos Syndrome, Type VIIC	*ADAMTS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 16,000
Ellis-Van Creveld Syndrome (*EVC2*-Related)	*EVC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 24,000
Ellis-van Creveld Syndrome (*EVC*-Related)	*EVC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,300
Emery-Dreifuss Myopathy 1	*EMD*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 833,000
Enhanced S-Cone Syndrome	*NR2E3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Ethylmalonic Encephalopathy	*ETHE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Fabry Disease	*GLA*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 7,700
Factor IX Deficiency	*F9*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
Factor VII Deficiency	*F7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 440
Factor XI Deficiency	*F11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 730
Familial Autosomal Recessive Hypercholesterolemia	*LDLRAP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 171,000
Familial Dysautonomia	*IKBKAP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,400
Familial Hypercholesterolemia	*LDLR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,000
Familial Hyperinsulinism (*ABCC8*-Related)	*ABCC8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 510
Familial Hyperinsulinism (*KCNJ11*-Related)	*KCNJ11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Familial Hyperphosphatemic Tumoral Calcinosis	*GALNT3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Familial Mediterranean Fever	*MEFV*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 720
Fanconi Anemia, Group A	*FANCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,500
Fanconi Anemia, Group C	*FANCC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,100
Fanconi Anemia, Group G	*FANCG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Fanconi-Bickel Syndrome	*SLC2A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Fragile X Syndrome	*FMR1*	XL	Reduced Risk	*FMR1* CGG repeat sizes: Not Performed *FMR1* Sequencing: Negative Fragile X CGG triplet repeat expansion testing was not performed at this time, as the patient has either been previously tested or is a male. **Personalized Residual Risk:** 1 in 8,300
Fructose-1,6-Bisphosphatase Deficiency	*FBP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Fucosidosis	*FUCA1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Fumarase Deficiency	*FH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,900
Fundus Albipunctatus	*RDH5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 41,000
GRACILE Syndrome and Other *BCS1L*-Related Disorders	*BCS1L*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Galactokinase Deficiency	*GALK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,300
Galactose Epimerase Deficiency	*GALE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,900
Galactosemia	*GALT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 23,000
Galactosialidosis	*CTSA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Generalized Thyrotropin-Releasing Hormone Resistance	*TRHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 162,000
Geroderma Osteodysplasticum	*GORAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 76,000
Gitelman Syndrome	*SLC12A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,000
Glanzmann Thrombasthenia (*ITGA2B*-Related)	*ITGA2B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Glanzmann Thrombasthenia (*ITGB3*-Related)	*ITGB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,300
Glutaric Acidemia, Type I	*GCDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Glutaric Acidemia, Type IIa	*ETFA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,400
Glutaric Acidemia, Type IIb	*ETFB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 49,000
Glutaric Acidemia, Type IIc	*ETFDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 123,000
Glutathione Synthetase Deficiency	*GSS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,600
Glycine Encephalopathy (*AMT*-Related)	*AMT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300

Glycine Encephalopathy (*GLDC*-Related)	*GLDC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 690
Glycogen Storage Disease, Type 0	*GYS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Glycogen Storage Disease, Type II	*GAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Glycogen Storage Disease, Type III	*AGL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	*GBE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Glycogen Storage Disease, Type IXb	*PHKB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Glycogen Storage Disease, Type Ia	*G6PC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,400
Glycogen Storage Disease, Type Ib	*SLC37A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 125,000
Glycogen Storage Disease, Type V	*PYGM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 420
Glycogen Storage Disease, Type VI	*PYGL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Glycogen Storage Disease, Type VII	*PFKM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,900
Gray Platelet Syndrome	*NBEAL2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Growth Hormone Deficiency, Type IB	*GHRHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
HMG-CoA Lyase Deficiency	*HMGCL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,400
Hemochromatosis, Type 2A	*HFE2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,400
Hemochromatosis, Type 3	*TFR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,400
Hereditary Fructose Intolerance	*ALDOB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,000
Hereditary Spastic Paraparesis 49	*TECPR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Hermansky-Pudlak Syndrome, Type 1	*HPS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,300
Hermansky-Pudlak Syndrome, Type 3	*HPS3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 27,000
Hermansky-Pudlak Syndrome, Type 4	*HPS4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000
Hermansky-Pudlak Syndrome, Type 6	*HPS6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,400
Hmg-CoA Synthase 2 Deficiency	*HMGCS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Holocarboxylase Synthetase Deficiency	*HLCS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,400
Homocystinuria (*CBS*-Related)	*CBS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,500
Homocystinuria due to *MTHFR* Deficiency	*MTHFR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Homocystinuria, cblE Type	*MTRR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 166,000
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	*MTR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Hydrocephalus	*L1CAM*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 40,000
Hydrolethalus Syndrome	*HYLS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 32,000
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 8,900
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	*SARS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 29,000
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 82,000
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 94,000
Hypoparathyroidism-Retardation-Dysmorphic Syndrome	*TBCE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Hypophosphatasia	*ALPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Hypophosphatemic Rickets with Hypercalciuria	*SLC34A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
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 120,000
Immunodeficiency 19	*CD3D*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 49,000
Inclusion Body Myopathy 2	*GNE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Infantile Cerebral and Cerebellar Atrophy	*MED17*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 130,000
Infantile Neuroaxonal Dystrophy 1 and other *PLA2G6*-Related Disorders	*PLA2G6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 600

