Donor 6390

Genetic Testing Summary

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

Last Updated: 05/06/22

Donor Reported Ancestry: Chinese

Jewish Ancestry: No

Genetic Test*	Result	Comments/Donor's Residual Risk**
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Expanded Genetic Disease Carrier Screening Panel attached- 502 diseases by gene sequencing. Personalized residual risk by gene is on attached report.	Carrier: Albinism, Oculocutaneous, Type III (TYRP1) Carrier: Phenylalanine Hydroxylase Deficiency (PAH) Carrier: Thyroid Dyshormonogenesis 6 (DUOX2) 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: 6390 Donor
Date of Birth: [redacted]
Sema4 ID: [redacted]
Client ID: [redacted]
Indication: Carrier Screening

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

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

Expanded Carrier Screen (502 genes)

with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
Carrier of Albinism, Oculocutaneous, Type III (AR) Associated gene(s): *TYRP1* Variant(s) Detected: c.1014_1017dupAGTT, p.G340SfsX5, Likely Pathogenic, Heterozygous (one copy) **Carrier of Phenylalanine Hydroxylase Deficiency (AR)** Associated gene(s): *PAH* Variant(s) Detected: c.1197A>T, p. V399=, Pathogenic, Heterozygous (one copy) **Carrier of Thyroid Dyshormonogenesis 6 (AR)** Associated gene(s): *DUOX2* Variant(s) Detected: c.364C>A, p.P122T, Likely 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

Albinism, Oculocutaneous, Type III (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic frameshift variant, c.1014_1017dupAGTT, p.G340SfsX5, was detected in the *TYRP1* gene (NM_000550.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for albinism, oculocutaneous, type III. Therefore, this individual is expected to be at least a carrier for albinism, oculocutaneous, type III. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Albinism, Oculocutaneous, Type III?

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

Phenylalanine Hydroxylase Deficiency (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic synonymous variant, c.1197A>T, p. V399=, was detected in the *PAH* gene (NM_000277.1). When this variant is present in trans with a pathogenic variant, it is considered to be causative for phenylalanine hydroxylase deficiency. Therefore, this individual is expected to be at least a carrier for phenylalanine hydroxylase deficiency. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Phenylalanine Hydroxylase Deficiency?

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

Thyroid Dyshormonogenesis 6 (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic missense variant, c.364C>A, p.P122T, was detected in the *DUOX2* gene (NM_014080.4). When this variant is present in trans with a pathogenic variant, it is considered to be causative for thyroid dyshormonogenesis 6. Therefore, this individual is expected to be at least a carrier for thyroid dyshormonogenesis 6. Heterozygous carriers may exhibit clinical symptoms, mainly transient hypothyroidism in infancy.

What is Thyroid Dyshormonogenesis 6?

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

Test description

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

Christie Buchovecky, Ph.D., Assistant Director, Reproductive Genomic
Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D

