



Donor 6911

Genetic Testing Summary

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

Last Updated: 02/24/23

Donor Reported Ancestry: African American, Irish

Jewish Ancestry: No

Genetic Test*	Result	Comments/Donor's Residual Risk**
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Low MCH Sickle Cell Trait (Hb S trait)	Alpha Thalassemia and Sickle Cell Disease carrier confirmed by DNA
Expanded Genetic Disease Carrier Screening Panel attached- 502 diseases by gene sequencing. Personalized residual risk by gene is on attached report.	Carrier: Alpha-Thalassemia (HBA1/HBA2) One copy of the alpha 3.7 deletion Carrier: Arthrogryposis, Intellectual Disability, and Seizures (SLC35A3) Carrier: Beta-Globin-Related Hemoglobinopathies (HBB) Variant HbS Unlikely Carrier: Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (CYP21A2) see report. Carrier: Multiple Sulfatase Deficiency (SUMF1) 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 6911
Date of Birth: [REDACTED]
Sema4 ID: [REDACTED]
Client ID: [REDACTED]
Indication: Carrier Screening

Specimen Information

Specimen Type: Blood
Date Collected: 08/05/2022
Date Received: 08/06/2022
Final Report: 08/19/2022

Referring Provider

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

Expanded Carrier Screen (502 genes) with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
<p>Carrier of Alpha-Thalassemia (AR) Associated gene(s): <i>HBA1/HBA2</i> Variant(s) Detected: One copy of the alpha 3,7 deletion</p> <p>Carrier of Arthrogryposis, Intellectual Disability, and Seizures (AR) Associated gene(s): <i>SLC35A3</i> Variant(s) Detected: c.680dupA, p.D227EfsX15, Likely Pathogenic, Heterozygous (one copy)</p> <p>Carrier of Beta-Globin-Related Hemoglobinopathies (AR) Associated gene(s): <i>HBB</i> Variant(s) Detected: c.20A>T, p.E7V (HbS), Pathogenic, Heterozygous (one copy)</p> <p>Unlikely Carrier of Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (AR) Associated gene(s): <i>CYP21A2</i> Variant(s) Detected: 3 copies of <i>CYP21A2</i> detected and c.952C>T, p.Q318X, Pathogenic, Heterozygous (one copy)</p> <p>Carrier of Multiple Sulfatase Deficiency (AR) Associated gene(s): <i>SUMF1</i> Variant(s) Detected: c.836C>T, p.A279V, Pathogenic, Heterozygous (one copy)</p>	<p>Negative for all other genes tested To view a full list of genes and diseases tested please see Table 1 in this report</p>

AR=Autosomal recessive; XL=X-linked

Recommendations

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

Interpretation of positive results

Alpha-Thalassemia (AR)

Results and Interpretation

HBA1 Copy Number: 2

HBA2 Copy Number: 1

One copy of the alpha 3.7 deletion detected

HBA1/HBA2 Sequencing: Negative

Gene(s) analyzed: *HBA1* (NM_000558.4) and *HBA2* (NM_000517.4)

Inheritance: Autosomal Recessive

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

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

What is Alpha-Thalassemia?

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

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

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

Arthrogryposis, Intellectual Disability, and Seizures (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic frameshift variant, c.680dupA, p.D227EfsX15, was detected in the *SLC35A3* gene (NM_012243.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for arthrogryposis, intellectual disability, and seizures. Therefore, this individual is expected to be at least a carrier for arthrogryposis, intellectual disability, and seizures. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Arthrogryposis, Intellectual Disability, and Seizures?

Pathogenic variants in the *SLC35A3* gene cause a syndrome characterized by arthrogryposis (congenital joint contractures), intellectual disability, autism spectrum disorder, and epilepsy. Patients also have microcephaly, small jaws, seizures and muscle hypotonia, as well as

developmental delay. To date, the disease has only been reported among individuals of Ashkenazi Jewish descent. At the moment, too few patients have been reported to determine a genotype-phenotype correlation.

Beta-Globin-Related Hemoglobinopathies (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.20A>T, p.E7V (HbS), was detected in the *HBB* gene (NM_000518.4). This variant is considered to be pathogenic and when present in trans with a pathogenic variant causative for sickle-cell disease or another beta-globin related hemoglobinopathy. Therefore, this individual is expected to be at least a carrier for sickle-cell disease. Carriers may be at risk for symptoms during physical exertion, high altitudes or when dehydrated.

What is Beta-Globin-Related Hemoglobinopathies?

Pathogenic variants in the beta-globin gene (*HBB*) cause a variety of autosomal recessive diseases of aberrant hemoglobin, the protein that carries oxygen in the blood. The most frequent hemoglobinopathies are beta-thalassemia, sickle cell disease and HbC disease.

- In individuals with beta-thalassemia, hemoglobin is not properly synthesized and results in small red blood cells that are inefficient at carrying oxygen. Individuals with severe beta-thalassemia require life-long blood transfusions and chelation therapy to remove the extra iron that results from the blood transfusions. Individuals with milder forms of beta-thalassemia may not require transfusions. Life expectancy may be shortened due to cardiac complications of iron overload. Individuals carrying one pathogenic allele causing beta-thalassemia in addition to 5 or more copies of HBA may develop a thalassemia intermedia phenotype with a variable clinical presentation, and may require recurrent transfusions.
- Sickle cell disease is caused by the inheritance of two copies of Hemoglobin S (HbS), encoded by a specific *HBB* variant. Symptoms typically first present in infancy or childhood and include chronic anemia, pain and/or swelling in the hands and feet, episodes of severe pain, and infections. The clinical presentation is highly variable between affected individuals. The life expectancy for individuals with sickle cell disease may be shortened. HbS can also cause related diseases if it is inherited along with a different type of variant in *HBB*.
- HbC disease is caused by the inheritance of two copies of Hemoglobin C (HbC), encoded by a specific *HBB* variant. HbC disease causes mild anemia in some patients, but the majority of affected individuals do not have any symptoms and have a normal life expectancy. HbC can also cause disease if it is inherited with another type of abnormal hemoglobin, the most common being HbS. The inheritance of one copy each of HbS and HbC result in SC disease, which may cause chronic anemia, pain and/or swelling in the hands and feet, episodes of severe pain, infections, and retinal disease. The life expectancy for individuals with SC disease may be shortened.

The type of disease that will develop can be predicted based on the variants inherited. Variants causing beta-thalassemia are prevalent in Mediterranean and South-East Asian populations, whereas HbS is most common in people of African, Mediterranean, Middle Eastern, and Indian ancestry. HbC is most common in people of African descent.

Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (AR)

Results and Interpretation

CYP21A2 copy number: 3

No pathogenic copy number variants detected

CYP21A2 sequencing: c.952C>T, p.Q318X, Pathogenic, Heterozygous (one copy)

Genes analyzed: *CYP21A2* (NM_000500.6)

Inheritance: Autosomal Recessive

A heterozygous pathogenic premature stop codon, c.952C>T, p.Q318X, was detected in the *CYP21A2* gene (NM_000500.6). In addition, MLPA results suggest that three copies of the *CYP21A2* gene are present in this patient. Genetic analyses indicate that this patient has one copy of *CYP21A2* on one chromosome, and two copies of *CYP21A2* on the other chromosome.

