



## Donor 7027

### Genetic Testing Summary

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

Last Updated: 08/07/23

Donor Reported Ancestry: African American

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 suggestive of <b>Alpha Thalassemia carrier status</b> - confirmed by DNA.	
Expanded Genetic Disease Carrier Screening Panel attached- 502 diseases by gene sequencing.  Personalized residual risk by gene is in the attached report.	<b>Carrier: Alpha-Thalassemia (HBA1/HBA2) One copy of the alpha 3.7 deletion</b>  <b>Carrier: Aspartylglycosaminuria (AGA)</b>  <b>Carrier: Bardet-Biedl Syndrome (BBS1-Related)</b>  <b>Carrier: Trichohepatoenteric Syndrome 1 (TTC37) Deletion of exons 5-43. Follow-up testing confirmed carrier status- attached.</b>  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: 7027 Donor  
Date of Birth: [REDACTED]  
Sema4 ID: [REDACTED]  
Client ID: [REDACTED]  
Indication: Carrier Screening

#### Specimen Information

Specimen Type: Blood  
Date Collected: 10/13/2022  
Date Received: 10/14/2022  
Final Report: 10/28/2022

#### Referring Provider

[REDACTED]  
Fairfax Cryobank, Inc.

## Expanded Carrier Screen Minus TSE (502 genes) with Personalized Residual Risk

### SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
<p><b>Carrier of Alpha-Thalassemia (AR)</b> Associated gene(s): <i>HBA1/HBA2</i> Variant(s) Detected: One copy of the alpha 3,7 deletion</p> <p><b>Carrier of Aspartylglycosaminuria (AR)</b> Associated gene(s): <i>AGA</i> Variant(s) Detected: c.319C&gt;T, p.R107X, Likely Pathogenic, Heterozygous (one copy)</p> <p><b>Carrier of Bardet-Biedl Syndrome (BBS1-Related) (AR)</b> Associated gene(s): <i>BBS1</i> Variant(s) Detected: c.1303_1313delGTGGATCAGAC, p.V435TfsX62, Likely Pathogenic, Heterozygous (one copy)</p> <p><b>Carrier of Trichohepatoenteric Syndrome 1 (AR)</b> Associated gene(s): <i>TTC37</i> Variant(s) Detected: Deletion of exons 5-43, Likely Pathogenic, Heterozygous (one copy)</p>	<p><b>Negative for all other genes tested</b> To view a full list of genes and diseases tested please see Table 1 in this report</p>

AR=Autosomal recessive; XL=X-linked

### Recommendations

- Testing the partner for the above positive disorder(s) and genetic counseling are recommended.
- Ultra-high resolution array (UHRMEA) may be considered to rule out the possibility of a larger deletion that includes additional disease genes.
- Please note that for female carriers of X-linked diseases, follow-up testing of a male partner is not indicated.
- CGG repeat analysis of *FMR1* for fragile X syndrome is not performed on males as repeat expansion of premutation alleles is not expected in the male germline.
- Individuals of Asian, African, Hispanic and Mediterranean ancestry should also be screened for hemoglobinopathies by CBC and hemoglobin electrophoresis.
- Consideration of residual risk by ethnicity after a negative carrier screen is recommended for the other diseases on the panel, especially in the case of a positive family history for a specific disorder. Please note that residual risks for X-linked diseases (including full repeat expansions for Fragile X syndrome) may not be accurate for males and the actual residual risk is likely to be lower.
- As genetic technologies may improve and variant classifications may change over time, it is recommended to obtain a new carrier screening test or reanalysis when a new pregnancy is being considered.

## Interpretation of positive results

### Alpha-Thalassemia (AR)

#### Results and Interpretation

*HBA1* Copy Number: 2

*HBA2* Copy Number: 1

One copy of the alpha 3,7 deletion detected

*HBA1/HBA2* Sequencing: Negative

**Gene(s) analyzed:** *HBA1* (NM\_000558.4) and *HBA2* (NM\_000517.4)

**Inheritance:** Autosomal Recessive

This patient carries a heterozygous alpha 3,7 deletion, resulting in the loss of one copy of the alpha-globin gene and is therefore a silent carrier of alpha-thalassemia (aa/-a). No pathogenic or likely pathogenic variants were identified by sequence analysis.

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

#### What is Alpha-Thalassemia?

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

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

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

### Aspartylglycosaminuria (AR)

#### Results and Interpretation

A heterozygous (one copy) likely pathogenic premature stop codon, c.319C>T, p.R107X, was detected in the *AGA* gene (NM\_000027.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for aspartylglycosaminuria. Therefore, this individual is expected to be at least a carrier for aspartylglycosaminuria. Heterozygous carriers are not expected to exhibit symptoms of this disease.

#### What is Aspartylglycosaminuria?

Aspartylglycosaminuria is an autosomal recessive disorder that is caused by pathogenic variants in the gene *AGA*. It is a pan-ethnic disease with high prevalence among individuals of Finnish descent. Symptoms become apparent within the first few years of life and include frequent diarrhea and infections, clumsiness, delayed speech, and hyperactivity. Over time, individuals will experience progressive intellectual disability, seizures, behavioral problems, and impaired motor function. Physically, individuals with aspartylglycosaminuria also have coarse facial features and spine and eye deformities. Due to the progressiveness of the disease, the life expectancy is estimated to be 30-40 years of age.

### Bardet-Biedl Syndrome (*BBS1*-Related) (AR)

#### Results and Interpretation

A heterozygous (one copy) likely pathogenic frameshift variant, c.1303\_1313delGTGGATCAGAC, p.V435TfsX62, was detected in the *BBS1* gene (NM\_024649.4). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Bardet-Biedl syndrome (*BBS1*-related). Therefore, this individual is expected to be at least a carrier for Bardet-Biedl syndrome (*BBS1*-related). Heterozygous carriers are not expected to exhibit symptoms of this disease.