Genes and diseases tested

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

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

	Disease	Gene	Inheritance Pattern	Status	Detailed Summary
⊕	**Positive**				
	Albinism, Oculocutaneous, Type III	*TYRP1*	AR	Carrier	c.1014_1017dupAGTT, p.G340SfsX5, Likely Pathogenic, Heterozygous (one copy)
	Phenylalanine Hydroxylase Deficiency	*PAH*	AR	Carrier	c.1197A>T, p. V399=, Pathogenic, Heterozygous (one copy)
	Thyroid Dyshormonogenesis 6	*DUOX2*	AR	Carrier	c.364C>A, p.P122T, Likely Pathogenic, Heterozygous (one copy)
⊖	**Negative**				
	2-Methylbutyrylglycinuria	*ACADSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 410
	3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	*HSD3B2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 181,000
	3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC1*-Related)	*MCCC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 930
	3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC2*-Related)	*MCCC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 500
	3-Methylglutaconic Aciduria, Type III	*OPA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 29,000
	3-Phosphoglycerate Dehydrogenase Deficiency	*PHGDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 123,000
	6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	*PTS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
	***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 7,500
	Achalasia-Addisonianism-Alacrimia Syndrome	*AAAS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
	Achromatopsia (*CNGA3*-Related)	*CNGA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 320
	Achromatopsia (*CNGB3*-related)	*CNGB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
	Acrodermatitis Enteropathica	*SLC39A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 62,000
	Acute Infantile Liver Failure	*TRMU*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 55,000
	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 59,000
	Adenosine Deaminase Deficiency	*ADA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 127,000
	Adrenocorticotropic Hormone Deficiency	*TBX19*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,500
	Adrenoleukodystrophy, X-Linked	*ABCD1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 19,000
	Agammaglobulinemia	*BTK*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 250,000
	Agenesis of the Corpus Callosum	*FRMD4A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 348,000
	Aicardi-Goutieres Syndrome (*RNASEH2C*-Related)	*RNASEH2C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
	Aicardi-Goutieres Syndrome (*SAMHD1*-Related)	*SAMHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
	Aicardi-Goutieres Syndrome (*TREX1*-Related)	*TREX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
	Alkaptonuria	*HGD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,200
	Alpha-Mannosidosis	*MAN2B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
	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 380

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 1,700
Alport Syndrome (*COL4A4*-Related)	*COL4A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 510
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 3,100
Andermann Syndrome	*SLC12A6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 287,000
Antley-Bixler Syndrome (*POR*-Related)	*POR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 650
Argininemia	*ARG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
Argininosuccinic Aciduria	*ASL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Aromatase Deficiency	*CYP19A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Arthrogryposis, Intellectual Disability, and Seizures	*SLC35A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240,000
Asparagine Synthetase Deficiency	*ASNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 178,000
Aspartylglycosaminuria	*AGA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Ataxia With Isolated Vitamin E Deficiency	*TTPA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Ataxia-Telangiectasia	*ATM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 540
Ataxia-Telangiectasia-Like Disorder 1	*MRE11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,700
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	*SACS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
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 15,000
Bardet-Biedl Syndrome (*ARL6*-Related)	*ARL6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Bardet-Biedl Syndrome (*BBS10*-Related)	*BBS10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Bardet-Biedl Syndrome (*BBS12*-Related)	*BBS12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 287,000
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 5,400
Bardet-Biedl Syndrome (*BBS4*-Related)	*BBS4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 287,000
Bare Lymphocyte Syndrome, Type II	*CIITA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 129,000
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 710
Bartter Syndrome, Type 4A	*BSND*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 69,000
Bernard-Soulier Syndrome, Type A1	*GP1BA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
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 1,200 **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 3,800
Beta-Mannosidosis	*MANBA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 57,000
Bilateral Frontoparietal Polymicrogyria	*GPR56*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 143,000
Biotinidase Deficiency	*BTD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
Bloom Syndrome	*BLM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 34,000
Canavan Disease	*ASPA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,200
Carbamoylphosphate Synthetase I Deficiency	*CPS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 690
Carnitine Acylcarnitine Translocase Deficiency	*SLC25A20*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,500
Carnitine Palmitoyltransferase IA Deficiency	*CPT1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 143,000
Carnitine Palmitoyltransferase II Deficiency	*CPT2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 930
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 450
Catecholaminergic Polymorphic Ventricular Tachycardia	*CASQ2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000
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 2,300
Cerebral Creatine Deficiency Syndrome 3	*GATM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
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 750
Charcot-Marie-Tooth Disease, Type 4D	*NDRG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 225,000
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 129,000
Chondrodysplasia Punctata	*ARSE*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 862,000
Choreoacanthocytosis	*VPS13A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
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 2,200
Citrullinemia, Type 1	*ASS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 81,000
Cockayne Syndrome, Type A	*ERCC8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 32,000
Cockayne Syndrome, Type B and other *ERCC6*-Related Disorders	*ERCC6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,300
Cohen Syndrome	*VPS13B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Combined Factor V and VIII Deficiency	*LMAN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 68,000
Combined Malonic and Methylmalonic Aciduria	*ACSF3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 23,000
Combined Oxidative Phosphorylation Deficiency 1	*GFM1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,100
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 1,900
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 121,000
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 720
Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency	*CYP11B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	*CYP17A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 840
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 300 **Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)):** 1 in 1,200
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 128,000
Congenital Amegakaryocytic Thrombocytopenia	*MPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 68,000
Congenital Bile Acid Synthesis Defect (*AKR1D1*-Related)	*AKR1D1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000

