



## Donor 6531

### Genetic Testing Summary

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

Last Updated: 04/05/23

Donor Reported Ancestry: Indian

Jewish Ancestry: No

Genetic Test*	Result	Comments/Donor's Residual Risk**
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Expanded Genetic Disease Carrier Screening Panel attached- 502 diseases by gene sequencing.  Personalized residual risk by gene is in the attached report.	<b>Carrier: Cystic Fibrosis (CFTR)</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: Donor 6531  
 Date of Birth: [REDACTED]  
 Sema4 ID: [REDACTED]  
 Client ID: [REDACTED]  
 Indication: Carrier Screening

**Specimen Information**

Specimen Type: Blood  
 Date Collected: 10/21/2022  
 Date Received: 10/22/2022  
 Final Report: 11/08/2022

**Referring Provider**

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

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

### SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
<p><b>Carrier of Cystic Fibrosis (AR)</b>            Associated gene(s): <i>CFTR</i>            Variant(s) Detected: c.1367T&gt;C, p.V456A, 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.
- 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

**Cystic Fibrosis (AR)**

**Results and Interpretation**

A heterozygous (one copy) likely pathogenic missense variant, c.1367T>C, p.V456A, was detected in the *CFTR* gene (NM\_000492.3). Please note that this variant is associated with a milder form of the disease when found in trans with a severe variant. When this variant is present in trans with a pathogenic variant, it is considered to be causative for cystic fibrosis. Therefore, this individual is expected to be at least a carrier for cystic fibrosis. Heterozygous carriers are not expected to exhibit symptoms of this disease.

**What is Cystic Fibrosis?**

Cystic fibrosis is an autosomal recessive disorder caused by pathogenic variants in the gene *CFTR*. It may be diagnosed in individuals worldwide, but has the highest prevalence in the Caucasian population, in individuals with Northern European ancestry. The clinical presentation includes thick mucus accumulation in the lungs leading to breathing difficulties and infection, poor digestion, and male infertility.



The average life expectancy is in the 30s. Although some genotype-phenotype correlations exist, individuals with two classic pathogenic variants in *CFTR* are expected to present with a more severe disease phenotype. Non-classic variants in *CFTR* may lead to less severe forms of disease or specific phenotypes, such as male infertility as a result of congenital absence or hypoplasia of the vas deferens.

## 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.

**Wei Kelly, M.D., Ph.D., DABMGG, Assistant 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
<b>Positive</b>				
Cystic Fibrosis	<i>CFTR</i>	AR	Carrier	c.1367T>C, p.V456A, Likely Pathogenic, Heterozygous (one copy)
<b>Negative</b>				
2-Methylbutyrylglycinuria	<i>ACADSB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	<i>HSD3B2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,200
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related)	<i>MCCC1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)	<i>MCCC2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
3-Methylglutaconic Aciduria, Type III	<i>OPA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000
3-Phosphoglycerate Dehydrogenase Deficiency	<i>PHGDH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	<i>PTS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
CD59-Mediated Hemolytic Anemia	<i>CD59</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 513,000
Abetalipoproteinemia	<i>MTTP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Achalasia-Addisonianism-Alacrimia Syndrome	<i>AAAS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Achromatopsia (CNGA3-Related)	<i>CNGA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 490
Achromatopsia (CNGB3-related)	<i>CNGB3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Acrodermatitis Enteropathica	<i>SLC39A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 55,000
Acute Infantile Liver Failure	<i>TRMU</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Acyl-CoA Oxidase I Deficiency	<i>ACOX1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 192,000
Adams-Oliver Syndrome 4	<i>EOGT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Adenosine Deaminase Deficiency	<i>ADA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Adrenocorticotrophic Hormone Deficiency	<i>TBX19</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Adrenoleukodystrophy, X-Linked	<i>ABCD1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Agammaglobulinemia	<i>BTK</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 250,000
Agenesis of the Corpus Callosum	<i>FRMD4A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 348,000
Aicardi-Goutieres Syndrome (RNASEH2C-Related)	<i>RNASEH2C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,000
Aicardi-Goutieres Syndrome (SAMHD1-Related)	<i>SAMHD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Aicardi-Goutieres Syndrome (TREX1-Related)	<i>TREX1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Albinism, Oculocutaneous, Type III	<i>TYRP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Alkaptonuria	<i>HGD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,800
Alpha-Mannosidosis	<i>MAN2B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Alpha-Thalassemia	<i>HBA1/HBA2</i>	AR	Reduced Risk	HBA1 Copy Number: 2 HBA2 Copy Number: 2 No pathogenic copy number variants detected HBA1/HBA2 Sequencing: Negative Personalized Residual Risk: 1 in 380
Alpha-Thalassemia Intellectual Disability Syndrome	<i>ATRX</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 48,000
Alport Syndrome (COL4A3-Related)	<i>COL4A3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500