#### What is Bardet-Biedl Syndrome (*BBS1*-Related)?

Bardet-Biedl syndrome (*BBS1*-related) is an autosomal recessive disease with symptoms including rod-cone dystrophy, truncal obesity, postaxial polydactyly, cognitive impairment, male hypogonadotropic hypogonadism, complex female genitourinary malformations, and renal abnormalities. Individuals experience night blindness by childhood and are diagnosed with legal blindness by an average age of 15 years. While most patients are expected to survive into adulthood, earlier death may occur when renal disease is severe. While there are a total of 18 genes associated with Bardet-Biedl syndrome, pathogenic *BBS1* variants tend to be associated with less severe ophthalmologic involvement. Pathogenic variants in *BBS1* are most commonly identified among individuals of Faroese descent. No genotype-phenotype correlation has been reported.

### Trichohepatoenteric Syndrome 1 (AR)

#### Results and Interpretation

A heterozygous (one copy) likely pathogenic deletion of exons 5-43 was detected in the *TTC37* gene (NM\_014639.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for trichohepatoenteric syndrome 1. As this deletion may extend past the 3' end of the *TTC37* gene, an ultra-high resolution array (UHRMEA) may be considered to determine the extent of the deletion. Therefore, this individual is expected to be at least a carrier for trichohepatoenteric syndrome 1. Heterozygous carriers are not expected to exhibit symptoms of this disease.

#### What is Trichohepatoenteric Syndrome 1?

Trichohepatoenteric syndrome 1 is an autosomal recessive disorder caused by pathogenic variants in the gene *TTC37*. The onset of this condition occurs at birth or in early infancy and is characterized by chronic, difficult-to-treat diarrhea that can lead to failure to thrive. Individuals typically have wooly, brittle, patchy, and easily pulled out hair. Other clinical features include liver disease, skin abnormalities, coarse facial features, immune system dysfunction, mild intellectual disability, and, less commonly, cardiac defects. This disorder is typically fatal in childhood due to complications from liver disease or severe infections. No clear genotype-phenotype correlation has been established.

## Test description

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



Fatimah Nahhas-Alwan, Ph.D., DABMGG, Laboratory Director

## Genes and diseases tested

The personalized residual risks listed below are specific to this individual. The complete residual risk table is available at [go.sema4.com/residualrisk](https://go.sema4.com/residualrisk)

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

Disease	Gene	Inheritance Pattern	Status	Detailed Summary
Positive				
Alpha-Thalassemia	HBA1/HBA2	AR	Silent Carrier	HBA1 Copy Number: 2 HBA2 Copy Number: 1 One copy of the alpha 3,7 deletion detected HBA1/HBA2 Sequencing: Negative
Aspartylglycosaminuria	AGA	AR	Carrier	c.319C>T, p.R107X, Likely Pathogenic, Heterozygous (one copy)
Bardet-Biedl Syndrome (BBS1-Related)	BBS1	AR	Carrier	c.1303_1313delGTGGATCAGAC, p.V435TfsX62, Likely Pathogenic, Heterozygous (one copy)
Trichohepatoenteric Syndrome 1	TTC37	AR	Carrier	Deletion of exons 5-43, Likely Pathogenic, Heterozygous (one copy)
Negative				
2-Methylbutyrylglycinuria	ACADSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	HSD3B2	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,000
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related)	MCCC1	AR	Reduced Risk	Personalized Residual Risk: 1 in 540
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)	MCCC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
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 4,600
6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	PTS	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
CD59-Mediated Hemolytic Anemia	CD59	AR	Reduced Risk	Personalized Residual Risk: 1 in 401,000
Abetalipoproteinemia	MTTP	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Achalasia-Addisonianism-Alacrimia Syndrome	AAAS	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Achromatopsia (CNGA3-Related)	CNGA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 410
Achromatopsia (CNGB3-related)	CNGB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Acrodermatitis Enteropathica	SLC39A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Acute Infantile Liver Failure	TRMU	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Acyl-CoA Oxidase I Deficiency	ACOX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 54,000
Adams-Oliver Syndrome 4	EOGT	AR	Reduced Risk	Personalized Residual Risk: 1 in 43,000
Adenosine Deaminase Deficiency	ADA	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Adrenocorticotrophic Hormone Deficiency	TBX19	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
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 10,000
Aicardi-Goutieres Syndrome (TREX1-Related)	TREX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600
Albinism, Oculocutaneous, Type III	TYRP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Alkaptonuria	HGD	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,600
Alpha-Mannosidosis	MAN2B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000

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 2,200
Alport Syndrome (COL4A4-Related)	COL4A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
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 2,300
Andermann Syndrome	SLC12A6	AR	Reduced Risk	Personalized Residual Risk: 1 in 161,000
Antley-Bixler Syndrome (POR-Related)	POR	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Argininemia	ARG1	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Argininosuccinic Aciduria	ASL	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Aromatase Deficiency	CYP19A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Arthrogryposis, Intellectual Disability, and Seizures	SLC35A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 400,000
Asparagine Synthetase Deficiency	ASNS	AR	Reduced Risk	Personalized Residual Risk: 1 in 84,000
Ataxia With Isolated Vitamin E Deficiency	TTPA	AR	Reduced Risk	Personalized Residual Risk: 1 in 32,000
Ataxia-Telangiectasia	ATM	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Ataxia-Telangiectasia-Like Disorder 1	MRE11	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	SACS	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Bardet-Biedl Syndrome (ARL6-Related)	ARL6	AR	Reduced Risk	Personalized Residual Risk: 1 in 20,000
Bardet-Biedl Syndrome (BBS10-Related)	BBS10	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,600
Bardet-Biedl Syndrome (BBS12-Related)	BBS12	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,100
Bardet-Biedl Syndrome (BBS2-Related)	BBS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,900
Bardet-Biedl Syndrome (BBS4-Related)	BBS4	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Bare Lymphocyte Syndrome, Type II	CLTA	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Barth Syndrome	TAZ	XL	Reduced Risk	Personalized Residual Risk: 1 in 183,000
Bartter Syndrome, Type 3	CLCNKB	AR	Reduced Risk	Personalized Residual Risk: 1 in 340
Bartter Syndrome, Type 4A	BSND	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Bernard-Soulier Syndrome, Type A1	GP1BA	AR	Reduced Risk	Personalized Residual Risk: 1 in 203,000
Bernard-Soulier Syndrome, Type C	GP9	AR	Reduced Risk	Personalized Residual Risk: 1 in 400
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 1,000 Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant): 1 in 3,700
Beta-Ketothiolase Deficiency	ACAT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Beta-Mannosidosis	MANBA	AR	Reduced Risk	Personalized Residual Risk: 1 in 60,000
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 8,000
Bilateral Frontoparietal Polymicrogyria	GPR56	AR	Reduced Risk	Personalized Residual Risk: 1 in 92,000
Biotinidase Deficiency	BTB	AR	Reduced Risk	Personalized Residual Risk: 1 in 790
Bloom Syndrome	BLM	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
Canavan Disease	ASPA	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Carbamoylphosphate Synthetase I Deficiency	CPS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Carnitine Acylcarnitine Translocase Deficiency	SLC25A20	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Carnitine Palmitoyltransferase IA Deficiency	CPT1A	AR	Reduced Risk	Personalized Residual Risk: 1 in 24,000
Carnitine Palmitoyltransferase II Deficiency	CPT2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Carpenter Syndrome	RAB23	AR	Reduced Risk	Personalized Residual Risk: 1 in 20,000
Cartilage-Hair Hypoplasia	RMRP	AR	Reduced Risk	Personalized Residual Risk: 1 in 570
Catecholaminergic Polymorphic Ventricular Tachycardia	CASQ2	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900