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

Ellis-van Creveld Syndrome (*EVC*-Related)	*EVC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Emery-Dreifuss Myopathy 1	*EMD*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 833,000
Enhanced S-Cone Syndrome	*NR2E3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Ethylmalonic Encephalopathy	*ETHE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Fabry Disease	*GLA*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 7,700
Factor IX Deficiency	*F9*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
Factor VII Deficiency	*F7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 300
Factor XI Deficiency	*F11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 440
Familial Autosomal Recessive Hypercholesterolemia	*LDLRAP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 171,000
Familial Dysautonomia	*IKBKAP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 78,000
Familial Hypercholesterolemia	*LDLR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 260
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,000
Familial Hyperinsulinism (*ABCC8*-Related)	*ABCC8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240
Familial Hyperinsulinism (*KCNJ11*-Related)	*KCNJ11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Familial Hyperphosphatemic Tumoral Calcinosis	*GALNT3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Familial Mediterranean Fever	*MEFV*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,400
Fanconi Anemia, Group A	*FANCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Fanconi Anemia, Group C	*FANCC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 34,000
Fanconi Anemia, Group G	*FANCG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Fanconi-Bickel Syndrome	*SLC2A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 295,000
Fragile X Syndrome	*FMR1*	XL	Reduced Risk	*FMR1* CGG repeat sizes: Not Performed *FMR1* Sequencing: Negative Fragile X CGG triplet repeat expansion testing was not performed at this time, as the patient has either been previously tested or is a male. **Personalized Residual Risk:** 1 in 222,000
Fructose-1,6-Bisphosphatase Deficiency	*FBP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Fucosidosis	*FUCA1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 49,000
Fumarase Deficiency	*FH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
Fundus Albipunctatus	*RDH5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 810
GRACILE Syndrome and Other *BCS1L*-Related Disorders	*BCS1L*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Galactokinase Deficiency	*GALK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Galactose Epimerase Deficiency	*GALE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 850
Galactosemia	*GALT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 390
Galactosialidosis	*CTSA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Gaucher Disease	*GBA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Generalized Thyrotropin-Releasing Hormone Resistance	*TRHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 296,000
Geroderma Osteodysplasticum	*GORAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 76,000
Gitelman Syndrome	*SLC12A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 230
Glanzmann Thrombasthenia (*ITGA2B*-Related)	*ITGA2B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Glanzmann Thrombasthenia (*ITGB3*-Related)	*ITGB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Glutaric Acidemia, Type I	*GCDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Glutaric Acidemia, Type IIa	*ETFA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Glutaric Acidemia, Type IIb	*ETFB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,800
Glutaric Acidemia, Type IIc	*ETFDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 260
Glutathione Synthetase Deficiency	*GSS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 48,000
Glycine Encephalopathy (*AMT*-Related)	*AMT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000
Glycine Encephalopathy (*GLDC*-Related)	*GLDC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240
Glycogen Storage Disease, Type 0	*GYS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 29,000