Alport Syndrome (COL4A4-Related)	COL4A4	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,700
Alport Syndrome (COL4A5-Related)	COL4A5	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 150,000
Alstrom Syndrome	ALMS1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,400
Andermann Syndrome	SLC12A6	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 256,000
Antley-Bixler Syndrome (POR-Related)	POR	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,300
Argininemia	ARG1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Argininosuccinic Aciduria	ASL	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,900
Aromatase Deficiency	CYP19A1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,200
Arthrogryposis, Intellectual Disability, and Seizures	SLC35A3	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 399,000
Asparagine Synthetase Deficiency	ASNS	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 307,000
Aspartylglycosaminuria	AGA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Ataxia With Isolated Vitamin E Deficiency	TTPA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 240,000
Ataxia-Telangiectasia	ATM	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 900
Ataxia-Telangiectasia-Like Disorder 1	MRE11	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	SACS	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Bardet-Biedl Syndrome (ARL6-Related)	ARL6	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
Bardet-Biedl Syndrome (BBS10-Related)	BBS10	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
Bardet-Biedl Syndrome (BBS12-Related)	BBS12	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,900
Bardet-Biedl Syndrome (BBS1-Related)	BBS1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,400
Bardet-Biedl Syndrome (BBS2-Related)	BBS2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Bardet-Biedl Syndrome (BBS4-Related)	BBS4	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Bare Lymphocyte Syndrome, Type II	CIITA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 35,000
Barth Syndrome	TAZ	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 183,000
Bartter Syndrome, Type 3	CLCNKB	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,700
Bartter Syndrome, Type 4A	BSND	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 73,000
Bernard-Soulier Syndrome, Type A1	GP1BA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 66,000
Bernard-Soulier Syndrome, Type C	GP9	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,300
Beta-Globin-Related Hemoglobinopathies	HBB	AR	Reduced Risk	<b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies):</b> 1 in 980 <b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant):</b> 1 in 81,000 <b>Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant):</b> 1 in 42,000
Beta-Ketothiolase Deficiency	ACAT1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,400
Beta-Mannosidosis	MANBA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,100
BH4-Deficient Hyperphenylalaninemia C	QDPR	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,500
BH4-Deficient Hyperphenylalaninemia D	PCBD1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Bilateral Frontoparietal Polymicrogyria	GPR56	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 64,000
Biotinidase Deficiency	BTD	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 370
Bloom Syndrome	BLM	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Canavan Disease	ASPA	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Carbamoylphosphate Synthetase I Deficiency	CPS1	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
Carnitine Acylcarnitine Translocase Deficiency	SLC25A20	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Carnitine Palmitoyltransferase IA Deficiency	CPT1A	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,500
Carnitine Palmitoyltransferase II Deficiency	CPT2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 670
Carpenter Syndrome	RAB23	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 28,000
Cartilage-Hair Hypoplasia	RMRP	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Catecholaminergic Polymorphic Ventricular Tachycardia	CASQ2	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000