Intellectual Disability, Autosomal Recessive 3	*CC2D1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
Intrahepatic Cholestasis	*ATP8B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Isovaleric Acidemia	*IVD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Joubert Syndrome 2	*TMEM216*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 14,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	*NPHP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,800
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	*RPGRIP1L*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,000
Junctional Epidermolysis Bullosa (*COL17A1*-Related)	*COL17A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Junctional Epidermolysis Bullosa (*ITGA6*-Related)	*ITGA6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 131,000
Junctional Epidermolysis Bullosa (*ITGB4*-Related)	*ITGB4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,500
Junctional Epidermolysis Bullosa (*LAMA3*-Related)	*LAMA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,300
Junctional Epidermolysis Bullosa (*LAMB3*-Related)	*LAMB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 98,000
Junctional Epidermolysis Bullosa (*LAMC2*-Related)	*LAMC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 78,000
Kohlschutter-Tonz Syndrome	*ROGDI*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 164,000
Krabbe Disease	*GALC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Lamellar Ichthyosis, Type 1	*TGM1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 62,000
Laron Dwarfism	*GHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,500
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	*CEP290*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Leber Congenital Amaurosis 13	*RDH12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	*TULP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	*RPE65*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Leber Congenital Amaurosis 4	*AIPL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Leber Congenital Amaurosis 5	*LCA5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 23,000
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	*CRB1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,400
Leigh Syndrome (*NDUFS7*-Related)	*NDUFS7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 38,000
Leigh Syndrome (*SURF1*-Related)	*SURF1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,900
Leigh Syndrome, French-Canadian Type	*LRPPRC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 14,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease	*GLE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Lethal Congenital Contracture Syndrome 2	*ERBB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 79,000
Lethal Congenital Contracture Syndrome 3	*PIP5K1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 151,000
Leukoencephalopathy with Vanishing White Matter	*EIF2B5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Limb-Girdle Muscular Dystrophy, Type 2A	*CAPN3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Limb-Girdle Muscular Dystrophy, Type 2B	*DYSF*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 25,000
Limb-Girdle Muscular Dystrophy, Type 2C	*SGCG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
Limb-Girdle Muscular Dystrophy, Type 2D	*SGCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 27,000
Limb-Girdle Muscular Dystrophy, Type 2E	*SGCB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Limb-Girdle Muscular Dystrophy, Type 2F	*SGCD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 36,000
Limb-Girdle Muscular Dystrophy, Type 2H	*TRIM32*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Limb-Girdle Muscular Dystrophy, Type 2I	*FKRP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Limb-Girdle Muscular Dystrophy, Type 2L	*ANO5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Lipoamide Dehydrogenase Deficiency	*DLD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Lipoid Adrenal Hyperplasia	*STAR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Lipoprotein Lipase Deficiency	*LPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600

Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADHA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,900
Lowe Syndrome	*OCRL*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 1,375,000
Lysinuric Protein Intolerance	*SLC7A7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
MEDNIK Syndrome	*AP1S1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 294,000
Malonyl-CoA Decarboxylase Deficiency	*MLYCD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Maple Syrup Urine Disease, Type 1a	*BCKDHA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Maple Syrup Urine Disease, Type 1b	*BCKDHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,100
Maple Syrup Urine Disease, Type 2	*DBT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 42,000
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	*MKS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 127,000
Medium Chain Acyl-CoA Dehydrogenase Deficiency	*ACADM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Megalencephalic Leukoencephalopathy with Subcortical Cysts	*MLC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 19,000
Megaloblastic Anemia 1	*AMN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Menkes Disease	*ATP7A*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Metachromatic Leukodystrophy	*ARSA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,600
Methionine Adenosyltransferase I/III Deficiency	*MAT1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Methylmalonic Acidemia (*MMAA*-Related)	*MMAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Methylmalonic Acidemia (*MMAB*-Related)	*MMAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Methylmalonic Acidemia (*MUT*-Related)	*MUT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 33,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	*MMACHC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	*MMADHC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 250,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	*LMBRD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,800
Methylmalonyl-CoA Epimerase Deficiency	*MCEE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 168,000
Microphthalmia / Anophthalmia	*VSX2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 44,000
Mitochondrial Complex I Deficiency (*ACAD9*-Related)	*ACAD9*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 124,000
Mitochondrial Complex I Deficiency (*NDUFA11*-Related)	*NDUFA11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 548,000
Mitochondrial Complex I Deficiency (*NDUFAF5*-Related)	*NDUFAF5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 49,000
Mitochondrial Complex I Deficiency (*NDUFS6*-Related)	*NDUFS6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 371,000
Mitochondrial Complex I Deficiency (*NDUFV1*-Related)	*NDUFV1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Mitochondrial Complex I Deficiency / Leigh Syndrome (*FOXRED1*-Related)	*FOXRED1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 56,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (*NDUFAF2*-Related)	*NDUFAF2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 192,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (*NDUFS4*-Related)	*NDUFS4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Mitochondrial Complex IV Deficiency (*COX20*-related)	*COX20*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 68,000
Mitochondrial Complex IV Deficiency (*COX6B1*-related)	*COX6B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,231,000
Mitochondrial Complex IV Deficiency (*APOPT1*-Related)	*APOPT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,600
Mitochondrial Complex IV Deficiency (*PET100*-Related)	*PET100*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 546,000
Mitochondrial Complex IV Deficiency (*SCO1*-related)	*SCO1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 25,000
Mitochondrial Complex IV Deficiency / Leigh Syndrome (*COX10*-Related)	*COX10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,900
Mitochondrial DNA Depletion Syndrome 2	*TK2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 70,000
Mitochondrial DNA Depletion Syndrome 3	*DGUOK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,100

Mitochondrial DNA Depletion Syndrome 4A and 4B and other *POLG*-Related Disorders	*POLG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 380
Mitochondrial DNA Depletion Syndrome 5	*SUCLA2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 65,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	*MPV17*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 162,000
Mitochondrial Myopathy and Sideroblastic Anemia 1	*PUS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 333,000
Mitochondrial Trifunctional Protein Deficiency (*HADHB*-Related)	*HADHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,400
Molybdenum Cofactor Deficiency A	*MOCS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 61,000
Mucolipidosis II / IIIA	*GNPTAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 166,000
Mucolipidosis III Gamma	*GNPTG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 51,000
Mucopolysaccharidosis Type I	*IDUA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 109,000
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 1,900
Mucopolysaccharidosis Type IIIB	*NAGLU*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Mucopolysaccharidosis Type IIIC	*HGSNAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,600
Mucopolysaccharidosis Type IIID	*GNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 201,000
Mucopolysaccharidosis Type IVa	*GALNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	*GLB1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Mucopolysaccharidosis VII	*GUSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Mucopolysaccharidosis type IX	*HYAL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 170,000
Mucopolysaccharidosis type VI	*ARSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Mulibrey Nanism	*TRIM37*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 164,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	*PIGN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,000
Multiple Pterygium Syndrome	*CHRNG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Multiple Sulfatase Deficiency	*SUMF1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 30,000
Muscle-Eye-Brain Disease and Other *POMGNT1*-Related Congenital Muscular Dystrophy-Dystroglycanopathies	*POMGNT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,500
Myoneurogastrointestinal Encephalopathy	*TYMP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 83,000
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 60,000
Nemaline Myopathy 2	*NEB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 660
Nephrogenic Diabetes Insipidus, Type II	*AQP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Nephrogenic Diabetes insipidus (*AVPR2*-related)/ Nephrogenic Syndrome of Inappropriate Antidiuresis	*AVPR2*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 471,000
Nephronophthisis 2	*INVS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Nephrotic Syndrome (*NPHS1*-Related) / Congenital Finnish Nephrosis	*NPHS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 880
Nephrotic Syndrome (*NPHS2*-Related) / Steroid-Resistant Nephrotic Syndrome	*NPHS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 850
Neurodegeneration due to Cerebral Folate Transport Deficiency	*FOLR1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	*PLAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 217,000
Neuronal Ceroid-Lipofuscinosis (*CLN3*-Related)	*CLN3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Neuronal Ceroid-Lipofuscinosis (*CLN5*-Related)	*CLN5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
Neuronal Ceroid-Lipofuscinosis (*CLN6*-Related)	*CLN6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 14,000
Neuronal Ceroid-Lipofuscinosis (*CLN8*-Related)	*CLN8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Neuronal Ceroid-Lipofuscinosis (*MFSD8*-Related)	*MFSD8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,200
Neuronal Ceroid-Lipofuscinosis (*PPT1*-Related)	*PPT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
Neuronal Ceroid-Lipofuscinosis (*TPP1*-Related)	*TPP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 127,000