Glycogen Storage Disease, Type II	*GAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 280
Glycogen Storage Disease, Type III	*AGL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 55,000
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	*GBE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 64,000
Glycogen Storage Disease, Type IXb	*PHKB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Glycogen Storage Disease, Type Ia	*G6PC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 410
Glycogen Storage Disease, Type Ib	*SLC37A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,900
Glycogen Storage Disease, Type V	*PYGM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Glycogen Storage Disease, Type VI	*PYGL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Glycogen Storage Disease, Type VII	*PFKM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,900
Gray Platelet Syndrome	*NBEAL2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,400
Growth Hormone Deficiency, Type IB	*GHRHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 104,000
HMG-CoA Lyase Deficiency	*HMGCL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 113,000
Hemochromatosis, Type 2A	*HFE2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 740
Hemochromatosis, Type 3	*TFR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 275,000
Hereditary Fructose Intolerance	*ALDOB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 35,000
Hereditary Spastic Paraparesis 49	*TECPR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 166,000
Hermansky-Pudlak Syndrome, Type 1	*HPS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 286,000
Hermansky-Pudlak Syndrome, Type 3	*HPS3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Hermansky-Pudlak Syndrome, Type 4	*HPS4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 287,000
Hermansky-Pudlak Syndrome, Type 6	*HPS6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 680
Hmg-CoA Synthase 2 Deficiency	*HMGCS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Holocarboxylase Synthetase Deficiency	*HLCS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,900
Homocystinuria (*CBS*-Related)	*CBS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Homocystinuria due to *MTHFR* Deficiency	*MTHFR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,000
Homocystinuria, cblE Type	*MTRR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 16,000
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	*MTR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 35,000
Hydrocephalus	*L1CAM*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 40,000
Hydrolethalus Syndrome	*HYLS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 296,000
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 30,000
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	*SARS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 220,000
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 86,000
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 66,000
Hypophosphatasia	*ALPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,200
Hypophosphatemic Rickets with Hypercalciuria	*SLC34A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Hypotrichosis 8 / Autosomal Recessive Woolly Hair 1	*LPAR6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Immunodeficiency 18	*CD3E*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 120,000
Immunodeficiency 19	*CD3D*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 69,000
Inclusion Body Myopathy 2	*GNE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
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 380
Intellectual Disability, Autosomal Recessive 3	*CC2D1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 108,000
Intrahepatic Cholestasis	*ATP8B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 580

Isovaleric Acidemia	*IVD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Joubert Syndrome 2	*TMEM216*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 133,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	*NPHP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	*RPGRIP1L*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Junctional Epidermolysis Bullosa (*COL17A1*-Related)	*COL17A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Junctional Epidermolysis Bullosa (*ITGA6*-Related)	*ITGA6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 287,000
Junctional Epidermolysis Bullosa (*ITGB4*-Related)	*ITGB4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 26,000
Junctional Epidermolysis Bullosa (*LAMA3*-Related)	*LAMA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 49,000
Junctional Epidermolysis Bullosa (*LAMB3*-Related)	*LAMB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,600
Junctional Epidermolysis Bullosa (*LAMC2*-Related)	*LAMC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Kohlschutter-Tonz Syndrome	*ROGDI*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 287,000
Krabbe Disease	*GALC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 340
Lamellar Ichthyosis, Type 1	*TGM1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Laron Dwarfism	*GHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	*CEP290*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Leber Congenital Amaurosis 13	*RDH12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 88,000
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	*TULP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	*RPE65*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Leber Congenital Amaurosis 4	*AIPL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,100
Leber Congenital Amaurosis 5	*LCA5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	*CRB1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 960
Leigh Syndrome (*NDUFS7*-Related)	*NDUFS7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 38,000
Leigh Syndrome (*SURF1*-Related)	*SURF1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Leigh Syndrome, French-Canadian Type	*LRPPRC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Lethal Congenital Contracture Syndrome 1 / Lethal 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 52,000
Lethal Congenital Contracture Syndrome 3	*PIP5K1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 304,000
Leukoencephalopathy with Vanishing White Matter	*EIF2B5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,200
Limb-Girdle Muscular Dystrophy, Type 2A	*CAPN3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Limb-Girdle Muscular Dystrophy, Type 2B	*DYSF*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Limb-Girdle Muscular Dystrophy, Type 2C	*SGCG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
Limb-Girdle Muscular Dystrophy, Type 2D	*SGCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Limb-Girdle Muscular Dystrophy, Type 2E	*SGCB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 72,000
Limb-Girdle Muscular Dystrophy, Type 2F	*SGCD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 36,000
Limb-Girdle Muscular Dystrophy, Type 2H	*TRIM32*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 123,000
Limb-Girdle Muscular Dystrophy, Type 2I	*FKRP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 460
Limb-Girdle Muscular Dystrophy, Type 2L	*ANO5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 920
Lipoamide Dehydrogenase Deficiency	*DLD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 225,000
Lipoid Adrenal Hyperplasia	*STAR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 36,000
Lipoprotein Lipase Deficiency	*LPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 800
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADHA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,500