Central Hypothyroidism and Testicular Enlargement	<i>IGSF1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 781,000
Cerebral Creatine Deficiency Syndrome 1	<i>SLC6A8</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 208,000
Cerebral Creatine Deficiency Syndrome 2	<i>GAMT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,800
Cerebral Creatine Deficiency Syndrome 3	<i>GATM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Cerebral Dysgenesis, Neuropathy, Ichthyosis, and Palmoplantar Keratoderma Syndrome	<i>SNAP29</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 154,000
Cerebrotendinous Xanthomatosis	<i>CYP27A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 960
Charcot-Marie-Tooth Disease, Type 4D	<i>NDRG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 479,000
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	<i>PRPS1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 114,000
Charcot-Marie-Tooth Disease, X-Linked	<i>GJB1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Chediak-Higashi Syndrome	<i>LYST</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Chondrodysplasia Punctata	<i>ARSE</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 862,000
Choreoacanthocytosis	<i>VPS13A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,900
Choroideremia	<i>CHM</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 125,000
Chronic Granulomatous Disease (CYBA-Related)	<i>CYBA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,800
Chronic Granulomatous Disease (CYBB-Related)	<i>CYBB</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 294,000
Citrin Deficiency	<i>SLC25A13</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,600
Citrullinemia, Type 1	<i>ASS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Cockayne Syndrome, Type A	<i>ERCC8</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,900
Cockayne Syndrome, Type B and other ERCC6-Related Disorders	<i>ERCC6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,500
Cohen Syndrome	<i>VPS13B</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 16,000
Combined Factor V and VIII Deficiency	<i>LMAN1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 168,000
Combined Malonic and Methylmalonic Aciduria	<i>ACSF3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 340
Combined Oxidative Phosphorylation Deficiency 1	<i>GFM1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Combined Oxidative Phosphorylation Deficiency 3	<i>TSMF</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 21,000
Combined Pituitary Hormone Deficiency 1	<i>POU1F1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,900
Combined Pituitary Hormone Deficiency 2	<i>PROP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,300
Combined Pituitary Hormone Deficiency 3	<i>LHX3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 197,000
Combined SAP Deficiency	<i>PSAP</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 78,000
Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1	<i>GUCY2D</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 920
Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency	<i>CYP11B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 510
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	<i>CYP17A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,000
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	<i>CYP21A2</i>	AR	Reduced Risk	<i>CYP21A2</i> copy number: 2 <i>CYP21A2</i> sequencing: Negative <b>Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)):</b> 1 in 300 <b>Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)):</b> 1 in 1,200
Congenital Adrenal Hypoplasia (NR0B1-Related)	<i>NR0B1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 353,000
Congenital Adrenal Insufficiency (CYP11A1-Related)	<i>CYP11A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,100
Congenital Amegakaryocytic Thrombocytopenia	<i>MPL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,100
Congenital Bile Acid Synthesis Defect (AKR1D1-Related)	<i>AKR1D1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Congenital Bile Acid Synthesis Defect (HSD3B7-Related)	<i>HSD3B7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Congenital Disorder of Deglycosylation	<i>NGLY1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Congenital Disorder of Glycosylation, Type Ia	<i>PMM2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,000

<b>Congenital Disorder of Glycosylation, Type Ib</b>	<i>MPI</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,500</b>
<b>Congenital Disorder of Glycosylation, Type Ic</b>	<i>ALG6</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,900</b>
<b>Congenital Disorder of Glycosylation, Type Im</b>	<i>DOLK</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 385,000</b>
<b>Congenital Dyserythropoietic Anemia Type 2</b>	<i>SEC23B</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,900</b>
<b>Congenital Dyserythropoietic Anemia, Type Ia</b>	<i>CDAN1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 900</b>
<b>Congenital Ichthyosis 4A and 4B</b>	<i>ABCA12</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,900</b>
<b>Congenital Insensitivity to Pain with Anhidrosis</b>	<i>NTRK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 15,000</b>
<b>Congenital Muscular Dystrophy (LAMA2-Related)</b>	<i>LAMA2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
<b>Congenital Myasthenic Syndrome (CHAT-Related)</b>	<i>CHAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,900</b>
<b>Congenital Myasthenic Syndrome (CHRNE-Related)</b>	<i>CHRNE</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,700</b>
<b>Congenital Myasthenic Syndrome (DOK7-Related)</b>	<i>DOK7</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,400</b>
<b>Congenital Myasthenic Syndrome (RAPSN-Related)</b>	<i>RAPSN</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 12,000</b>
<b>Congenital Neutropenia (HAX1-Related)</b>	<i>HAX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 82,000</b>
<b>Congenital Neutropenia (VPS45-Related)</b>	<i>VPS45</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 170,000</b>
<b>Congenital Nongoitrous Hypothyroidism 1</b>	<i>TSHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,000</b>
<b>Congenital Nongoitrous Hypothyroidism 4</b>	<i>TSHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 227,000</b>
<b>Congenital Secretory Chloride Diarrhea 1</b>	<i>SLC26A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,400</b>
<b>Corneal Dystrophy and Perceptive Deafness</b>	<i>SLC4A11</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,500</b>
<b>Corticosterone Methyloxidase Deficiency</b>	<i>CYP11B2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,200</b>
<b>Cystinosis</b>	<i>CTNS</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,900</b>
<b>Cystinuria (SLC3A1-Related)</b>	<i>SLC3A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,100</b>
<b>Cytochrome C Oxidase Deficiency / Leigh Syndrome (COX15-Related)</b>	<i>COX15</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,300</b>
<b>D-Bifunctional Protein Deficiency</b>	<i>HSD17B4</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 8,200</b>
<b>Deafness, Autosomal Recessive 3</b>	<i>MYO15A</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 240</b>
<b>Deafness, Autosomal Recessive 59</b>	<i>PJVK</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,700</b>
<b>Deafness, Autosomal Recessive 7</b>	<i>TMC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,700</b>
<b>Deafness, Autosomal Recessive 76</b>	<i>SYNE4</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 76,000</b>
<b>Deafness, Autosomal Recessive 77</b>	<i>LOXHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 35,000</b>
<b>Deafness, Autosomal Recessive 8/10</b>	<i>TMPRSS3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 360</b>
<b>Deafness, Autosomal Recessive 9</b>	<i>OTOF</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
<b>Desbuquois Dysplasia 1</b>	<i>CANT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 24,000</b>
<b>Desmosterolosis</b>	<i>DHCR24</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 28,000</b>
<b>Diaphanospondylodysostosis</b>	<i>BMPER</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 18,000</b>
<b>Distal Renal Tubular Acidosis and other SLC4A1-related Disorders</b>	<i>SLC4A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,700</b>
<b>Duchenne Muscular Dystrophy / Becker Muscular Dystrophy</b>	<i>DMD</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 10,000</b>
<b>Dyskeratosis Congenita (DKC1-related)</b>	<i>DKC1</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 9,259,000</b>
<b>Dyskeratosis Congenita (RTEL1-Related)</b>	<i>RTEL1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 9,800</b>
<b>Dystrophic Epidermolysis Bullosa</b>	<i>COL7A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 980</b>
<b>Ehlers-Danlos Syndrome, Type VI</b>	<i>PLOD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 20,000</b>
<b>Ehlers-Danlos Syndrome, Type VIIC</b>	<i>ADAMTS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 380,000</b>
<b>Ellis-Van Creveld Syndrome (EVC2-Related)</b>	<i>EVC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,700</b>
<b>Ellis-van Creveld Syndrome (EVC-Related)</b>	<i>EVC</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 9,500</b>
<b>Emery-Dreifuss Myopathy 1</b>	<i>EMD</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 833,000</b>
<b>Enhanced S-Cone Syndrome</b>	<i>NR2E3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,100</b>
<b>Ethylmalonic Encephalopathy</b>	<i>ETHE1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,400</b>
<b>Fabry Disease</b>	<i>GLA</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,700</b>