The p.Q318X variant is reported to be causative for the classic salt-wasting/severe virilizing form of congenital adrenal hyperplasia (PMID: 29450859). Variants associated with the classic form usually cause classic congenital adrenal hyperplasia when found in trans with a second classic allele, or non-classic congenital adrenal hyperplasia when found in trans with a non-classic allele (PMID: 29450859). However, the p.Q318X variant has been frequently identified on chromosomes with two copies of *CYP21A2* (PMIDs: 12384784, 17042033). In the absence of other variants, these individuals are not considered to be carriers of congenital adrenal hyperplasia, as the chromosome with the non-functional copy is still expected to carry one functional copy of *CYP21A2*. Chromosomes with one copy of *CYP21A2* that carry p.Q318X have

been reported much less frequently. Therefore, to ensure that this patient is not a carrier of classic congenital adrenal hyperplasia, testing of parents or other close family members may be helpful, if indicated.

What is congenital adrenal hyperplasia (due to 21-hydroxylase deficiency)?

Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders resulting from deficiency in the enzymes involved in cortisol biosynthesis. The majority (95%) of CAH cases are due to 21-hydroxylase deficiency (21-OHD CAH), which is caused by homozygous or compound heterozygous pathogenic variants in the gene *CYP21A2*. Approximately 20% of mutant alleles have deletions of 30 kb that have been generated by unequal meiotic crossing-over between the two genes. Another 75% of mutant alleles are due to gene conversion events, where an inactivating mutation from the *CYP21A1P* pseudogene is introduced into one copy of the *CYP21A2* gene, thus making the gene non-functional. Three different forms of 21-OHD CAH have been reported: a classic salt wasting form, a classic simple virilizing form, and a non-classic form.

- The classic salt wasting form results from a nonfunctional enzyme and is the most severe. The phenotype includes prenatal onset of virilization and inadequate adrenal aldosterone secretion that can result in fatal salt-wasting crises.
- The classic simple virilizing form results from low levels of functional enzyme and involves prenatal virilization but no salt-wasting.
- The non-classic form, which results from a mild enzyme deficiency, occurs postnatally and involves phenotypes associated with hyperandrogenism, such as hirsutism, delayed menarche, and infertility.

Treatment for the classic forms of the disorder include glucocorticoid and mineralocorticoid replacement therapy, as well as the possibility of feminizing genitoplasty, while patients with the non-classic form usually do not require treatment. The life expectancy for this disorder can be normal with treatment, however the occurrence of salt-wasting crises can be fatal.

Multiple Sulfatase Deficiency (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.836C>T, p.A279V, was detected in the *SUMF1* gene (NM_182760.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for multiple sulfatase deficiency. Therefore, this individual is expected to be at least a carrier for multiple sulfatase deficiency. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Multiple Sulfatase Deficiency?

Multiple sulfatase deficiency is an autosomal recessive disorder that is caused by pathogenic variants in the gene *SUMF1*. While it is found in different ethnicities around the world, it may be more prevalent in individuals of Ashkenazi Jewish descent due to the presence of a founder mutation. Clinical symptoms usually appear at the age of 1 or 2 years, but may appear earlier or later. These symptoms include leukodystrophy, seizures, developmental delay, slow growth, and progressive loss of mental abilities. Skeletal defects, coarse facial features, and enlarged organs and hearing loss are often present. Patients with onset in the neonatal period often die within the first year of life, and patients with later onset usually die in childhood. It is not currently possible to predict the severity of the disease based on the genotype.

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.

Hongli Zhan

Hongli Zhan, Ph.D., Director

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

Genes and diseases tested

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

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

Disease	Gene	Inheritance Pattern	Status	Detailed Summary
Positive				
Alpha-Thalassemia	<i>HBA1/HBA2</i>	AR	Silent Carrier	<i>HBA1</i> Copy Number: 2 <i>HBA2</i> Copy Number: 1 One copy of the alpha 3,7 deletion detected <i>HBA1/HBA2</i> Sequencing: Negative
Arthrogryposis, Intellectual Disability, and Seizures	<i>SLC35A3</i>	AR	Carrier	c.680dupA, p.D227EfsX15, Likely Pathogenic, Heterozygous (one copy)
Beta-Globin-Related Hemoglobinopathies	<i>HBB</i>	AR	Carrier	c.20A>T, p.E7V (HbS), Pathogenic, Heterozygous (one copy)
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	<i>CYP21A2</i>	AR	Unlikely Carrier	<i>CYP21A2</i> copy number: 3 No pathogenic copy number variants detected <i>CYP21A2</i> sequencing: c.952C>T, p.Q318X, Pathogenic, Heterozygous (one copy)
Multiple Sulfatase Deficiency	<i>SUMF1</i>	AR	Carrier	c.836C>T, p.A279V, Pathogenic, Heterozygous (one copy)
Negative				
2-Methylbutyrylglycinuria	<i>ACADSB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	<i>HSD3B2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,000
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related)	<i>MCCC1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 540
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)	<i>MCCC2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
3-Methylglutaconic Aciduria, Type III	<i>OPA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000
3-Phosphoglycerate Dehydrogenase Deficiency	<i>PHGDH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,600
6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	<i>PTS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
CD59-Mediated Hemolytic Anemia	<i>CD59</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 401,000
Abetalipoproteinemia	<i>MTTP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Achalasia-Addisonianism-Alacrimia Syndrome	<i>AAAS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Achromatopsia (CNGA3-Related)	<i>CNGA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 410
Achromatopsia (CNGB3-related)	<i>CNGB3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Acrodermatitis Enteropathica	<i>SLC39A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Acute Infantile Liver Failure	<i>TRMU</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Acyl-CoA Oxidase I Deficiency	<i>ACOX1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 54,000
Adams-Oliver Syndrome 4	<i>EOGT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 43,000
Adenosine Deaminase Deficiency	<i>ADA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Adrenocorticotrophic Hormone Deficiency	<i>TBX19</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Adrenoleukodystrophy, X-Linked	<i>ABCD1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Agammaglobulinemia	<i>BTK</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 250,000
Agenesis of the Corpus Callosum	<i>FRMD4A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 348,000
Aicardi-Goutieres Syndrome (RNASEH2C-Related)	<i>RNASEH2C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Aicardi-Goutieres Syndrome (SAMHD1-Related)	<i>SAMHD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Aicardi-Goutieres Syndrome (TREX1-Related)	<i>TREX1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600