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 72,000
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 4,000
Maple Syrup Urine Disease, Type 1b	*BCKDHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Maple Syrup Urine Disease, Type 2	*DBT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 790
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	*MKS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Medium Chain Acyl-CoA Dehydrogenase Deficiency	*ACADM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Megalencephalic Leukoencephalopathy with Subcortical Cysts	*MLC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 171,000
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 2,600
Methionine Adenosyltransferase I/III Deficiency	*MAT1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Methylmalonic Acidemia (*MMAA*-Related)	*MMAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 216,000
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 830
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	*MMACHC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	*MMADHC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	*LMBRD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 43,000
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 83,000
Mitochondrial Complex I Deficiency (*ACAD9*-Related)	*ACAD9*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,100
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 770
Mitochondrial Complex I Deficiency (*NDUFS6*-Related)	*NDUFS6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 211,000
Mitochondrial Complex I Deficiency (*NDUFV1*-Related)	*NDUFV1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,100
Mitochondrial Complex I Deficiency / Leigh Syndrome (*FOXRED1*-Related)	*FOXRED1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,900
Mitochondrial Complex I Deficiency / Leigh Syndrome (*NDUFAF2*-Related)	*NDUFAF2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 114,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (*NDUFS4*-Related)	*NDUFS4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 31,000
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 22,000
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 74,000
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 5,700
Mitochondrial DNA Depletion Syndrome 3	*DGUOK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,500
Mitochondrial DNA Depletion Syndrome 4A and 4B and other *POLG*-Related Disorders	*POLG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 180
Mitochondrial DNA Depletion Syndrome 5	*SUCLA2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 152,000

Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	*MPV17*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	*PUS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 333,000
Mitochondrial Trifunctional Protein Deficiency (*HADHB*-Related)	*HADHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Molybdenum Cofactor Deficiency A	*MOCS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 215,000
Mucolipidosis II / IIIA	*GNPTAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Mucolipidosis III Gamma	*GNPTG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 213,000
Mucolipidosis IV	*MCOLN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,500
Mucopolysaccharidosis Type I	*IDUA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 630
Mucopolysaccharidosis Type II	*IDS*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 76,000
Mucopolysaccharidosis Type IIIA	*SGSH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 700
Mucopolysaccharidosis Type IIIB	*NAGLU*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 900
Mucopolysaccharidosis Type IIIC	*HGSNAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 42,000
Mucopolysaccharidosis Type IIID	*GNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 201,000
Mucopolysaccharidosis Type IVa	*GALNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 440
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	*GLB1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Mucopolysaccharidosis VII	*GUSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Mucopolysaccharidosis type IX	*HYAL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000
Mucopolysaccharidosis type VI	*ARSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000
Mulibrey Nanism	*TRIM37*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 36,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	*PIGN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 19,000
Multiple Pterygium Syndrome	*CHRNG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Multiple Sulfatase Deficiency	*SUMF1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000
Muscle-Eye-Brain Disease and Other *POMGNT1*-Related Congenital Muscular Dystrophy-Dystroglycanopathies	*POMGNT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,100
Myoneurogastrointestinal Encephalopathy	*TYMP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Myotubular Myopathy 1	*MTM1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 192,000
N-Acetylglutamate Synthase Deficiency	*NAGS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,700
Nemaline Myopathy 2	*NEB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 300
Nephrogenic Diabetes Insipidus, Type II	*AQP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,700
Nephrogenic Diabetes insipidus (*AVPR2*-related)/ Nephrogenic Syndrome of Inappropriate Antidiuresis	*AVPR2*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 471,000
Nephronophthisis 2	*INVS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 24,000
Nephrotic Syndrome (*NPHS1*-Related) / Congenital Finnish Nephrosis	*NPHS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 980
Nephrotic Syndrome (*NPHS2*-Related) / Steroid-Resistant Nephrotic Syndrome	*NPHS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Neurodegeneration due to Cerebral Folate Transport Deficiency	*FOLR1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	*PLAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 217,000
Neuronal Ceroid-Lipofuscinosis (*CLN3*-Related)	*CLN3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 59,000
Neuronal Ceroid-Lipofuscinosis (*CLN5*-Related)	*CLN5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 75,000
Neuronal Ceroid-Lipofuscinosis (*CLN6*-Related)	*CLN6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 91,000
Neuronal Ceroid-Lipofuscinosis (*CLN8*-Related)	*CLN8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Neuronal Ceroid-Lipofuscinosis (*MFSD8*-Related)	*MFSD8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 87,000
Neuronal Ceroid-Lipofuscinosis (*PPT1*-Related)	*PPT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,300
Neuronal Ceroid-Lipofuscinosis (*TPP1*-Related)	*TPP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Niemann-Pick Disease (*SMPD1*-Related)	*SMPD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300