Factor IX Deficiency	<i>F9</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,100
Factor VII Deficiency	<i>F7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 290
Factor XI Deficiency	<i>F11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Familial Autosomal Recessive Hypercholesterolemia	<i>LDLRAP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 192,000
Familial Dysautonomia	<i>IKBKAP</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 85,000
Familial Hypercholesterolemia	<i>LDLR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 270
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	<i>HADH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,000
Familial Hyperinsulinism (ABCC8-Related)	<i>ABCC8</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Familial Hyperinsulinism (KCNJ11-Related)	<i>KCNJ11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Familial Hyperphosphatemic Tumoral Calcinosis	<i>GALNT3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
Familial Mediterranean Fever	<i>MEFV</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,000
Fanconi Anemia, Group A	<i>FANCA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Fanconi Anemia, Group C	<i>FANCC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Fanconi Anemia, Group G	<i>FANCG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 128,000
Fanconi-Bickel Syndrome	<i>SLC2A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Fragile X Syndrome	<i>FMR1</i>	XL	Reduced Risk	FMR1 CGG repeat sizes: Not Performed FMR1 Sequencing: Negative Fragile X CGG triplet repeat expansion testing was not performed at this time, as the patient has either been previously tested or is a male. <b>Personalized Residual Risk:</b> 1 in 17,000
Fructose-1,6-Bisphosphatase Deficiency	<i>FBP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Fucosidosis	<i>FUCA1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 48,000
Fumarase Deficiency	<i>FH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,900
Fundus Albipunctatus	<i>RDH5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Galactokinase Deficiency	<i>GALK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Galactose Epimerase Deficiency	<i>GALE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,500
Galactosemia	<i>GALT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,500
Galactosialidosis	<i>CTSA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Gaucher Disease	<i>GBA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Generalized Thyrotropin-Releasing Hormone Resistance	<i>TRHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 192,000
Geroderma Osteodysplasticum	<i>GORAB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 308,000
Gitelman Syndrome	<i>SLC12A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 460
Glanzmann Thrombasthenia (ITGA2B-Related)	<i>ITGA2B</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Glanzmann Thrombasthenia (ITGB3-Related)	<i>ITGB3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,900
Glutaric Acidemia, Type I	<i>GCDH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,400
Glutaric Acidemia, Type IIa	<i>ETFA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,700
Glutaric Acidemia, Type IIb	<i>ETFB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,200
Glutaric Acidemia, Type IIc	<i>ETFDH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
Glutathione Synthetase Deficiency	<i>GSS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,500
Glycine Encephalopathy (AMT-Related)	<i>AMT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,700
Glycine Encephalopathy (GLDC-Related)	<i>GLDC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Glycogen Storage Disease, Type 0	<i>GYS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,100
Glycogen Storage Disease, Type Ia	<i>G6PC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Glycogen Storage Disease, Type Ib	<i>SLC37A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Glycogen Storage Disease, Type II	<i>GAA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
Glycogen Storage Disease, Type III	<i>AGL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	<i>GBE1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,600
Glycogen Storage Disease, Type IXb	<i>PHKB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,400