Albinism, Oculocutaneous, Type III	<i>TYRP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Alkaptonuria	<i>HGD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,600
Alpha-Mannosidosis	<i>MAN2B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000
Alpha-Thalassemia Intellectual Disability Syndrome	<i>ATRX</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 48,000
Alport Syndrome (<i>COL4A3</i> -Related)	<i>COL4A3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
Alport Syndrome (<i>COL4A4</i> -Related)	<i>COL4A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Alport Syndrome (<i>COL4A5</i> -Related)	<i>COL4A5</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 150,000
Alstrom Syndrome	<i>ALMS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Andermann Syndrome	<i>SLC12A6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 161,000
Antley-Bixler Syndrome (<i>POR</i> -Related)	<i>POR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Argininemia	<i>ARG1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Argininosuccinic Aciduria	<i>ASL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Aromatase Deficiency	<i>CYP19A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Asparagine Synthetase Deficiency	<i>ASNS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 84,000
Aspartylglycosaminuria	<i>AGA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Ataxia With Isolated Vitamin E Deficiency	<i>TTPA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 32,000
Ataxia-Telangiectasia	<i>ATM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Ataxia-Telangiectasia-Like Disorder 1	<i>MRE11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	<i>SACS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Bardet-Biedl Syndrome (<i>ARL6</i> -Related)	<i>ARL6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 20,000
Bardet-Biedl Syndrome (<i>BBS10</i> -Related)	<i>BBS10</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,600
Bardet-Biedl Syndrome (<i>BBS12</i> -Related)	<i>BBS12</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,100
Bardet-Biedl Syndrome (<i>BBS1</i> -Related)	<i>BBS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 25,000
Bardet-Biedl Syndrome (<i>BBS2</i> -Related)	<i>BBS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,900
Bardet-Biedl Syndrome (<i>BBS4</i> -Related)	<i>BBS4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Bare Lymphocyte Syndrome, Type II	<i>CIITA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Barth Syndrome	<i>TAZ</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 183,000
Bartter Syndrome, Type 3	<i>CLCNKB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 340
Bartter Syndrome, Type 4A	<i>BSND</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Bernard-Soulier Syndrome, Type A1	<i>GP1BA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 203,000
Bernard-Soulier Syndrome, Type C	<i>GP9</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 400
Beta-Ketothiolase Deficiency	<i>ACAT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Beta-Mannosidosis	<i>MANBA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,100
BH4-Deficient Hyperphenylalaninemia C	<i>QDPR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
BH4-Deficient Hyperphenylalaninemia D	<i>PCBD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,000
Bilateral Frontoparietal Polymicrogyria	<i>GPR56</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 92,000
Biotinidase Deficiency	<i>BTBD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 790
Bloom Syndrome	<i>BLM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
Canavan Disease	<i>ASPA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Carbamoylphosphate Synthetase I Deficiency	<i>CPS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Carnitine Acylcarnitine Translocase Deficiency	<i>SLC25A20</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Carnitine Palmitoyltransferase IA Deficiency	<i>CPT1A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,200
Carnitine Palmitoyltransferase II Deficiency	<i>CPT2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Carpenter Syndrome	<i>RAB23</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 20,000
Cartilage-Hair Hypoplasia	<i>RMRP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 570
Catecholaminergic Polymorphic Ventricular Tachycardia	<i>CASQ2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Central Hypothyroidism and Testicular Enlargement	<i>IGSF1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 781,000

Cerebral Creatine Deficiency Syndrome 1	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 2,000
Cerebral Creatine Deficiency Syndrome 3	GATM	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
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 6,100
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 38,000
Chondrodysplasia Punctata	ARSE	XL	Reduced Risk	Personalized Residual Risk: 1 in 862,000
Choreoacanthocytosis	VPS13A	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
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 3,600
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 1,700
Citrullinemia, Type 1	ASS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Cockayne Syndrome, Type A	ERCC8	AR	Reduced Risk	Personalized Residual Risk: 1 in 31,000
Cockayne Syndrome, Type B and other ERCC6-Related Disorders	ERCC6	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,800
Cohen Syndrome	VPS13B	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,500
Combined Factor V and VIII Deficiency	LMAN1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,900
Combined Malonic and Methylmalonic Aciduria	ACSF3	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Combined Oxidative Phosphorylation Deficiency 1	GFM1	AR	Reduced Risk	Personalized Residual Risk: 1 in 51,000
Combined Oxidative Phosphorylation Deficiency 3	TSFM	AR	Reduced Risk	Personalized Residual Risk: 1 in 68,000
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 194,000
Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1	GUCY2D	AR	Reduced Risk	Personalized Residual Risk: 1 in 400
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 5,200
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 6,600
Congenital Amegakaryocytic Thrombocytopenia	MPL	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
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 8,900
Congenital Disorder of Deglycosylation	NGLY1	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,200
Congenital Disorder of Glycosylation, Type Ia	PMM2	AR	Reduced Risk	Personalized Residual Risk: 1 in 540
Congenital Disorder of Glycosylation, Type Ib	MPI	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Congenital Disorder of Glycosylation, Type Ic	ALG6	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
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 1,000
Congenital Dyserythropoietic Anemia, Type Ia	CDAN1	AR	Reduced Risk	Personalized Residual Risk: 1 in 330
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 4,100

Congenital Muscular Dystrophy (LAMA2-Related)	LAMA2	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
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 4,100
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 5,700
Congenital Neutropenia (HAX1-Related)	HAX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 80,000
Congenital Neutropenia (VPS45-Related)	VPS45	AR	Reduced Risk	Personalized Residual Risk: 1 in 112,000
Congenital Nongoitrous Hypothyroidism 1	TSHR	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
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 2,000
Corneal Dystrophy and Perceptive Deafness	SLC4A11	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Corticosterone Methyloxidase Deficiency	CYP11B2	AR	Reduced Risk	Personalized Residual Risk: 1 in 940
Cystic Fibrosis	CFTR	AR	Reduced Risk	Personalized Residual Risk: 1 in 630
Cystinosis	CTNS	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Cystinuria (SLC3A1-Related)	SLC3A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 960
Cytochrome C Oxidase Deficiency / Leigh Syndrome (COX15-Related)	COX15	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
D-Bifunctional Protein Deficiency	HSD17B4	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
Deafness, Autosomal Recessive 3	MYO15A	AR	Reduced Risk	Personalized Residual Risk: 1 in 400
Deafness, Autosomal Recessive 59	PJVK	AR	Reduced Risk	Personalized Residual Risk: 1 in 52,000
Deafness, Autosomal Recessive 7	TMC1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,100
Deafness, Autosomal Recessive 76	SYNE4	AR	Reduced Risk	Personalized Residual Risk: 1 in 69,000
Deafness, Autosomal Recessive 77	LOXHD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Deafness, Autosomal Recessive 8/10	TMPRSS3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Deafness, Autosomal Recessive 9	OTOF	AR	Reduced Risk	Personalized Residual Risk: 1 in 580
Desbuquois Dysplasia 1	CANT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 100,000
Desmosterolosis	DHCR24	AR	Reduced Risk	Personalized Residual Risk: 1 in 28,000
Diaphanospondylodysostosis	BMPER	AR	Reduced Risk	Personalized Residual Risk: 1 in 27,000
Distal Renal Tubular Acidosis and other SLC4A1-related Disorders	SLC4A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
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 9,800
Dystrophic Epidermolysis Bullosa	COL7A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 690
Ehlers-Danlos Syndrome, Type VI	PLOD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 102,000
Ehlers-Danlos Syndrome, Type VIIC	ADAMTS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 142,000
Ellis-Van Creveld Syndrome (EVC2-Related)	EVC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Ellis-van Creveld Syndrome (EVC-Related)	EVC	AR	Reduced Risk	Personalized Residual Risk: 1 in 18,000
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 1,000
Ethylmalonic Encephalopathy	ETHE1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
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 570
Factor XI Deficiency	F11	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Familial Autosomal Recessive Hypercholesterolemia	LDLRAP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 144,000
Familial Dysautonomia	IKBKAP	AR	Reduced Risk	Personalized Residual Risk: 1 in 41,000