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 2,000
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 Hyperplasia due to 21-Hydroxylase Deficiency	CYP21A2	AR	Reduced Risk	CYP21A2 copy number: 2 CYP21A2 sequencing: Negative <b>Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)): 1 in 300</b> <b>Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)): 1 in 1,200</b>
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	<p>FMR1 CGG repeat sizes: Not Performed</p> <p>FMR1 Sequencing: Negative</p> <p>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.</p> <p>Personalized Residual Risk: 1 in 27,000</p>
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 7,800
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 <i>BCS1L</i> -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 IB	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 ( <i>CBS</i> -Related)	CBS	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Homocystinuria due to <i>MTHFR</i> 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
Hydroletharus Syndrome	HYLS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 109,000
Hyper-Igm Syndrome	CD40LG	XL	Reduced Risk	Personalized Residual Risk: 1 in 1167,000
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	GENE	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 <i>PLA2G6</i> -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 (LAMB3-Related)	LAMB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,300
Junctional Epidermolysis Bullosa (LAMC2-Related)	LAMC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 82,000
Kohlschutter-Tonz Syndrome	ROGDI	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
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 900
Laron Dwarfism	GHR	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,700
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	CEP290	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Leber Congenital Amaurosis 13	RDH12	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,100
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	TULP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 380
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	RPE65	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Leber Congenital Amaurosis 4	AIP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Leber Congenital Amaurosis 5	LCA5	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,800
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	CRB1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
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 3,700
Leigh Syndrome, French-Canadian Type	LRPPRC	AR	Reduced Risk	Personalized Residual Risk: 1 in 65,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease	GLE1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Lethal Congenital Contracture Syndrome 2	ERBB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 79,000
Lethal Congenital Contracture Syndrome 3	PIP5K1C	AR	Reduced Risk	Personalized Residual Risk: 1 in 67,000
Leukoencephalopathy with Vanishing White Matter	EIF2B5	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Limb-Girdle Muscular Dystrophy, Type 2A	CAPN3	AR	Reduced Risk	Personalized Residual Risk: 1 in 450
Limb-Girdle Muscular Dystrophy, Type 2B	DYSF	AR	Reduced Risk	Personalized Residual Risk: 1 in 600
Limb-Girdle Muscular Dystrophy, Type 2C	SGCG	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,800
Limb-Girdle Muscular Dystrophy, Type 2D	SGCA	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Limb-Girdle Muscular Dystrophy, Type 2E	SGCB	AR	Reduced Risk	Personalized Residual Risk: 1 in 33,000
Limb-Girdle Muscular Dystrophy, Type 2F	SGCD	AR	Reduced Risk	Personalized Residual Risk: 1 in 142,000
Limb-Girdle Muscular Dystrophy, Type 2H	TRIM32	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Limb-Girdle Muscular Dystrophy, Type 2I	FKRP	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Limb-Girdle Muscular Dystrophy, Type 2L	ANO5	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Lipoamide Dehydrogenase Deficiency	DLD	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Lipoid Adrenal Hyperplasia	STAR	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Lipoprotein Lipase Deficiency	LPL	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	HADHA	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
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 3,200
Malonyl-CoA Decarboxylase Deficiency	MLYCD	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Maple Syrup Urine Disease, Type 1a	BCKDHA	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	<i>AMN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 36,000
Menkes Disease	<i>ATP7A</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 172,000
Metachromatic Leukodystrophy	<i>ARSA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Methionine Adenosyltransferase I/III Deficiency	<i>MAT1A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Methylmalonic Acidemia (MMAA-Related)	<i>MMAA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 20,000
Methylmalonic Acidemia (MMAB-Related)	<i>MMAB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Methylmalonic Acidemia (MUT-Related)	<i>MUT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	<i>MMACHC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	<i>MMADHC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 336,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	<i>LMBRD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Methylmalonyl-CoA Epimerase Deficiency	<i>MCEE</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 168,000
Microphthalmia / Anophthalmia	<i>VSX2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
Mitochondrial Complex I Deficiency (ACAD9-Related)	<i>ACAD9</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,600
Mitochondrial Complex I Deficiency (NDUFA11-Related)	<i>NDUFA11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 548,000
Mitochondrial Complex I Deficiency (NDUFAF5-Related)	<i>NDUFAF5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 149,000
Mitochondrial Complex I Deficiency (NDUFS6-Related)	<i>NDUFS6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 371,000
Mitochondrial Complex I Deficiency (NDUFV1-Related)	<i>NDUFV1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Mitochondrial Complex I Deficiency / Leigh Syndrome (FOXRED1-Related)	<i>FOXRED1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,800
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFAF2-Related)	<i>NDUFAF2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 176,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFS4-Related)	<i>NDUFS4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 70,000
Mitochondrial Complex IV Deficiency (COX20-related)	<i>COX20</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 177,000
Mitochondrial Complex IV Deficiency (COX6B1-related)	<i>COX6B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,231,000
Mitochondrial Complex IV Deficiency (APOPT1-Related)	<i>APOPT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,200
Mitochondrial Complex IV Deficiency (PET100-Related)	<i>PET100</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 546,000
Mitochondrial Complex IV Deficiency (SCO1-related)	<i>SCO1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Mitochondrial Complex IV Deficiency / Leigh Syndrome (COX10-Related)	<i>COX10</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,600
Mitochondrial DNA Depletion Syndrome 2	<i>TK2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Mitochondrial DNA Depletion Syndrome 3	<i>DGUK</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,200
Mitochondrial DNA Depletion Syndrome 4A and 4B and other POLG-Related Disorders	<i>POLG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 180
Mitochondrial DNA Depletion Syndrome 5	<i>SUCLA2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 82,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	<i>MPV17</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	<i>PUS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 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
Multiple Sulfatase Deficiency	SUMF1	AR	Reduced Risk	Personalized Residual Risk: 1 in 40,000
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 2,400
Nephrogenic Diabetes insipidus (AVPR2-related) / Nephrogenic Syndrome of Inappropriate Antidiuresis	AVPR2	XL	Reduced Risk	Personalized Residual Risk: 1 in 471,000
Nephrogenic Diabetes Insipidus, Type II	AQP2	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Nephronophthisis 2	INVS	AR	Reduced Risk	Personalized Residual Risk: 1 in 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 ( <i>GJB2</i> -Related)	<i>GJB2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 360
Oculocutaneous Albinism, Type IA / IB	<i>TYR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 240
Oculocutaneous Albinism, Type IV	<i>SLC45A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	<i>WNT10A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Omenn Syndrome ( <i>RAG2</i> -Related)	<i>RAG2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 95,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	<i>DCLRE1C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,300
Omenn Syndrome and other <i>RAG1</i> -Related Disorders	<i>RAG1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Ornithine Aminotransferase Deficiency	<i>OAT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Ornithine Transcarbamylase Deficiency	<i>OTC</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 103,000
Osteogenesis Imperfecta, Type XI	<i>FKBP10</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,500
Osteopetrosis 1	<i>TCIRG1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Osteopetrosis 8	<i>SNX10</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 34,000
Otospondylomegapiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	<i>COL11A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Papillon-Lefevre Syndrome	<i>CTSC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Pendred Syndrome	<i>SLC26A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 490
Peroxisome Biogenesis Disorder 3A and 3B	<i>PEX12</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Peroxisome Biogenesis Disorder 7A and 7B	<i>PEX26</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 84,000
Phenylalanine Hydroxylase Deficiency	<i>PAH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Polycystic Kidney Disease, Autosomal Recessive	<i>PKHD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 320
Polyglandular Autoimmune Syndrome, Type 1	<i>AIRE</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Pontocerebellar Hypoplasia, Type 1A	<i>VRK1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 47,000
Pontocerebellar Hypoplasia, Type 1B	<i>EXOSC3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Pontocerebellar Hypoplasia, Type 2A and Type 4	<i>TSEN54</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,700
Pontocerebellar Hypoplasia, Type 2E	<i>VPS53</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 94,000
Pontocerebellar Hypoplasia, Type 6	<i>RARS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 38,000
Primary Carnitine Deficiency	<i>SLC22A5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Primary Ciliary Dyskinesia ( <i>CCDC103</i> -Related)	<i>CCDC103</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 49,000
Primary Ciliary Dyskinesia ( <i>CCDC151</i> -Related)	<i>CCDC151</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 98,000
Primary Ciliary Dyskinesia ( <i>CCDC39</i> -Related)	<i>CCDC39</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 50,000
Primary Ciliary Dyskinesia ( <i>DNAH5</i> -Related)	<i>DNAH5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Primary Ciliary Dyskinesia ( <i>DNAI1</i> -Related)	<i>DNAI1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,500
Primary Ciliary Dyskinesia ( <i>DNAI2</i> -Related)	<i>DNAI2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 41,000
Primary Ciliary Dyskinesia ( <i>RSPH9</i> -Related)	<i>RSPH9</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 54,000
Primary Coenzyme Q10 Deficiency 7	<i>COQ4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Primary Congenital Glaucoma 3A	<i>CYP1B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Primary Hyperoxaluria, Type 1	<i>AGXT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Primary Hyperoxaluria, Type 2	<i>GRHPR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Primary Hyperoxaluria, Type 3	<i>HOGA1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,300
Progressive Cerebello-Cerebral Atrophy	<i>SEPSECS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Progressive Familial Intrahepatic Cholestasis, Type 2	<i>ABCB11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 610
Progressive Myoclonic Epilepsy, Type 1B	<i>PRICKLE1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 136,000
Progressive Pseudorheumatoid Dysplasia	<i>WISP3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Prolidase Deficiency	<i>PEPD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,300
Propionic Acidemia ( <i>PCCA</i> -Related)	<i>PCCA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Propionic Acidemia ( <i>PCCB</i> -Related)	<i>PCCB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Pulmonary Surfactant Dysfunction	<i>ABCA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800