Niemann-Pick Disease, Type C (*NPC1*-Related)	*NPC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
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 214,000
Non-Syndromic Hearing Loss (*GJB2*-Related)	*GJB2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 280
Oculocutaneous Albinism, Type IA / IB	*TYR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 220
Oculocutaneous Albinism, Type IV	*SLC45A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 980
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	*WNT10A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 900
Omenn Syndrome (*RAG2*-Related)	*RAG2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 32,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	*DCLRE1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 48,000
Omenn Syndrome and other *RAG1*-Related Disorders	*RAG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 180
Ornithine Aminotransferase Deficiency	*OAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,900
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 8,100
Osteopetrosis 1	*TCIRG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,700
Osteopetrosis 8	*SNX10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 215,000
Otospondylomegaepiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	*COL11A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,800
Papillon-Lefevre Syndrome	*CTSC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,400
Pendred Syndrome	*SLC26A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 72
Peroxisome Biogenesis Disorder 3A and 3B	*PEX12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 225,000
Peroxisome Biogenesis Disorder 7A and 7B	*PEX26*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 23,000
Polycystic Kidney Disease, Autosomal Recessive	*PKHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 350
Polyglandular Autoimmune Syndrome, Type 1	*AIRE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Pontocerebellar Hypoplasia, Type 1A	*VRK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 215,000
Pontocerebellar Hypoplasia, Type 1B	*EXOSC3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 54,000
Pontocerebellar Hypoplasia, Type 2A and Type 4	*TSEN54*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,800
Pontocerebellar Hypoplasia, Type 2E	*VPS53*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 146,000
Pontocerebellar Hypoplasia, Type 6	*RARS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 52,000
Primary Carnitine Deficiency	*SLC22A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 600
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 215,000
Primary Ciliary Dyskinesia (*CCDC39*-Related)	*CCDC39*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 84,000
Primary Ciliary Dyskinesia (*DNAH5*-Related)	*DNAH5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 19,000
Primary Ciliary Dyskinesia (*DNAI1*-Related)	*DNAI1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,300
Primary Ciliary Dyskinesia (*DNAI2*-Related)	*DNAI2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000
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 31,000
Primary Congenital Glaucoma 3A	*CYP1B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 130
Primary Hyperoxaluria, Type 1	*AGXT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Primary Hyperoxaluria, Type 2	*GRHPR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 68,000
Primary Hyperoxaluria, Type 3	*HOGA1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Progressive Cerebello-Cerebral Atrophy	*SEPSECS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 247,000
Progressive Familial Intrahepatic Cholestasis, Type 2	*ABCB11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 390
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 287,000
Prolidase Deficiency	*PEPD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,900
Propionic Acidemia (*PCCA*-Related)	*PCCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600