Familial Hypercholesterolemia	LDLR	AR	Reduced Risk	Personalized Residual Risk: 1 in 450
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	HADH	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Familial Hyperinsulinism (ABCC8-Related)	ABCC8	AR	Reduced Risk	Personalized Residual Risk: 1 in 480
Familial Hyperinsulinism (KCNJ11-Related)	KCNJ11	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Familial Hyperphosphatemic Tumoral Calcinosis	GALNT3	AR	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Familial Mediterranean Fever	MEFV	AR	Reduced Risk	Personalized Residual Risk: 1 in 870
Fanconi Anemia, Group A	FANCA	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Fanconi Anemia, Group C	FANCC	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Fanconi Anemia, Group G	FANCG	AR	Reduced Risk	Personalized Residual Risk: 1 in 49,000
Fanconi-Bickel Syndrome	SLC2A2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
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 27,000
Fructose-1,6-Bisphosphatase Deficiency	FBP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Fucosidosis	FUCA1	AR	Reduced Risk	Personalized Residual Risk: 1 in 25,000
Fumarase Deficiency	FH	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Fundus Albipunctatus	RDH5	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Galactokinase Deficiency	GALK1	AR	Reduced Risk	Personalized Residual Risk: 1 in 910
Galactose Epimerase Deficiency	GALE	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Galactosemia	GALT	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Galactosialidosis	CTSA	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,400
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 162,000
Geroderma Osteodysplasticum	GORAB	AR	Reduced Risk	Personalized Residual Risk: 1 in 60,000
Gitelman Syndrome	SLC12A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 620
Glanzmann Thrombasthenia (ITGA2B-Related)	ITGA2B	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Glanzmann Thrombasthenia (ITGB3-Related)	ITGB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Glutaric Acidemia, Type I	GCDH	AR	Reduced Risk	Personalized Residual Risk: 1 in 560
Glutaric Acidemia, Type IIa	ETFA	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,300
Glutaric Acidemia, Type IIb	ETFB	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Glutaric Acidemia, Type IIc	ETFDH	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Glutathione Synthetase Deficiency	GSS	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
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 1,000
Glycogen Storage Disease, Type 0	GYS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Glycogen Storage Disease, Type Ia	G6PC	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,000
Glycogen Storage Disease, Type Ib	SLC37A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,300
Glycogen Storage Disease, Type II	GAA	AR	Reduced Risk	Personalized Residual Risk: 1 in 380
Glycogen Storage Disease, Type III	AGL	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	GBE1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Glycogen Storage Disease, Type IXb	PHKB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Glycogen Storage Disease, Type V	PYGM	AR	Reduced Risk	Personalized Residual Risk: 1 in 940
Glycogen Storage Disease, Type VI	PYGL	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Glycogen Storage Disease, Type VII	PFKM	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
GRACILE Syndrome and Other BCS1L-Related Disorders	BCS1L	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Gray Platelet Syndrome	NBEAL2	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200

Growth Hormone Deficiency, Type 1B	GHRHR	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Hemochromatosis, Type 2A	HFE2	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Hemochromatosis, Type 3	TFR2	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Hereditary Fructose Intolerance	ALDOB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Hereditary Spastic Paraparesis 49	TECPR2	AR	Reduced Risk	Personalized Residual Risk: 1 in 187,000
Hermansky-Pudlak Syndrome, Type 1	HPS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,700
Hermansky-Pudlak Syndrome, Type 3	HPS3	AR	Reduced Risk	Personalized Residual Risk: 1 in 80,000
Hermansky-Pudlak Syndrome, Type 4	HPS4	AR	Reduced Risk	Personalized Residual Risk: 1 in 179,000
Hermansky-Pudlak Syndrome, Type 6	HPS6	AR	Reduced Risk	Personalized Residual Risk: 1 in 62,000
HMG-CoA Lyase Deficiency	HMGCL	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Hmg-CoA Synthase 2 Deficiency	HMGCS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,200
Holocarboxylase Synthetase Deficiency	HLCS	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,800
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 1,000
Homocystinuria, cblE Type	MTRR	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,600
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	MTR	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
Hydrocephalus	L1CAM	XL	Reduced Risk	Personalized Residual Risk: 1 in 40,000
Hydrolethrus Syndrome	HYLS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 109,000
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 6,800
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 32,000
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 51,000
Hypoparathyroidism-Retardation-Dysmorphic Syndrome	TBCE	AR	Reduced Risk	Personalized Residual Risk: 1 in 83,000
Hypophosphatasia	ALPL	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,400
Hypophosphatemic Rickets with Hypercalciuria	SLC34A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Hypotrichosis 8 / Autosomal Recessive Woolly Hair 1	LPAR6	AR	Reduced Risk	Personalized Residual Risk: 1 in 76,000
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 820
Infantile Cerebral and Cerebellar Atrophy	MED17	AR	Reduced Risk	Personalized Residual Risk: 1 in 75,000
Infantile Neuroaxonal Dystrophy 1 and other PLA2G6-Related Disorders	PLA2G6	AR	Reduced Risk	Personalized Residual Risk: 1 in 340
Intellectual Disability, Autosomal Recessive 3	CC2D1A	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
Intrahepatic Cholestasis	ATP8B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Isovaleric Acidemia	IVD	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Joubert Syndrome 2	TMEM216	AR	Reduced Risk	Personalized Residual Risk: 1 in 336,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	NPHP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,100
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	RPGRIP1L	AR	Reduced Risk	Personalized Residual Risk: 1 in 26,000
Junctional Epidermolysis Bullosa (COL17A1-Related)	COL17A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Junctional Epidermolysis Bullosa (ITGA6-Related)	ITGA6	AR	Reduced Risk	Personalized Residual Risk: 1 in 145,000
Junctional Epidermolysis Bullosa (ITGB4-Related)	ITGB4	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Junctional Epidermolysis Bullosa (LAMA3-Related)	LAMA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 78,000