Pycnodysostosis	CTSK	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,100
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 13,000
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	SMARCA1	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	SMN1 copy number: 2 SMN2 copy number: 2 c.*3>80T>G: Negative SMN1 Sequencing: Negative Personalized Residual Risk: 1 in 618
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	<i>DLL3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
Spondylometaphyseal Dysplasia (DDR2-Related)	<i>DDR2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 122,000
Spondylothoracic Dysostosis	<i>MESP2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 225,000
Steel Syndrome	<i>COL27A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 173,000
Stuve-Wiedemann Syndrome	<i>LIFR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,000
Sulfate Transporter-Related Osteochondrodysplasia	<i>SLC26A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Tay-Sachs Disease	<i>HEXA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 400
Thiamine-Responsive Megaloblastic Anemia Syndrome	<i>SLC19A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Thyroid Dysmorphogenesis 1	<i>SLC5A5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Thyroid Dysmorphogenesis 2A	<i>TPO</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 400
Thyroid Dysmorphogenesis 3	<i>TG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 940
Thyroid Dysmorphogenesis 4	<i>IYD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Thyroid Dysmorphogenesis 5	<i>DUOXA2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Thyroid Dysmorphogenesis 6	<i>DUOX2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 480
Tyrosinemia, Type I	<i>FAH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,900
Tyrosinemia, Type II	<i>TAT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 27,000
Tyrosinemia, Type III	<i>HPD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Usher Syndrome, Type IB	<i>MYO7A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Usher Syndrome, Type IC	<i>USH1C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Usher Syndrome, Type ID	<i>CDH23</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 530
Usher Syndrome, Type IF	<i>PCDH15</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Usher Syndrome, Type IIA	<i>USH2A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 390
Usher Syndrome, Type III	<i>CLRN1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADVL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 600
Vitamin D-Dependent Rickets, Type I	<i>CYP27B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Vitamin D-Resistant Rickets, Type IIA	<i>VDR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 78,000
Walker-Warburg Syndrome and Other <i>FKTN</i> -Related Dystrophies	<i>FKTN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Werner Syndrome	<i>WRN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 40,000
Wilson Disease	<i>ATP7B</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 540
Wiskott-Aldrich Syndrome (WAS-Related)	<i>WAS</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 1,203,000
Wolcott-Rallison Syndrome	<i>EIF2AK3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 113,000
Wolman Disease / Cholesteryl Ester Storage Disease	<i>LIPA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,600
Woodhouse-Sakati Syndrome	<i>DCAF17</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 311,000
X-Linked Juvenile Retinoschisis	<i>RS1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 40,000
X-Linked Severe Combined Immunodeficiency	<i>IL2RG</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 250,000
Xeroderma Pigmentosum (POLH-Related)	<i>POLH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
Xeroderma Pigmentosum, Group A	<i>XPA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 65,000
Xeroderma Pigmentosum, Group C	<i>XPC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Xeroderma Pigmentosum, Group G	<i>ERCC5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,800
Zellweger Syndrome Spectrum (PEX10-Related)	<i>PEX10</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Zellweger Syndrome Spectrum (PEX1-Related)	<i>PEX1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Zellweger Syndrome Spectrum (PEX2-Related)	<i>PEX2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 87,000
Zellweger Syndrome Spectrum (PEX6-Related)	<i>PEX6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,900