Niemann-Pick Disease (*SMPD1*-Related)	*SMPD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,700
Niemann-Pick Disease, Type C (*NPC1*-Related)	*NPC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Niemann-Pick Disease, Type C (*NPC2*-Related)	*NPC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Nijmegen Breakage Syndrome	*NBN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 43,000
Non-Syndromic Hearing Loss (*GJB2*-Related)	*GJB2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 210
Oculocutaneous Albinism, Type IA / IB	*TYR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Oculocutaneous Albinism, Type IV	*SLC45A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,600
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	*WNT10A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Omenn Syndrome (*RAG2*-Related)	*RAG2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	*DCLRE1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,400
Omenn Syndrome and other *RAG1*-Related Disorders	*RAG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Ornithine Aminotransferase Deficiency	*OAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 61,000
Ornithine Transcarbamylase Deficiency	*OTC*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 103,000
Osteogenesis Imperfecta, Type XI	*FKBP10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Osteopetrosis 1	*TCIRG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Osteopetrosis 8	*SNX10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 34,000
Otospondylomegaepiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	*COL11A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,500
Papillon-Lefevre Syndrome	*CTSC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Pendred Syndrome	*SLC26A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Peroxisome Biogenesis Disorder 3A and 3B	*PEX12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Peroxisome Biogenesis Disorder 7A and 7B	*PEX26*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 26,000
Phenylalanine Hydroxylase Deficiency	*PAH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Polycystic Kidney Disease, Autosomal Recessive	*PKHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,600
Polyglandular Autoimmune Syndrome, Type 1	*AIRE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Pontocerebellar Hypoplasia, Type 1A	*VRK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 31,000
Pontocerebellar Hypoplasia, Type 1B	*EXOSC3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Pontocerebellar Hypoplasia, Type 2A and Type 4	*TSEN54*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 50,000
Pontocerebellar Hypoplasia, Type 2E	*VPS53*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 135,000
Pontocerebellar Hypoplasia, Type 6	*RARS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Primary Carnitine Deficiency	*SLC22A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 50,000
Primary Ciliary Dyskinesia (*CCDC103*-Related)	*CCDC103*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 33,000
Primary Ciliary Dyskinesia (*CCDC151*-Related)	*CCDC151*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 98,000
Primary Ciliary Dyskinesia (*CCDC39*-Related)	*CCDC39*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
Primary Ciliary Dyskinesia (*DNAH5*-Related)	*DNAH5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,500
Primary Ciliary Dyskinesia (*DNAI1*-Related)	*DNAI1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 38,000
Primary Ciliary Dyskinesia (*DNAI2*-Related)	*DNAI2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
Primary Ciliary Dyskinesia (*RSPH9*-Related)	*RSPH9*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 73,000
Primary Coenzyme Q10 Deficiency 7	*COQ4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 16,000
Primary Congenital Glaucoma 3A	*CYP1B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Primary Hyperoxaluria, Type 1	*AGXT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Primary Hyperoxaluria, Type 2	*GRHPR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,500
Primary Hyperoxaluria, Type 3	*HOGA1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,600
Progressive Cerebello-Cerebral Atrophy	*SEPSECS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 164,000
Progressive Familial Intrahepatic Cholestasis, Type 2	*ABCB11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 880
Progressive Myoclonic Epilepsy, Type 1B	*PRICKLE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 136,000
Progressive Pseudorheumatoid Dysplasia	*WISP3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000