Junctional Epidermolysis Bullosa (<i>LAMB3</i> -Related)	<i>LAMB3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,300
Junctional Epidermolysis Bullosa (<i>LAMC2</i> -Related)	<i>LAMC2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 82,000
Kohlschutter-Tonz Syndrome	<i>ROGDI</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Krabbe Disease	<i>GALC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 340
Lamellar Ichthyosis, Type 1	<i>TGM1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 900
Laron Dwarfism	<i>GHR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,700
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	<i>CEP290</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Leber Congenital Amaurosis 13	<i>RDH12</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,100
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	<i>TULP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 380
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	<i>RPE65</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Leber Congenital Amaurosis 4	<i>AIPL1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Leber Congenital Amaurosis 5	<i>LCA5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,800
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	<i>CRB1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Leigh Syndrome (<i>NDUFS7</i> -Related)	<i>NDUFS7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 38,000
Leigh Syndrome (<i>SURF1</i> -Related)	<i>SURF1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Leigh Syndrome, French-Canadian Type	<i>LRPPRC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 65,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease	<i>GLE1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Lethal Congenital Contracture Syndrome 2	<i>ERBB3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 79,000
Lethal Congenital Contracture Syndrome 3	<i>PIP5K1C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 67,000
Leukoencephalopathy with Vanishing White Matter	<i>EIF2B5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Limb-Girdle Muscular Dystrophy, Type 2A	<i>CAPN3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 450
Limb-Girdle Muscular Dystrophy, Type 2B	<i>DYSF</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 600
Limb-Girdle Muscular Dystrophy, Type 2C	<i>SGCG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,800
Limb-Girdle Muscular Dystrophy, Type 2D	<i>SGCA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Limb-Girdle Muscular Dystrophy, Type 2E	<i>SGCB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 33,000
Limb-Girdle Muscular Dystrophy, Type 2F	<i>SGCD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 142,000
Limb-Girdle Muscular Dystrophy, Type 2H	<i>TRIM32</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Limb-Girdle Muscular Dystrophy, Type 2I	<i>FKRP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Limb-Girdle Muscular Dystrophy, Type 2L	<i>ANO5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Lipoamide Dehydrogenase Deficiency	<i>DLD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Lipoid Adrenal Hyperplasia	<i>STAR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Lipoprotein Lipase Deficiency	<i>LPL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	<i>HADHA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
Lowe Syndrome	<i>OCRL</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 1,375,000
Lysinuric Protein Intolerance	<i>SLC7A7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Malonyl-CoA Decarboxylase Deficiency	<i>MLYCD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Maple Syrup Urine Disease, Type 1a	<i>BCKDHA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Maple Syrup Urine Disease, Type 1b	<i>BCKDHB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Maple Syrup Urine Disease, Type 2	<i>DBT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,700
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	<i>MKS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Medium Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
MEDNIK Syndrome	<i>AP1S1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 294,000
Megalencephalic Leukoencephalopathy with Subcortical Cysts	<i>MLC1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200

Megaloblastic Anemia 1	AMN	AR	Reduced Risk	Personalized Residual Risk: 1 in 36,000
Menkes Disease	ATP7A	XL	Reduced Risk	Personalized Residual Risk: 1 in 172,000
Metachromatic Leukodystrophy	ARSA	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Methionine Adenosyltransferase I/III Deficiency	MAT1A	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
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 1,200
Methylmalonic Acidemia (MUT-Related)	MUT	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	MMACHC	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	MMADHC	AR	Reduced Risk	Personalized Residual Risk: 1 in 336,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	LMBRD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
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 7,400
Mitochondrial Complex I Deficiency (ACAD9-Related)	ACAD9	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,600
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 9,800
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 2,400
Mitochondrial Complex I Deficiency / Leigh Syndrome (FOXRED1-Related)	FOXRED1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,800
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFAF2-Related)	NDUFAF2	AR	Reduced Risk	Personalized Residual Risk: 1 in 176,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFS4-Related)	NDUFS4	AR	Reduced Risk	Personalized Residual Risk: 1 in 70,000
Mitochondrial Complex IV Deficiency (COX20-related)	COX20	AR	Reduced Risk	Personalized Residual Risk: 1 in 177,000
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 9,200
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 13,000
Mitochondrial Complex IV Deficiency / Leigh Syndrome (COX10-Related)	COX10	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,600
Mitochondrial DNA Depletion Syndrome 2	TK2	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Mitochondrial DNA Depletion Syndrome 3	DGUK	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,200
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 82,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	MPV17	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	PUS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 204,000
Mitochondrial Trifunctional Protein Deficiency (HADHB-Related)	HADHB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Molybdenum Cofactor Deficiency A	MOCS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,600
Mucopolipidosis II / IIIA	GNPTAB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Mucopolipidosis III Gamma	GNPTG	AR	Reduced Risk	Personalized Residual Risk: 1 in 49,000
Mucopolipidosis IV	MCOLN1	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,400
Mucopolysaccharidosis Type I	IDUA	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
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 2,000
Mucopolysaccharidosis Type IIIB	NAGLU	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Mucopolysaccharidosis Type IIIC	HGSNAT	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
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 800
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	GLB1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Mucopolysaccharidosis type IX	HYAL1	AR	Reduced Risk	Personalized Residual Risk: 1 in 254,000
Mucopolysaccharidosis type VI	ARSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Mucopolysaccharidosis VII	GUSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Mulibrey Nanism	TRIM37	AR	Reduced Risk	Personalized Residual Risk: 1 in 20,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	PIGN	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Multiple Pterygium Syndrome	CHRNA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 38,000
Muscle-Eye-Brain Disease and Other POMGNT1-Related Congenital Muscular Dystrophy-Dystroglycanopathies	POMGNT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Myoneurogastrointestinal Encephalopathy	TYMP	AR	Reduced Risk	Personalized Residual Risk: 1 in 920
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 4,300
Nemaline Myopathy 2	NEB	AR	Reduced Risk	Personalized Residual Risk: 1 in 660
Nephrogenic Diabetes insipidus (AVPR2-related) / Nephrogenic Syndrome of Inappropriate Antidiuresis	AVPR2	XL	Reduced Risk	Personalized Residual Risk: 1 in 471,000
Nephrogenic Diabetes Insipidus, Type II	AQP2	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Nephronophthisis 2	INVS	AR	Reduced Risk	Personalized Residual Risk: 1 in 26,000
Nephrotic Syndrome (NPHS1-Related) / Congenital Finnish Nephrosis	NPHS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 830
Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome	NPHS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Neurodegeneration due to Cerebral Folate Transport Deficiency	FOLR1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	PLAA	AR	Reduced Risk	Personalized Residual Risk: 1 in 122,000
Neuronal Ceroid-Lipofuscinosis (CLN3-Related)	CLN3	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
Neuronal Ceroid-Lipofuscinosis (CLN5-Related)	CLN5	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Neuronal Ceroid-Lipofuscinosis (CLN6-Related)	CLN6	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,300
Neuronal Ceroid-Lipofuscinosis (CLN8-Related)	CLN8	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Neuronal Ceroid-Lipofuscinosis (MFSD8-Related)	MFSD8	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,300
Neuronal Ceroid-Lipofuscinosis (PPT1-Related)	PPT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,900
Neuronal Ceroid-Lipofuscinosis (TPP1-Related)	TPP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Niemann-Pick Disease (SMPD1-Related)	SMPD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Niemann-Pick Disease, Type C (NPC1-Related)	NPC1	AR	Reduced Risk	Personalized Residual Risk: 1 in 740
Niemann-Pick Disease, Type C (NPC2-Related)	NPC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600
Nijmegen Breakage Syndrome	NBN	AR	Reduced Risk	Personalized Residual Risk: 1 in 50,000
Non-Syndromic Hearing Loss (GJB2-Related)	GJB2	AR	Reduced Risk	Personalized Residual Risk: 1 in 360
Oculocutaneous Albinism, Type IA / IB	TYR	AR	Reduced Risk	Personalized Residual Risk: 1 in 240
Oculocutaneous Albinism, Type IV	SLC45A2	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	WNT10A	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Omenn Syndrome (RAG2-Related)	RAG2	AR	Reduced Risk	Personalized Residual Risk: 1 in 95,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	DCLRE1C	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,300
Omenn Syndrome and other RAG1-Related Disorders	RAG1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200