Glycogen Storage Disease, Type V	<i>PYGM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,600
Glycogen Storage Disease, Type VI	<i>PYGL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 820
Glycogen Storage Disease, Type VII	<i>PFKM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
GRACILE Syndrome and Other <i>BCS1L</i> -Related Disorders	<i>BCS1L</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,800
Gray Platelet Syndrome	<i>NBEAL2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,800
Growth Hormone Deficiency, Type IB	<i>GHRHR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,800
Hemochromatosis, Type 2A	<i>HFE2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,800
Hemochromatosis, Type 3	<i>TFR2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Hereditary Fructose Intolerance	<i>ALDOB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,700
Hereditary Spastic Paraparesis 49	<i>TECPR2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 112,000
Hermansky-Pudlak Syndrome, Type 1	<i>HPS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,500
Hermansky-Pudlak Syndrome, Type 3	<i>HPS3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Hermansky-Pudlak Syndrome, Type 4	<i>HPS4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 35,000
Hermansky-Pudlak Syndrome, Type 6	<i>HPS6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,400
HMG-CoA Lyase Deficiency	<i>HMGCL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Hmg-CoA Synthase 2 Deficiency	<i>HMGCS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,500
Holocarboxylase Synthetase Deficiency	<i>HLCS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,500
Homocystinuria (CBS-Related)	<i>CBS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Homocystinuria due to <i>MTHFR</i> Deficiency	<i>MTHFR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,700
Homocystinuria, cblE Type	<i>MTRR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,600
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	<i>MTR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,700
Hydrocephalus	<i>L1CAM</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
Hydroletharus Syndrome	<i>HYLS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 220,000
Hyper-Igm Syndrome	<i>CD40LG</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,167,000
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	<i>SLC25A15</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,500
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	<i>SARS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 23,000
Hypohidrotic Ectodermal Dysplasia 1	<i>EDA</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 22,000
Hypomagnesemia 1	<i>TRPM6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Hypomyelinating Leukodystrophy 3	<i>AIMP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 308,000
Hypomyelinating Leukodystrophy 12	<i>VPS11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 94,000
Hypoparathyroidism-Retardation-Dysmorphic Syndrome	<i>TBCE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Hypophosphatasia	<i>ALPL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,500
Hypophosphatemic Rickets with Hypercalciuria	<i>SLC34A3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,300
Hypotrichosis 8 / Autosomal Recessive Woolly Hair 1	<i>LPAR6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,500
Immunodeficiency 18	<i>CD3E</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 120,000
Immunodeficiency 19	<i>CD3D</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 49,000
Inclusion Body Myopathy 2	<i>GNE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,600
Infantile Cerebral and Cerebellar Atrophy	<i>MED17</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 308,000
Infantile Neuroaxonal Dystrophy 1 and other <i>PLA2G6</i> -Related Disorders	<i>PLA2G6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
Intellectual Disability, Autosomal Recessive 3	<i>CC2D1A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 150,000
Intrahepatic Cholestasis	<i>ATP8B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
Isovaleric Acidemia	<i>IVD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,000
Joubert Syndrome 2	<i>TMEM216</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 353,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	<i>NPHP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,800
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	<i>RPGRIPL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,800