Prolidase Deficiency	*PEPD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 158,000
Propionic Acidemia (*PCCA*-Related)	*PCCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Propionic Acidemia (*PCCB*-Related)	*PCCB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
Pulmonary Surfactant Dysfunction	*ABCA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Pycnodysostosis	*CTSK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Pyridoxamine 5'-Phosphate Oxidase Deficiency	*PNPO*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Pyridoxine-Dependent Epilepsy	*ALDH7A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Pyruvate Carboxylase Deficiency	*PC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Pyruvate Dehydrogenase E1-Alpha Deficiency	*PDHA1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 139,000
Pyruvate Dehydrogenase E1-Beta Deficiency	*PDHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Renal Tubular Acidosis and Deafness	*ATP6V1B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,500
Retinitis Pigmentosa 25	*EYS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,400
Retinitis Pigmentosa 26	*CERKL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,000
Retinitis Pigmentosa 28	*FAM161A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 24,000
Retinitis Pigmentosa 36	*PRCD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 422,000
Retinitis Pigmentosa 59	*DHDDS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,900
Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16	*C8ORF37*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 50,000
Rh Deficiency Syndrome	*RHAG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Rhizomelic Chondrodysplasia Punctata, Type 1	*PEX7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 23,000
Rhizomelic Chondrodysplasia Punctata, Type 3	*AGPS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,024,000
Roberts Syndrome	*ESCO2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000
Salla Disease	*SLC17A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,700
Salt and Pepper Developmental Regression Syndrome	*ST3GAL5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Sandhoff Disease	*HEXB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Schimke Immunoosseous Dysplasia	*SMARCAL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Seckel Syndrome 5 / Microcephaly 9	*CEP152*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 45,000
Segawa Syndrome	*TH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,700
Sepiapterin Reductase Deficiency	*SPR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 43,000
Severe Combined Immunodeficiency (*IL7R*-Related)	*IL7R*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
Severe Combined Immunodeficiency (*JAK3*-Related)	*JAK3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
Severe Combined Immunodeficiency (*PTPRC*-Related)	*PTPRC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,500
Severe Congenital Neutropenia 4	*G6PC3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Severe Neonatal Hyperparathyroidism	*CASR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis	*POC1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 135,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	*ACADS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,500
Shwachman-Diamond Syndrome	*SBDS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 19,000
Sialidosis, Type I and Type II	*NEU1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 61,000
Sjogren-Larsson Syndrome	*ALDH3A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,800
Smith-Lemli-Opitz Syndrome	*DHCR7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Spastic Paraplegia 15	*ZFYVE26*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 164,000
Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly	*SLC1A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Spherocytosis, Type 5	*EPB42*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Spinal Muscular Atrophy	*SMN1*	AR	Reduced Risk	*SMN1* copy number: 2 *SMN2* copy number: 2 c.*3+80T>G: Negative *SMN1* Sequencing: Negative **Personalized Residual Risk:** 1 in 1,246

Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S	*IGHMBP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,900
Spinocerebellar Ataxia with Axonal Neuropathy 3	*COA7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000
Spondylocostal Dysostosis 1	*DLL3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 43,000
Spondylometaepiphyseal Dysplasia (*DDR2*-Related)	*DDR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 220,000
Spondylothoracic Dysostosis	*MESP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 225,000
Steel Syndrome	*COL27A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 118,000
Stuve-Wiedemann Syndrome	*LIFR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000
Sulfate Transporter-Related Osteochondrodysplasia	*SLC26A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Tay-Sachs Disease	*HEXA*	AR	Reduced Risk	Tay-Sachs disease enzyme: Non-carrier White blood cells: Non-carrier • Hex A%: 66.8% (Non-carrier : 55.0 - 72.0%; Carrier: <50%) • Total hexosaminidase activity: 2183 nmol/hr/mg Plasma: Non-carrier • Hex A%: 66.5 (Non-carrier : 58.0 - 72.0%; Carrier: <54%) • Total hexosaminidase activity: 799 nmol/hr/ml *HEXA* Sequencing: Negative **Personalized Residual Risk:** 1 in 3,000
Thiamine-Responsive Megaloblastic Anemia Syndrome	*SLC19A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 101,000
Thyroid Dyshormonogenesis 1	*SLC5A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,400
Thyroid Dyshormonogenesis 2A	*TPO*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 440
Thyroid Dyshormonogenesis 3	*TG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Thyroid Dyshormonogenesis 4	*IYD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
Thyroid Dyshormonogenesis 5	*DUOXA2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,700
Thyroid Dyshormonogenesis 6	*DUOX2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Trichohepatoenteric Syndrome 1	*TTC37*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 42,000
Tyrosinemia, Type I	*FAH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Tyrosinemia, Type II	*TAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,100
Tyrosinemia, Type III	*HPD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Usher Syndrome, Type IB	*MYO7A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Usher Syndrome, Type IC	*USH1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,900
Usher Syndrome, Type ID	*CDH23*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 97,000
Usher Syndrome, Type IF	*PCDH15*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,800
Usher Syndrome, Type IIA	*USH2A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Usher Syndrome, Type III	*CLRN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,200
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	*ACADVL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
Vitamin D-Dependent Rickets, Type I	*CYP27B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,500
Vitamin D-Resistant Rickets, Type IIA	*VDR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
Walker-Warburg Syndrome and Other *FKTN*-Related Dystrophies	*FKTN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Werner Syndrome	*WRN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 38,000
Wilson Disease	*ATP7B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Wiskott-Aldrich Syndrome (*WAS*-Related)	*WAS*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 1,203,000
Wolcott-Rallison Syndrome	*EIF2AK3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 142,000

Wolman Disease / Cholesteryl Ester Storage Disease	*LIPA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 32,000
Woodhouse-Sakati Syndrome	*DCAF17*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 111,000
X-Linked Juvenile Retinoschisis	*RS1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 40,000
X-Linked Severe Combined Immunodeficiency	*IL2RG*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 250,000
Xeroderma Pigmentosum (*POLH*-Related)	*POLH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Xeroderma Pigmentosum, Group A	*XPA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 19,000
Xeroderma Pigmentosum, Group C	*XPC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 18,000
Xeroderma Pigmentosum, Group G	*ERCC5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
Zellweger Syndrome Spectrum (*PEX10*-Related)	*PEX10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,100
Zellweger Syndrome Spectrum (*PEX1*-Related)	*PEX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 59,000
Zellweger Syndrome Spectrum (*PEX2*-Related)	*PEX2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,700
Zellweger Syndrome Spectrum (*PEX6*-Related)	*PEX6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 910

AR=Autosomal recessive; XL=X-linked

Test methods and comments

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

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

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

Genotyping (Analytical Detection Rate >99%)

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

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

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

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

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

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

For spinal muscular atrophy (SMA), the copy numbers of the *SMN1* and *SMN2* genes were analyzed. The individual dosage of exons 7 and 8 as well as the combined dosage of exons 1, 4, 6 and 8 of *SMN1* and *SMN2* were assessed. Copy number gains and losses can be detected with this assay. Depending on ethnicity, 6 - 29 % of carriers will not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *SMN1* gene on one chromosome and loss of *SMN1* (deletion) on the other chromosome (silent 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^{TM}XT Low Input technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Libraries were pooled and sequenced on the Illumina NovaSeq 9000 platform, using paired-end 100 bp reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house.

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

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 ΔΔCt formula.

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

Long-range PCR was performed to generate locus-specific amplicons for *CYP21A2*, *HBA1* and *HBA2* and *GBA*. The PCR products were then prepared for short-read NGS sequencing and sequenced. Sequenced reads were mapped back to the original genomic locus and run through the bioinformatics pipeline. If indicated, copy number from MLPA was correlated with the sequencing output to analyze the results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where two copies of a gene are located on the same chromosome in tandem, only the second copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in the tandem allele and this patient is therefore less likely to be a carrier. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to determine the phase (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^{TM}XT Low-Input technology was utilized in order to create whole-genome libraries for each patient sample. Libraries were then pooled and sequenced on the Illumina NovaSeq platform. Each sequencing lane was multiplexed to achieve 0.4-2x genome coverage, using paired-end 100 bp reads. The sequencing data underwent ancestral analysis using a customized, licensed bioinformatics algorithm that was validated in house. Identified sub-ethnic groupings were binned into one of 7 continental-level groups (African, East Asian, South Asian, Non-Finnish European, Finnish, Native American, and Ashkenazi Jewish) or, for those ethnicities that matched poorly to the continental-level groups, an 8th "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.