AR=Autosomal recessive; XL=X-linked

## Test methods and comments

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

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

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

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

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

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

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

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

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

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

For spinal muscular atrophy (SMA), the copy numbers of the *SMN1* and *SMN2* genes were analyzed. The individual dosage of exons 7 and 8 as well as the combined dosage of exons 1, 4, 6 and 8 of *SMN1* and *SMN2* were assessed. Copy number gains and losses can be detected with this assay. Depending on ethnicity, 6 - 29 % of carriers will not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *SMN1* gene on one chromosome and loss of *SMN1* (deletion) on the other chromosome (silent 2+0 carrier) or individuals that carry an intragenic mutation in *SMN1*. Please also note that 2% of individuals diagnosed with SMA have a causative *SMN1* variant that occurred de novo, and therefore cannot be picked up by carrier screening in the parents. Analysis of *SMN1* is performed in association with short-read sequencing of exons 2a-7, followed by confirmation using long-range PCR (described below).

In individuals with two copies of *SMN1* with Ashkenazi Jewish, East Asian, African American, Native American or Caucasian ancestry, the presence or absence of c.\*3+80T>G significantly increases or decreases, respectively, the likelihood of being a silent 2+0 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<sup>™</sup>XT Low Input technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Libraries were pooled and sequenced on the Illumina NovaSeq 6000 platform, using paired-end 100 bp reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house.

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

**Exceptions:** *ABCD1* (NM\_000033.3) exons 8 and 9; *ACADSB* (NM\_001609.3) chr10:124,810,695-124,810,707 (partial exon 9); *ADA* (NM\_000022.2) exon 1; *ADAMTS2* (NM\_014244.4) exon 1; *AGPS* (NM\_003659.3) chr2:178,257,512-178,257,649 (partial exon 1); *ALDH7A1* (NM\_001182.4) chr5:125,911,150-125,911,163 (partial exon 7) and chr5:125,896,807-125,896,821 (partial exon 10); *ALMS1* (NM\_015120.4) chr2:73,612,990-73,613,041 (partial exon 1); *APOPT1* (NM\_032374.4) chr14:104,040,437-104,040,455 (partial exon 3); *CDAN1* (NM\_138477.2) exon 2; *CEP152* (NM\_014985.3) chr15:49,061,146-49,061,165 (partial exon 14) and exon 22; *CEP290* (NM\_025114.3) exon 5, exon 7, chr12:88,519,017-88,519,039 (partial exon 13), chr12:88,514,049-88,514,058 (partial exon 15), chr12:88,502,837-88,502,841 (partial exon 23), chr12:88,481,551-88,481,589 (partial exon 32), chr12:88,471,605-88,471,700 (partial exon 40); *CFTR* (NM\_000492.3) exon 10; *COL4A4* (NM\_000092.4) chr2:227,942,604-227,942,619 (partial exon 25); *COX10* (NM\_001303.3) exon 6; *CYP11B1* (NM\_000497.3) exons 3-7; *CYP11B2* (NM\_000498.3) exons 3-7; *DNAI2* (NM\_023036.4) chr17:72,308,136-72,308,147 (partial exon 12); *DOK7* (NM\_173660.4) chr4:3,465,131-3,465,161 (partial exon 1) and exon 2; *DUOX2* (NM\_014080.4) exons 6-8; *EIF2AK3* (NM\_004836.5) exon 8; *EVC* (NM\_153717.2) exon 1; *F5* (NM\_000130.4) chr1:169,551,662-169,551,679 (partial exon 2); *FH* (NM\_000143.3) exon 1; *GAMT* (NM\_000156.5) exon 1; *GLDC* (NM\_000170.2) exon 1; *GNPTAB* (NM\_024312.4) chr17:4,837,000-4,837,400 (partial exon 2); *GNPTG* (NM\_032520.4) exon 1; *GHR* (NM\_000163.4) exon 3; *GYS2* (NM\_021957.3) chr12:21,699,370-21,699,409 (partial exon 12); *HGSNAT* (NM\_152419.2) exon 1; *IDS* (NM\_000202.6) exon 3; *ITGB4* (NM\_000213.4) chr17:73,749,976-73,750,060 (partial exon 33); *JAK3* (NM\_000215.3) chr19:17,950,462-17,950,483 (partial exon 10); *LIFR* (NM\_002310.5) exon 19; *LMBRD1* (NM\_018368.3) chr6:70,459,226-70,459,257 (partial exon 5), chr6:70,447,828-70,447,836 (partial exon 7) and exon 12; *LYST* (NM\_000081.3) chr1:235,944,158-235,944,176 (partial exon 16) and chr1:235,875,350-235,875,362 (partial exon 43); *MLYCD* (NM\_012213.2) chr16:83,933,242-83,933,282 (partial exon 1); *MTR* (NM\_000254.2) chr1:237,024,418-237,024,439 (partial exon 20) and chr1:237,038,019-237,038,029 (partial exon 24); *NBEAL2* (NM\_015175.2) chr3:47,021,385-47,021,407 (partial exon 1); *NEB* (NM\_001271208.1) exons 82-105; *NPC1* (NM\_000271.4) chr18:21,123,519-21,123,538 (partial exon 14); *NPHP1* (NM\_000272.3) chr2:110,937,251-110,937,263 (partial exon 3); *OCRL* (NM\_000276.3) chrX:128,674,450-128,674,460 (partial exon 1); *PHKB* (NM\_000293.2) exon 1 and chr16:47,732,498-47,732,504 (partial exon 30); *PIGN* (NM\_176787.4) chr18:59,815,547-59,815,576 (partial exon 8); *PIP5K1C* (NM\_012398.2) exon 1 and chr19:363,760-363,761 (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\_020734.6.2) exon 1; *TYR* (NM\_000372.4) exon 5; *VWF* (NM\_000552.3) exons 24-26, chr12:6,125,675-6,125,684 (partial exon 30), chr12:6,121,244-6,121,265 (partial exon 33), and exon 34.