Junctional Epidermolysis Bullosa (COL17A1-Related)	COL17A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Junctional Epidermolysis Bullosa (ITGA6-Related)	ITGA6	AR	Reduced Risk	Personalized Residual Risk: 1 in 165,000
Junctional Epidermolysis Bullosa (ITGB4-Related)	ITGB4	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Junctional Epidermolysis Bullosa (LAMA3-Related)	LAMA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 81,000
Junctional Epidermolysis Bullosa (LAMB3-Related)	LAMB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Junctional Epidermolysis Bullosa (LAMC2-Related)	LAMC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 171,000
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 390
Lamellar Ichthyosis, Type 1	TGM1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,600
Laron Dwarfism	GHR	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	CEP290	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Leber Congenital Amaurosis 13	RDH12	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	TULP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	RPE65	AR	Reduced Risk	Personalized Residual Risk: 1 in 490
Leber Congenital Amaurosis 4	AIP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Leber Congenital Amaurosis 5	LCA5	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	CRB1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
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 3,000
Leigh Syndrome, French-Canadian Type	LRPPRC	AR	Reduced Risk	Personalized Residual Risk: 1 in 76,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogyposis with Anterior Horn Cell Disease	GLE1	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Lethal Congenital Contracture Syndrome 2	ERBB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 118,000
Lethal Congenital Contracture Syndrome 3	PIP5K1C	AR	Reduced Risk	Personalized Residual Risk: 1 in 151,000
Leukoencephalopathy with Vanishing White Matter	EIF2B5	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,600
Limb-Girdle Muscular Dystrophy, Type 2A	CAPN3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Limb-Girdle Muscular Dystrophy, Type 2B	DYSF	AR	Reduced Risk	Personalized Residual Risk: 1 in 930
Limb-Girdle Muscular Dystrophy, Type 2C	SGCG	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,900
Limb-Girdle Muscular Dystrophy, Type 2D	SGCA	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Limb-Girdle Muscular Dystrophy, Type 2E	SGCB	AR	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Limb-Girdle Muscular Dystrophy, Type 2F	SGCD	AR	Reduced Risk	Personalized Residual Risk: 1 in 36,000
Limb-Girdle Muscular Dystrophy, Type 2H	TRIM32	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Limb-Girdle Muscular Dystrophy, Type 2I	FKRP	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Limb-Girdle Muscular Dystrophy, Type 2L	ANO5	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Lipoamide Dehydrogenase Deficiency	DLD	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Lipoid Adrenal Hyperplasia	STAR	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
Lipoprotein Lipase Deficiency	LPL	AR	Reduced Risk	Personalized Residual Risk: 1 in 900
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	HADHA	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Lowe Syndrome	OCRL	XL	Reduced Risk	Personalized Residual Risk: 1 in 1,375,000
Lysinuric Protein Intolerance	SLC7A7	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Malonyl-CoA Decarboxylase Deficiency	MLYCD	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
Maple Syrup Urine Disease, Type 1a	BCKDHA	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,100
Maple Syrup Urine Disease, Type 1b	BCKDHB	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100

Maple Syrup Urine Disease, Type 2	<i>DBT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,500
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	<i>MKS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,400
Medium Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADM</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 550
MEDNIK Syndrome	<i>AP1S1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 294,000
Megalencephalic Leukoencephalopathy with Subcortical Cysts	<i>MLC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,300
Megaloblastic Anemia 1	<i>AMN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 29,000
Menkes Disease	<i>ATP7A</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 172,000
Metachromatic Leukodystrophy	<i>ARSA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
Methionine Adenosyltransferase I/III Deficiency	<i>MAT1A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
Methylmalonic Acidemia (MMAA-Related)	<i>MMAA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Methylmalonic Acidemia (MMAB-Related)	<i>MMAB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Methylmalonic Acidemia (MUT-Related)	<i>MUT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	<i>MMACHC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	<i>MMADHC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 128,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	<i>LMBRD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
Methylmalonyl-CoA Epimerase Deficiency	<i>MCEE</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 168,000
Microphthalmia / Anophthalmia	<i>VSX2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
Mitochondrial Complex I Deficiency (ACAD9-Related)	<i>ACAD9</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,500
Mitochondrial Complex I Deficiency (NDUFA11-Related)	<i>NDUFA11</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 244,000
Mitochondrial Complex I Deficiency (NDUFAF5-Related)	<i>NDUFAF5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 118,000
Mitochondrial Complex I Deficiency (NDUFS6-Related)	<i>NDUFS6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 216,000
Mitochondrial Complex I Deficiency (NDUFV1-Related)	<i>NDUFV1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 600
Mitochondrial Complex I Deficiency / Leigh Syndrome (FOXRED1-Related)	<i>FOXRED1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,700
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFAF2-Related)	<i>NDUFAF2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 161,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFS4-Related)	<i>NDUFS4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Mitochondrial Complex IV Deficiency (COX20-related)	<i>COX20</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 78,000
Mitochondrial Complex IV Deficiency (COX6B1-related)	<i>COX6B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,231,000
Mitochondrial Complex IV Deficiency (APOPT1-Related)	<i>APOPT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,200
Mitochondrial Complex IV Deficiency (PET100-Related)	<i>PET100</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 284,000
Mitochondrial Complex IV Deficiency (SCO1-related)	<i>SCO1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Mitochondrial Complex IV Deficiency / Leigh Syndrome (COX10-Related)	<i>COX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
Mitochondrial DNA Depletion Syndrome 2	<i>TK2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,900
Mitochondrial DNA Depletion Syndrome 3	<i>DGUOK</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,200
Mitochondrial DNA Depletion Syndrome 4A and 4B and other POLG-Related Disorders	<i>POLG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 290
Mitochondrial DNA Depletion Syndrome 5	<i>SUCLA2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 256,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	<i>MPV17</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Mitochondrial Myopathy and Sideroblastic Anemia 1	<i>PUS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 513,000
Mitochondrial Trifunctional Protein Deficiency (HADHB-Related)	<i>HADHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000