Ornithine Aminotransferase Deficiency	OAT	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
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 9,500
Osteopetrosis 1	TCIRG1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
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 1,700
Papillon-Lefevre Syndrome	CTSC	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Pendred Syndrome	SLC26A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 490
Peroxisome Biogenesis Disorder 3A and 3B	PEX12	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Peroxisome Biogenesis Disorder 7A and 7B	PEX26	AR	Reduced Risk	Personalized Residual Risk: 1 in 84,000
Phenylalanine Hydroxylase Deficiency	PAH	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Polycystic Kidney Disease, Autosomal Recessive	PKHD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 320
Polyglandular Autoimmune Syndrome, Type 1	AIRE	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Pontocerebellar Hypoplasia, Type 1A	VRK1	AR	Reduced Risk	Personalized Residual Risk: 1 in 47,000
Pontocerebellar Hypoplasia, Type 1B	EXOSC3	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Pontocerebellar Hypoplasia, Type 2A and Type 4	TSEN54	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,700
Pontocerebellar Hypoplasia, Type 2E	VPS53	AR	Reduced Risk	Personalized Residual Risk: 1 in 94,000
Pontocerebellar Hypoplasia, Type 6	RARS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 38,000
Primary Carnitine Deficiency	SLC22A5	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Primary Ciliary Dyskinesia (CCDC103-Related)	CCDC103	AR	Reduced Risk	Personalized Residual Risk: 1 in 49,000
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 50,000
Primary Ciliary Dyskinesia (DNAH5-Related)	DNAH5	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Primary Ciliary Dyskinesia (DNAI1-Related)	DNAI1	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,500
Primary Ciliary Dyskinesia (DNAI2-Related)	DNAI2	AR	Reduced Risk	Personalized Residual Risk: 1 in 41,000
Primary Ciliary Dyskinesia (RSPH9-Related)	RSPH9	AR	Reduced Risk	Personalized Residual Risk: 1 in 54,000
Primary Coenzyme Q10 Deficiency 7	COQ4	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Primary Congenital Glaucoma 3A	CYP1B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Primary Hyperoxaluria, Type 1	AGXT	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Primary Hyperoxaluria, Type 2	GRHPR	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Primary Hyperoxaluria, Type 3	HOGA1	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,300
Progressive Cerebello-Cerebral Atrophy	SEPSECS	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Progressive Familial Intrahepatic Cholestasis, Type 2	ABCB11	AR	Reduced Risk	Personalized Residual Risk: 1 in 610
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 6,300
Propionic Acidemia (PCCA-Related)	PCCA	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Propionic Acidemia (PCCB-Related)	PCCB	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Pulmonary Surfactant Dysfunction	ABCA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
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 28,000
Pyridoxine-Dependent Epilepsy	ALDH7A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 860
Pyruvate Carboxylase Deficiency	PC	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,000
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 1,700
Renal Tubular Acidosis and Deafness	ATP6V1B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,700
Retinitis Pigmentosa 25	EYS	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
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 89,000
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 50,000
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 49,000
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 67,000
Salla Disease	SLC17A5	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
Salt and Pepper Developmental Regression Syndrome	ST3GAL5	AR	Reduced Risk	Personalized Residual Risk: 1 in 66,000
Sandhoff Disease	HEXB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Schimke Immunoosseous Dysplasia	SMARCAL1	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,000
Seckel Syndrome 5 / Microcephaly 9	CEP152	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,800
Segawa Syndrome	TH	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
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 17,000
Severe Combined Immunodeficiency (JAK3-Related)	JAK3	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
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 7,300
Severe Neonatal Hyperparathyroidism	CASR	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis	POC1A	AR	Reduced Risk	Personalized Residual Risk: 1 in 170,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	ACADS	AR	Reduced Risk	Personalized Residual Risk: 1 in 530
Shwachman-Diamond Syndrome	SBDS	AR	Reduced Risk	Personalized Residual Risk: 1 in 940
Sialidosis, Type I and Type II	NEU1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Sjogren-Larsson Syndrome	ALDH3A2	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Smith-Lemli-Opitz Syndrome	DHCR7	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Spastic Paraplegia 15	ZFYVE26	AR	Reduced Risk	Personalized Residual Risk: 1 in 61,000
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 2,000
Spinal Muscular Atrophy	SMN1	AR	Reduced Risk	<p>SMN1 copy number: >=3 SMN2 copy number: 1 c.'3>80T>G: Detected SMN1 Sequencing: Negative Personalized Residual Risk: 1 in 618 As additional gene copies are present, the patient's residual risk is expected to be lower than displayed</p>
Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S	IGHMBP2	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,500
Spinocerebellar Ataxia with Axonal Neuropathy 3	COA7	AR	Reduced Risk	Personalized Residual Risk: 1 in 42,000
Spondylocostal Dysostosis 1	DLL3	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
Spondylometaepiphyseal Dysplasia (DDR2-Related)	DDR2	AR	Reduced Risk	Personalized Residual Risk: 1 in 122,000
Spondyl thoracic Dysostosis	MESP2	AR	Reduced Risk	Personalized Residual Risk: 1 in 225,000
Steel Syndrome	COL27A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 173,000
Stuve-Wiedemann Syndrome	LIFR	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,000
Sulfate Transporter-Related Osteochondrodysplasia	SLC26A2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800

Tay-Sachs Disease	HEXA	AR	Reduced Risk	Tay-Sachs disease enzyme: Non-carrier
				White blood cells: Non-carrier
				<ul style="list-style-type: none">Hex A%: 65.4% (Non-carrier : 55.0 - 72.0%; Carrier: <50%)Total hexosaminidase activity: 1096 nmol/hr/mg
				Plasma: Non-carrier
				<ul style="list-style-type: none">Hex A%: 60.5 (Non-carrier : 58.0 - 72.0%; Carrier: <54%)Total hexosaminidase activity: 811 nmol/hr/ml
HEXA Sequencing: Negative				
Personalized Residual Risk: 1 in 400				
Thiamine-Responsive Megaloblastic Anemia Syndrome	SLC19A2	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Thyroid Dysmorphogenesis 1	SLC5A5	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Thyroid Dysmorphogenesis 2A	TPO	AR	Reduced Risk	Personalized Residual Risk: 1 in 400
Thyroid Dysmorphogenesis 3	TG	AR	Reduced Risk	Personalized Residual Risk: 1 in 940
Thyroid Dysmorphogenesis 4	IYD	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Thyroid Dysmorphogenesis 5	DUOXA2	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Thyroid Dysmorphogenesis 6	DUOX2	AR	Reduced Risk	Personalized Residual Risk: 1 in 480
Trichohepatoenteric Syndrome 1	TTC37	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Tyrosinemia, Type I	FAH	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,900
Tyrosinemia, Type II	TAT	AR	Reduced Risk	Personalized Residual Risk: 1 in 27,000
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 1,600
Usher Syndrome, Type IC	USH1C	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Usher Syndrome, Type ID	CDH23	AR	Reduced Risk	Personalized Residual Risk: 1 in 530
Usher Syndrome, Type IF	PCDH15	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Usher Syndrome, Type IIA	USH2A	AR	Reduced Risk	Personalized Residual Risk: 1 in 390
Usher Syndrome, Type III	CLRN1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	ACADVL	AR	Reduced Risk	Personalized Residual Risk: 1 in 600
Vitamin D-Dependent Rickets, Type I	CYP27B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Vitamin D-Resistant Rickets, Type IIA	VDR	AR	Reduced Risk	Personalized Residual Risk: 1 in 78,000
Walker-Warburg Syndrome and Other FKTN-Related Dystrophies	FKTN	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Werner Syndrome	WRN	AR	Reduced Risk	Personalized Residual Risk: 1 in 40,000
Wilson Disease	ATP7B	AR	Reduced Risk	Personalized Residual Risk: 1 in 540
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 113,000
Wolman Disease / Cholesteryl Ester Storage Disease	LIPA	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,600
Woodhouse-Sakati Syndrome	DCAF17	AR	Reduced Risk	Personalized Residual Risk: 1 in 311,000
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 11,000
Xeroderma Pigmentosum, Group C	XPC	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Xeroderma Pigmentosum, Group G	ERCC5	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,800
Zellweger Syndrome Spectrum (PEX10-Related)	PEX10	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Zellweger Syndrome Spectrum (PEX1-Related)	PEX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Zellweger Syndrome Spectrum (PEX2-Related)	PEX2	AR	Reduced Risk	Personalized Residual Risk: 1 in 87,000