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

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

#### Next Generation Sequencing for *SMN1*

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

#### Copy Number Variant 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. Deletions and duplications near the lower limit of detection may not be detected due to run variability.

**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%)**

The 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. Please note that in rare cases, allele drop-out may occur, which has the potential to lead to false negative results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where multiple copies of *CYP21A2* are located on the same chromosome in tandem, only the last copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in the tandem allele and this patient is therefore less likely to be a carrier. A *CYP21A1P/CYP21A2* hybrid gene detected only by MLPA but not by long-range PCR will not be reported when the long-range PCR indicates the presence of two full *CYP21A2* gene copies (one on each chromosome), as the additional hybrid gene is nonfunctional. Classic 30-kb deletions are identified by MLPA and are also identified by the presence of multiple common pathogenic *CYP21A2* variants by long-range PCR. Since multiple pseudogene-derived variants are detected in all cases with the classic 30kb deletion, we cannot rule out the possibility that some variant(s) detected could be present in trans with the chimeric *CYP21A1P/CYP21A2* gene created by the 30kb deletion. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to determine the phase (cis/trans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing is required to determine the carrier status.

**Residual Risk Calculations**

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

**Personalized Residual Risk Calculations**

Agilent SureSelect<sup>TM</sup>XT Low-Input technology was utilized in order to create whole-genome libraries for each patient sample. Libraries were then pooled and sequenced on the Illumina NovaSeq platform. Each sequencing lane was multiplexed to achieve 0.4-2x genome coverage, using paired-end 100 bp reads. The sequencing data underwent ancestral analysis using a customized, licensed bioinformatics algorithm that was validated in house. Identified sub-ethnic groupings were binned into one of 7 continental-level groups (African, East Asian, South Asian, Non-Finnish European, Finnish, Native American, and Ashkenazi Jewish) or, for those ethnicities that matched poorly to the continental-level groups, an 8<sup>th</sup> "unassigned" group, which were then used to select residual risk values for each gene. For individuals belonging to multiple high-level ethnic groupings, a weighting strategy was used to select the most appropriate residual risk. For genes that had insufficient data to calculate ethnic-specific residual risk values, or for sub-ethnic groupings that fell into the "unassigned" group, a "worldwide" residual risk was used. This "worldwide" residual risk was calculated using data from all available continental-level groups.

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

**Sanger Sequencing (Confirmation method) (Accuracy >99%)**

Sanger sequencing, as indicated, was performed using BigDye Terminator chemistry with the ABI 3730 DNA analyzer with target specific amplicons. It also may be used to supplement specific guaranteed target regions that fail NGS sequencing due to poor quality or low depth of coverage (<20 reads) or as a confirmatory method for NGS positive results. False negative results may occur if rare variants interfere with amplification or annealing.

#### Tay-Sachs Disease (TSD) Enzyme Analysis (Analytical Detection Rate $\geq 98\%$ )

Hexosaminidase activity and Hex A% activity were measured by a standard heat-inactivation, fluorometric method using artificial 4-MU- $\beta$ -N-acetyl glucosaminide (4-MUG) substrate. This assay is highly sensitive and accurate in detecting Tay-Sachs carriers and individuals affected with TSD. Normal ranges of Hex A% activity are 55.0-72.0 for white blood cells and 58.0-72.0 for plasma. It is estimated that less than 0.5% of Tay-Sachs carriers have non-carrier levels of percent Hex A activity, and therefore may not be identified by this assay. In addition, this assay may detect individuals that are carriers of or are affected with Sandhoff disease. False positive results may occur if benign variants, such as pseudodeficiency alleles, interfere with the enzymatic assay. False negative results may occur if both *HEXA* and *HEXB* pathogenic or pseudodeficiency variants are present in the same individual.

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

This test was developed, and its performance characteristics determined by Sema4 Opco, Inc. It has not been cleared or approved by the US Food and Drug Administration. FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. These analyses generally provide highly accurate information regarding the patient's carrier or affected status. Despite this high level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, or other rare genetic variants that interfere with analysis. Families should understand that rare diagnostic errors may occur for these reasons.