Molybdenum Cofactor Deficiency A	<i>MOCS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,200
Mucopolipidosis II / IIIA	<i>GNPTAB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
Mucopolipidosis III Gamma	<i>GNPTG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,400
Mucopolipidosis IV	<i>MCOLN1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Mucopolysaccharidosis Type I	<i>IDUA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,300
Mucopolysaccharidosis Type II	<i>IDS</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 76,000
Mucopolysaccharidosis Type IIIA	<i>SGSH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Mucopolysaccharidosis Type IIIB	<i>NAGLU</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Mucopolysaccharidosis Type IIIC	<i>HGSNAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,200
Mucopolysaccharidosis Type IIID	<i>GNS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 201,000
Mucopolysaccharidosis Type IVa	<i>GALNS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 530
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	<i>GLB1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Mucopolysaccharidosis type IX	<i>HYAL1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 128,000
Mucopolysaccharidosis type VI	<i>ARSB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Mucopolysaccharidosis VII	<i>GUSB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,300
Mulibrey Nanism	<i>TRIM37</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 31,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	<i>PIGN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Multiple Pterygium Syndrome	<i>CHRNA3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Multiple Sulfatase Deficiency	<i>SUMF1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Muscle-Eye-Brain Disease and Other <i>POMGNT1</i> -Related Congenital Muscular Dystrophy-Dystroglycanopathies	<i>POMGNT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,300
Myoneurogastrointestinal Encephalopathy	<i>TYMP</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Myotubular Myopathy 1	<i>MTM1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 192,000
N-Acetylglutamate Synthase Deficiency	<i>NAGS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,300
Nemaline Myopathy 2	<i>NEB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,200
Nephrogenic Diabetes insipidus ( <i>AVPR2</i> -related) / Nephrogenic Syndrome of Inappropriate Antidiuresis	<i>AVPR2</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 471,000
Nephrogenic Diabetes Insipidus, Type II	<i>AQP2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,600
Nephronophthisis 2	<i>INVS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 51,000
Nephrotic Syndrome ( <i>NPHS1</i> -Related) / Congenital Finnish Nephrosis	<i>NPHS1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 620
Nephrotic Syndrome ( <i>NPHS2</i> -Related) / Steroid-Resistant Nephrotic Syndrome	<i>NPHS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,000
Neurodegeneration due to Cerebral Folate Transport Deficiency	<i>FOLR1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	<i>PLAA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 217,000
Neuronal Ceroid-Lipofuscinosis ( <i>CLN3</i> -Related)	<i>CLN3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,200
Neuronal Ceroid-Lipofuscinosis ( <i>CLN5</i> -Related)	<i>CLN5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Neuronal Ceroid-Lipofuscinosis ( <i>CLN6</i> -Related)	<i>CLN6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 13,000
Neuronal Ceroid-Lipofuscinosis ( <i>CLN8</i> -Related)	<i>CLN8</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,500
Neuronal Ceroid-Lipofuscinosis ( <i>MFSD8</i> -Related)	<i>MFSD8</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,700
Neuronal Ceroid-Lipofuscinosis ( <i>PPT1</i> -Related)	<i>PPT1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Neuronal Ceroid-Lipofuscinosis ( <i>TPP1</i> -Related)	<i>TPP1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,300
Niemann-Pick Disease ( <i>SMPD1</i> -Related)	<i>SMPD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Niemann-Pick Disease, Type C ( <i>NPC1</i> -Related)	<i>NPC1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,000
Niemann-Pick Disease, Type C ( <i>NPC2</i> -Related)	<i>NPC2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Nijmegen Breakage Syndrome	<i>NBN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Non-Syndromic Hearing Loss ( <i>GJB2</i> -Related)	<i>GJB2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 970
Oculocutaneous Albinism, Type IA / IB	<i>TYR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 580