Propionic Acidemia (*PCCB*-Related)	*PCCB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 920
Pulmonary Surfactant Dysfunction	*ABCA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,300
Pycnodysostosis	*CTSK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,200
Pyridoxamine 5'-Phosphate Oxidase Deficiency	*PNPO*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Pyridoxine-Dependent Epilepsy	*ALDH7A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Pyruvate Carboxylase Deficiency	*PC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 215,000
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 8,300
Renal Tubular Acidosis and Deafness	*ATP6V1B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,800
Retinitis Pigmentosa 25	*EYS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 580
Retinitis Pigmentosa 26	*CERKL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Retinitis Pigmentosa 28	*FAM161A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 145,000
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 201,000
Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16	*C8ORF37*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Rh Deficiency Syndrome	*RHAG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 94,000
Rhizomelic Chondrodysplasia Punctata, Type 1	*PEX7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 55,000
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 95,000
Salla Disease	*SLC17A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Salt and Pepper Developmental Regression Syndrome	*ST3GAL5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 108,000
Sandhoff Disease	*HEXB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 680
Schimke Immunoosseous Dysplasia	*SMARCAL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 56,000
Seckel Syndrome 5 / Microcephaly 9	*CEP152*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Segawa Syndrome	*TH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
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 48,000
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 2,300
Severe Congenital Neutropenia 4	*G6PC3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 296,000
Severe Neonatal Hyperparathyroidism	*CASR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 216,000
Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis	*POC1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 98,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	*ACADS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 340
Shwachman-Diamond Syndrome	*SBDS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Sialidosis, Type I and Type II	*NEU1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Sjogren-Larsson Syndrome	*ALDH3A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Smith-Lemli-Opitz Syndrome	*DHCR7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
Spastic Paraplegia 15	*ZFYVE26*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly	*SLC1A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 136,000
Spherocytosis, Type 5	*EPB42*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
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 1,115
Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S	*IGHMBP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100

Spinocerebellar Ataxia with Axonal Neuropathy 3	*COA7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Spondylocostal Dysostosis 1	*DLL3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 156,000
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 53,000
Steel Syndrome	*COL27A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 275,000
Stuve-Wiedemann Syndrome	*LIFR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Sulfate Transporter-Related Osteochondrodysplasia	*SLC26A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Tay-Sachs Disease	*HEXA*	AR	Reduced Risk	Tay-Sachs disease enzyme: Non-carrier White blood cells: Non-carrier • Hex A%: 59.6% (Non-carrier : 55.0 - 72.0%; Carrier: < 50.0%) • Total hexosaminidase activity: 1751 nmol/hr/mg *HEXA* Sequencing: Negative **Personalized Residual Risk:** 1 in 2,700
Thiamine-Responsive Megaloblastic Anemia Syndrome	*SLC19A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000
Thyroid Dyshormonogenesis 1	*SLC5A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,300
Thyroid Dyshormonogenesis 2A	*TPO*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 350
Thyroid Dyshormonogenesis 3	*TG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 130
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 1,300
Trichohepatoenteric Syndrome 1	*TTC37*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Tyrosinemia, Type I	*FAH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
Tyrosinemia, Type II	*TAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
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 180
Usher Syndrome, Type IC	*USH1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 400
Usher Syndrome, Type ID	*CDH23*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 880
Usher Syndrome, Type IF	*PCDH15*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Usher Syndrome, Type IIA	*USH2A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 54
Usher Syndrome, Type III	*CLRN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	*ACADVL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 380
Vitamin D-Dependent Rickets, Type I	*CYP27B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
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 390
Werner Syndrome	*WRN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Wilson Disease	*ATP7B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 150
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 287,000
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 59,000
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 4,300
Xeroderma Pigmentosum, Group A	*XPA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 170,000
Xeroderma Pigmentosum, Group C	*XPC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Xeroderma Pigmentosum, Group G	*ERCC5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,900

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

AR=Autosomal recessive; XL=X-linked

Test methods and comments

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

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

PCR amplification using Asuragen, Inc. AmplideX® *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™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.