Test methods and comments

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

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

PCR amplification using Asuragen, Inc. AmpliX[®] *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; *DNAL2* (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 chr19:363,7602-363,7616 (partial exon 17); *POU1F1* (NM_000306.3) exon 5; *PTPRC* (NM_002838.4) exons 11 and 23; *PUS1* (NM_025215.5) chr12:132,414,446-132,414,532 (partial exon 2); *RPGRIP1L* (NM_015272.2) exon 23; *SGSH* (NM_000199.3) chr17:78,194,022-78,194,072 (partial exon 1); *SLC6A8* (NM_005629.3) exons 3 and 4; *ST3GAL5* (NM_003896.3) exon 1; *SURF1* (NM_003172.3) chr9:136,223,269-136,223,307 (partial exon 1); *TRPM6* (NM_017662.4) chr9:77,362,800-77,362,811 (partial exon 31); *TSEN54* (NM_207346.2) exon 1; *TYR* (NM_000372.4) exon 5; *VWF* (NM_000552.3) exons 24-26, chr12:6,125,675-6,125,684 (partial exon 30), chr12:6,121,244-6,121,265 (partial exon 33), and exon 34.

This test will detect variants within the exons and the intron-exon boundaries of the target regions. Variants outside these regions may not be detected, including, but not limited to, UTRs, promoters, and deep intronic areas, or regions that fall into the Exceptions mentioned above. This technology may not detect all small insertion/deletions and is not diagnostic for repeat expansions and structural genomic variation. In addition, a mutation(s) in a gene not included on the panel could be present in this patient.

Variant interpretation and classification was performed based on the American College of Medical Genetics Standards and Guidelines for the Interpretation of Sequence Variants (Richards et al, 2015). All potentially pathogenic variants may be confirmed by either a specific genotyping assay or Sanger sequencing, if indicated. Any benign variants, likely benign variants or variants of uncertain significance identified during this analysis will not be reported.

Next Generation Sequencing for SMN1

Exonic regions and intron/exon splice junctions of *SMN1* and *SMN2* were captured, sequenced, and analyzed as described above. Any variants located within exons 2a-7 and classified as pathogenic or likely pathogenic were confirmed to be in either *SMN1* or *SMN2* using gene-specific long-range PCR analysis followed by Sanger sequencing. Variants located in exon 1 cannot be accurately assigned to either *SMN1* or *SMN2* using our current methodology, and so these variants are considered to be of uncertain significance and are not reported.

Copy Number Variant Analysis (Analytical Detection Rate >95%)

Large duplications and deletions were called from the relative read depths on an exon-by-exon basis using a custom exome hidden Markov model (XHMM) algorithm. Deletions or duplications determined to be pathogenic or likely pathogenic were confirmed by either a custom arrayCGH platform, quantitative PCR, or MLPA (depending on CNV size and gene content). While this algorithm is designed to pick up deletions and duplications of 2 or more exons in length, potentially pathogenic single-exon CNVs will be confirmed and reported, if detected.

Exon Array (Confirmation method) (Accuracy >99%)

The customized oligonucleotide microarray (Oxford Gene Technology) is a highly-targeted exon-focused array capable of detecting medically relevant microdeletions and microduplications at a much higher resolution than traditional aCGH methods. Each array matrix has approximately 180,000 60-mer oligonucleotide probes that cover the entire genome. This platform is designed based on human genome NCBI Build 37 (hg19) and the CGH probes are enriched to target the exonic regions of the genes in this panel.

Quantitative PCR (Confirmation method) (Accuracy >99%)

Th relative quantification PCR is utilized on a Roche Universal Library Probe (UPL) system, which relates the PCR signal of the target region in one group to another. To test for genomic imbalances, both sample DNA and reference DNA is amplified with primer/probe sets that specific to the target region and a control region with known genomic copy number. Relative genomic copy numbers are calculated based on the standard $\Delta\Delta C_t$ formula.

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

Long-range PCR was performed to generate locus-specific amplicons for *CYP21A2*, *HBA1* and *HBA2* and *GBA*. The PCR products were then prepared for short-read NGS sequencing and sequenced. Sequenced reads were mapped back to the original genomic locus and run through the bioinformatics pipeline. If indicated, copy number from MLPA was correlated with the sequencing output to analyze the results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where two copies of a gene are located on the same chromosome in tandem, only the second copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in the tandem allele and this patient is therefore less likely to be a carrier. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to determine the phase (cis/trans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing is required to determine the carrier status.

Residual Risk Calculations

Carrier frequencies and detection rates for each ethnicity were calculated through the combination of internal curations of >30,000 variants and genomic frequency data from >138,000 individuals across seven ethnic groups in the gnomAD database. Additional variants in HGMD and novel deleterious variants were also incorporated into the calculation. Residual risk values are calculated using a Bayesian analysis combining the *a priori* risk of being a pathogenic mutation carrier (carrier frequency) and the detection rate. They are provided only as a guide for assessing approximate risk given a negative result, and values will vary based on the exact ethnic background of an individual. This report does not represent medical advice but should be interpreted by a genetic counselor, medical geneticist or physician skilled in genetic result interpretation and the relevant medical literature.

Personalized Residual Risk Calculations

Agilent SureSelectTMXT 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.

SELECTED REFERENCES

Carrier Screening

Grody W et al. ACMG position statement on prenatal/preconception expanded carrier screening. *Genet Med*. 2013 15:482-3.

Fragile X syndrome:

Chen L et al. An information-rich CGG repeat primed PCR that detects the full range of Fragile X expanded alleles and minimizes the need for Southern blot analysis. *J Mol Diag* 2010 12:589-600.