## 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.

Akler G et al. Towards a unified approach for comprehensive reproductive carrier screening in the Ashkenazi, Sephardi, and Mizrahi Jewish populations. *Mol Genet Genomic Med*. 2020 Feb 8(2):e1053.

### 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

Name: 7027 Donor

Date of Birth: [REDACTED]

Sema4 ID: [REDACTED]

Client ID: [REDACTED]

Indication: Chromosomal Microarray

Testing

## Specimen Information

Specimen Type: Blood

Date Collected: 10/13/2022

Date Received: 10/14/2022

Final Report: 11/30/2022

## Referring Provider

[REDACTED]

Fairfax Cryobank, Inc.

[REDACTED]

[REDACTED]

[REDACTED]

## Ultra-High Resolution Medical Exome Array Analysis

## Results

Gender: Male

A heterozygous likely pathogenic 94.8 kb deletion was detected on chromosome 5q15

(No additional disease genes were detected within the deletion)

Gene	Exon (s)	CNV type	Size	ISCN nomenclature	Zygosity	Classification	Disease (inheritance)
See interpretation	See interpretation	Deletion	94.8 kb	arr[GRCh37] 5q15(94785719_94880544)x1	Heterozygous	Likely pathogenic	Trichohepatoenteric syndrome 1 (AR)

## Interpretation

The OGT Medical Exome oligonucleotide array comparative genomic hybridization (aCGH) assay was used to investigate copy number variation (CNV) at the *TTC37* gene locus.

A heterozygous likely pathogenic 94.8 kb deletion was detected by aCGH. There are two genes included within the deleted region (exons 5-43 of *TTC37* and exon 10 of *FAM81B*), and of these, *TTC37* is a known Mendelian disease gene. Mutations in *TTC37* are an autosomal recessive (AR) cause trichohepatoenteric syndrome 1. Consequently, this aberration is considered likely pathogenic and may result in disease phenotype when present *in trans* with a pathogenic variant of *TTC37*.

Please note that this individual is at least a heterozygous carrier for the AR disease mentioned above. This finding confirmed the Expanded Carrier Screening results previously reported for this individual (see laboratory report 22207614).

Genetic counseling is recommended to discuss the implications of this finding.

## References:

- Hartley JL, Zachos NC, Dawood B, et al. Mutations in *TTC37* cause trichohepatoenteric syndrome (phenotypic diarrhea of infancy). *Gastroenterology*. 2010;138(7):2388-2398.e23982.

## Test Methodology

The Medical Exome 1M 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 one million 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 selected to target the exonic regions of 4,645 genes. For the majority of genes there are a minimum of 4 probes per exon. For very large exons, probes are distributed evenly along the exon with 1 probe every 125 bp. In the untargeted backbone regions, this array has one probe every 42kb. All genomic

coordinates are reported using human genome NCBI Build 37 (hg19). Copy number aberrations are identified using the Aberration Detection Method-2 (ADM2) algorithm with a sensitivity threshold of 6.0 (Agilent Technologies). The  $\log_2$  ratio threshold values to detect aberrations are  $\leq -0.25$  for copy number losses and  $\geq 0.25$  for copy number gains. Please note that any inconsistencies in the reported biological familial relationships could significantly change the interpretation of these results. For reported CNVs with uncertain clinical significance, continued surveillance of the medical literature for new information is recommended.

The sensitivity of this assay is estimated to be greater than 99% for microdeletions and microduplications in the exonic regions of 4,645 medically-relevant genes. Variant interpretation and classification is performed based on the American College of Medical Genetics standards and guidelines for the interpretation of sequence variants (Richards et al, 2015). Frequency in control populations is evaluated based on the Exome Aggregation Consortium (ExAC; <http://exac.broadinstitute.org/>), the Database of Genomic Variants (<http://dgv.tcag.ca/dgv/app/home>), and 1000 genomes (<http://www.1000genomes.org/>) databases. Any benign polymorphisms identified during this analysis will not be reported. Variant interpretations, based on current knowledge, may change over time as more information arises.

#### Reporting Criteria for Medical Exome aCGH Analysis

The following aberrations will **NOT** be reported and parental studies will **NOT** be performed:

- CNVs that are considered benign based on coverage in the Database of Genomic Variants (DGV; <http://dgv.tcag.ca/>) and/or our internal laboratory CNV database
- Gains or losses of <500 kb that do not include any known genes (<http://www.ncbi.nlm.nih.gov/refseq/>)
- Gains or losses with no known clinical significance (based on gene content and/or coverage in the DGV)
- Copy number gains of *KAL1*, *NPHP1*, *NIPA1*, *STS* or *SHOX* (full gene)
- Copy number gains and losses associated with genetic susceptibility, quantitative trait loci, pharmacogenetic alleles, and cancer predisposition
- Copy number gains and losses that are < 1.0 Mb in size and that appear to be mosaic by aCGH due to atypical  $\log_2$  ratios, unless the affected region is determined to be clinically significant based on gene content and/or coverage in the DGV

#### Test limitations

This array cannot detect balanced rearrangements, such as reciprocal translocations, Robertsonian translocations, inversions and balanced insertions, or imbalances that are below the resolution of this array. This technology will also not detect point mutations or small insertion/deletions below this array's resolution that cause frameshifts, imprinting defects or other epigenetic mutations, and may not detect low level mosaicism. The failure to detect an alteration at any locus does not exclude the diagnosis of any of the disorders represented on the microarray.

#### Disclaimer

This test was developed and its performance characteristics were determined by Sema4 Opco, Inc and were considered acceptable for patient testing. It has not been cleared or approved by the FDA. The FDA has determined that such clearance or approval is not necessary. This type of mutation analysis generally provides highly accurate genotype information for point mutations and single nucleotide polymorphisms. Despite this level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, rare polymorphisms, or other rare genetic variants that interfere with analysis. In addition, families should understand the limitations of the testing and that rare diagnostic errors may occur for the reasons described.