Spinal Muscular Atrophy:

Luo M et al. An Ashkenazi Jewish SMN1 haplotype specific to duplication alleles improves pan-ethnic carrier screening for spinal muscular atrophy. *Genet Med*. 2014 16:149-56.

Ashkenazi Jewish Disorders:

Scott SA et al. Experience with carrier screening and prenatal diagnosis for sixteen Ashkenazi Jewish Genetic Diseases. *Hum. Mutat*. 2010 31:1-11.

Duchenne Muscular Dystrophy:

Flanigan KM et al. Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. *Hum Mutat*. 2009 30:1657-66.

Variant Classification:

Richards S et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015 May;17(5):405-24

Additional disease-specific references available upon request.



Patient Information	Specimen Information	Client Information
6911, DONOR DOB: [REDACTED] AGE: [REDACTED] Gender: M Phone: NG Patient ID: [REDACTED]	Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED] Collected: 08/05/2022 Received: 08/06/2022 / 20:18 EDT Reported: 08/16/2022 / 13:14 EDT	Client #: 48041578 NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229

Ward:	FFAXCB
-------	--------

Cytogenetic Report

CHROMOSOME ANALYSIS, BLOOD - 14596

Lab:EZ

CHROMOSOME ANALYSIS, BLOOD

Order ID: [REDACTED]
Specimen Type: Blood
Clinical Indication: Encounter of male for testing for
disease carrier status for procrea management

RESULT:
NORMAL MALE KARYOTYPE

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

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

NOMENCLATURE:
46,XY

ASSAY INFORMATION:

Method: G-Band (Digital Analysis: MetaSyst)
Cells Counted: 20
Band Level: 450
Cells Analyzed: 6
Cells Karyotyped: 6

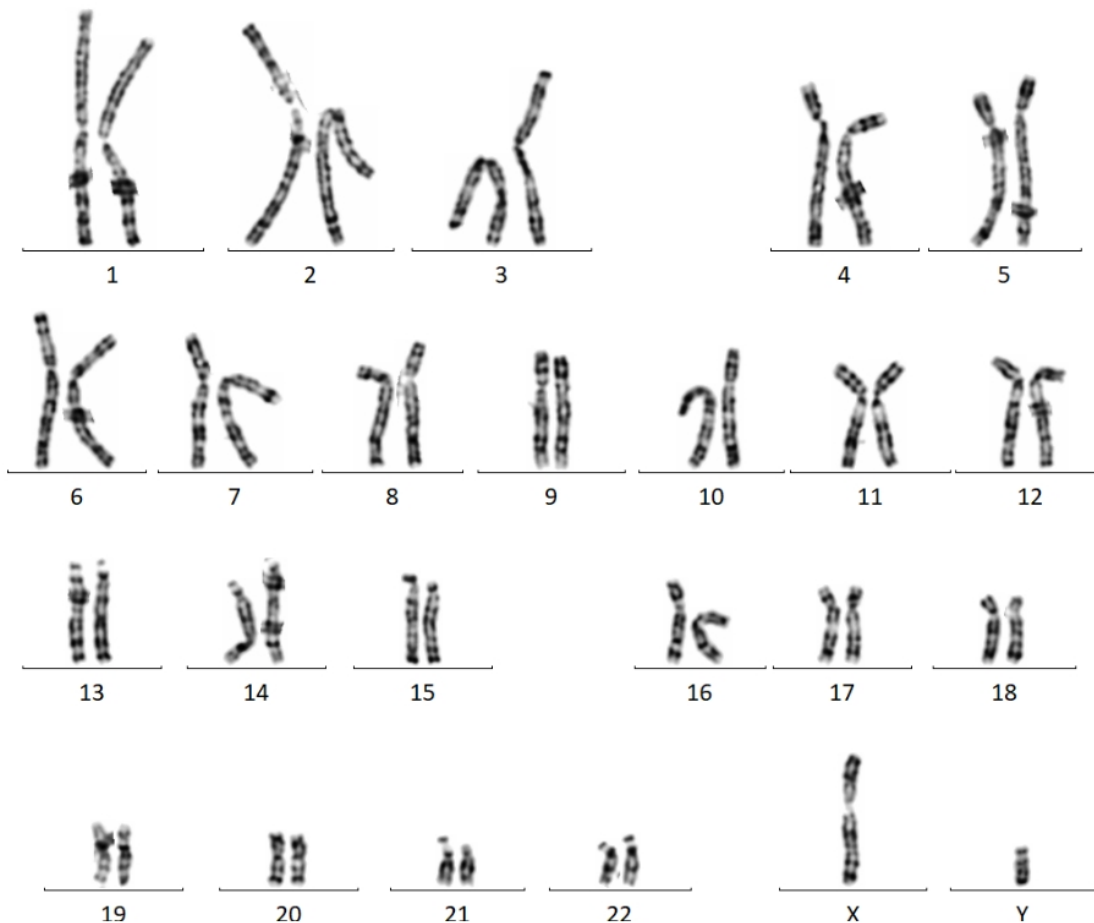
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

Lakshmi J. Nemana, Ph.D., FACMG

Electronic Signature: 8/16/2022 12:17 PM



Patient Information	Specimen Information	Client Information
6911, DONOR DOB: [REDACTED] AGE: [REDACTED] Gender: M Patient ID: [REDACTED]	Specimen: [REDACTED] Collected: 08/05/2022 Received: 08/06/2022 / 20:18 EDT Reported: 08/16/2022 / 13:14 EDT	Client #: 48041578 GENOMICS, SEMA4



PERFORMING SITE:

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



Patient Information	Specimen Information	Client Information
6911, DONOR DOB: [REDACTED] AGE: [REDACTED] Gender: M Phone: NG Patient ID: [REDACTED]	Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED] Collected: 08/05/2022 Received: 08/06/2022 / 20:43 EDT Reported: 08/08/2022 / 22:38 EDT	Client #: 48041578 NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229

Ward: FFXCB

Test Name	In Range	Out Of Range	Reference Range	Lab
HEMOGLOBINOPATHY EVALUATION				
RED BLOOD CELL COUNT	5.62		4.20-5.80 Million/uL	Z99
HEMOGLOBIN	14.4		13.2-17.1 g/dL	
HEMATOCRIT	45.8		38.5-50.0 %	
MCV	81.5		80.0-100.0 fL	
MCH		25.6 L	27.0-33.0 pg	
RDW	13.1		11.0-15.0 %	
HEMOGLOBIN A		61.5 L	>96.0 %	Z99
HEMOGLOBIN F	0.3		<2.0 %	
HEMOGLOBIN A2 (QUANT)		3.4 H	2.2-3.2 %	
HEMOGLOBIN S		34.8 H	%	
INTERPRETATION	*			
Consistent with Hb S trait. The RBC parameters are suggestive of microcytosis/hypochromia. Concurrent iron deficiency, thalassemic trait, or other causes of microcytosis should be clinically excluded.				

PERFORMING SITE:

Z99 QUEST DIAGNOSTICS CLIFTON, 1 INSIGHTS DRIVE, CLIFTON, NJ 07012-2355 Laboratory Director: SHELLA K MONGIA,MD, CLIA: 31D0696246