#### References

1. Kearney HM, et al. American College of Medical Genetics standards and guidelines for interpretation and reporting of postnatal constitutional copy number variants. *Genet Med*. 2011;13:680-5.
2. South ST, et al. ACMG Standards and Guidelines for constitutional cytogenomic microarray analysis, including postnatal and prenatal applications: revision 2013. *Genet Med*. 2013;15:901-9.



Oscar Cano, M.D., Laboratory Director

Laboratory Medical Consultant: Bryn Webb, M.D.





Patient Information	Specimen Information	Client Information
<b>DONOR, 7027</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] Gender: M Phone: NG Patient ID: [REDACTED]	Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED]  Collected: 10/13/2022 Received: 10/15/2022 / 20:55 EDT Reported: 10/26/2022 / 01:24 EDT	Client #: 48041578     NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229

Ward:	FFAXCB
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## Cytogenetic Report

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

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

**RESULT:**  
NORMAL MALE KARYOTYPE

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

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

**NOMENCLATURE:**  
46,XY

**ASSAY INFORMATION:**

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

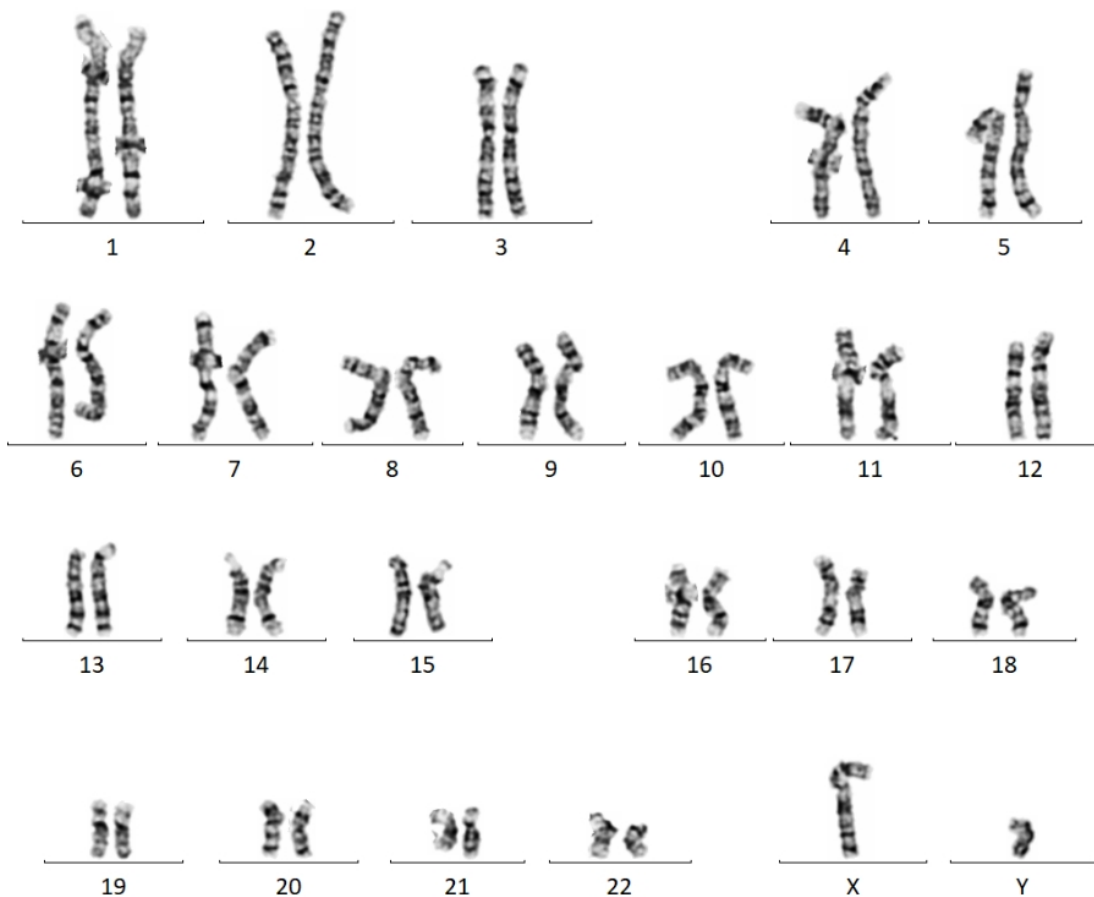
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

Lakshmi J. Nemana, Ph.D., FACMG

Electronic Signature: 10/26/2022 12:20 AM



Patient Information	Specimen Information	Client Information
<b>DONOR, 7027</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] <b>Gender:</b> M <b>Patient ID:</b> [REDACTED]	<b>Specimen:</b> [REDACTED] <b>Collected:</b> 10/13/2022 <b>Received:</b> 10/15/2022 / 20:55 EDT <b>Reported:</b> 10/26/2022 / 01:24 EDT	<b>Client #:</b> 48041578 <b>GENOMICS, SEMA4</b>



**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
<b>DONOR, 7027</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] Gender: M Phone: NG Patient ID: [REDACTED]	Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED]  Collected: 10/13/2022 Received: 10/15/2022 / 20:56 EDT Reported: 10/18/2022 / 22:10 EDT	Client #: 48041578    NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229

Ward:	FFAXCB
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Test Name	In Range	Out Of Range	Reference Range	Lab
HEMOGLOBINOPATHY EVALUATION				
RED BLOOD CELL COUNT	5.40		4.20-5.80 Million/uL	Z99
HEMOGLOBIN	14.1		13.2-17.1 g/dL	
HEMATOCRIT	45.1		38.5-50.0 %	
MCV	83.5		80.0-100.0 fL	
<b>MCH</b>		<b>26.1 L</b>	27.0-33.0 pg	
RDW	13.4		11.0-15.0 %	
HEMOGLOBIN A	97.3		>96.0 %	Z99
HEMOGLOBIN F	<1.0		<2.0 %	
HEMOGLOBIN A2 (QUANT)	2.7		2.2-3.2 %	
INTERPRETATION	*			
The red blood cell indices are suggestive of microcytosis and or hypochromia. Complete interpretation requires clinical correlation, review of family history and exclusion of possible etiologies for microcytosis and hypochromia, such as iron deficiency and alpha thalassemia.				

**PERFORMING SITE:**

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