Oculocutaneous Albinism, Type IV	<i>SLC45A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 830</b>
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	<i>WNT10A</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,400</b>
Omenn Syndrome ( <i>RAG2</i> -Related)	<i>RAG2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 96,000</b>
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	<i>DCLRE1C</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,900</b>
Omenn Syndrome and other <i>RAG1</i> -Related Disorders	<i>RAG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,300</b>
Ornithine Aminotransferase Deficiency	<i>OAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,700</b>
Ornithine Transcarbamylase Deficiency	<i>OTC</i>	XL	Reduced Risk	<b>Personalized Residual Risk: 1 in 103,000</b>
Osteogenesis Imperfecta, Type XI	<i>FKBP10</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 9,500</b>
Osteopetrosis 1	<i>TCIRG1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,500</b>
Osteopetrosis 8	<i>SNX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 34,000</b>
Otospondylomegaepiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	<i>COL11A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,700</b>
Papillon-Lefevre Syndrome	<i>CTSC</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,200</b>
Pendred Syndrome	<i>SLC26A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 430</b>
Peroxisome Biogenesis Disorder 3A and 3B	<i>PEX12</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 14,000</b>
Peroxisome Biogenesis Disorder 7A and 7B	<i>PEX26</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 160,000</b>
Phenylalanine Hydroxylase Deficiency	<i>PAH</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 640</b>
Polycystic Kidney Disease, Autosomal Recessive	<i>PKHD1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,300</b>
Polyglandular Autoimmune Syndrome, Type 1	<i>AIRE</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,000</b>
Pontocerebellar Hypoplasia, Type 1A	<i>VRK1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 47,000</b>
Pontocerebellar Hypoplasia, Type 1B	<i>EXOSC3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 12,000</b>
Pontocerebellar Hypoplasia, Type 2A and Type 4	<i>TSEN54</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 4,700</b>
Pontocerebellar Hypoplasia, Type 2E	<i>VPS53</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 256,000</b>
Pontocerebellar Hypoplasia, Type 6	<i>RARS2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 8,600</b>
Primary Carnitine Deficiency	<i>SLC22A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,300</b>
Primary Ciliary Dyskinesia ( <i>CCDC103</i> -Related)	<i>CCDC103</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 16,000</b>
Primary Ciliary Dyskinesia ( <i>CCDC151</i> -Related)	<i>CCDC151</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 255,000</b>
Primary Ciliary Dyskinesia ( <i>CCDC39</i> -Related)	<i>CCDC39</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 12,000</b>
Primary Ciliary Dyskinesia ( <i>DNAH5</i> -Related)	<i>DNAH5</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 3,500</b>
Primary Ciliary Dyskinesia ( <i>DNAI1</i> -Related)	<i>DNAI1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,000</b>
Primary Ciliary Dyskinesia ( <i>DNAI2</i> -Related)	<i>DNAI2</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 67,000</b>
Primary Ciliary Dyskinesia ( <i>RSPH9</i> -Related)	<i>RSPH9</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 171,000</b>
Primary Coenzyme Q10 Deficiency 7	<i>COQ4</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,600</b>
Primary Congenital Glaucoma 3A	<i>CYP11B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 650</b>
Primary Hyperoxaluria, Type 1	<i>AGXT</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,900</b>
Primary Hyperoxaluria, Type 2	<i>GRHPR</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 11,000</b>
Primary Hyperoxaluria, Type 3	<i>HOGA1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,000</b>
Progressive Cerebello-Cerebral Atrophy	<i>SEPSECS</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 15,000</b>
Progressive Familial Intrahepatic Cholestasis, Type 2	<i>ABCB11</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,500</b>
Progressive Myoclonic Epilepsy, Type 1B	<i>PRICKLE1</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 136,000</b>
Progressive Pseudorheumatoid Dysplasia	<i>WISP3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 5,600</b>
Prolidase Deficiency	<i>PEPD</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 7,000</b>
Propionic Acidemia ( <i>PCCA</i> -Related)	<i>PCCA</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 2,300</b>
Propionic Acidemia ( <i>PCCB</i> -Related)	<i>PCCB</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,400</b>
Pulmonary Surfactant Dysfunction	<i>ABCA3</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 1,700</b>
Pycnodysostosis	<i>CTSK</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 450</b>
Pyridoxamine 5'-Phosphate Oxidase Deficiency	<i>PNPO</i>	AR	Reduced Risk	<b>Personalized Residual Risk: 1 in 6,600</b>

Pyridoxine-Dependent Epilepsy	<i>ALDH7A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
Pyruvate Carboxylase Deficiency	<i>PC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Pyruvate Dehydrogenase E1-Alpha Deficiency	<i>PDHA1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 139,000
Pyruvate Dehydrogenase E1-Beta Deficiency	<i>PDHB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Renal Tubular Acidosis and Deafness	<i>ATP6V1B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,600
Retinitis Pigmentosa 25	<i>EYS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 600
Retinitis Pigmentosa 26	<i>CERKL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
Retinitis Pigmentosa 28	<i>FAM161A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 79,000
Retinitis Pigmentosa 36	<i>PRCD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 422,000
Retinitis Pigmentosa 59	<i>DHDDS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 201,000
Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16	<i>C8ORF37</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 256,000
Rh Deficiency Syndrome	<i>RHAG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 94,000
Rhizomelic Chondrodysplasia Punctata, Type 1	<i>PEX7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
Rhizomelic Chondrodysplasia Punctata, Type 3	<i>AGPS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,024,000
Roberts Syndrome	<i>ESCO2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 138,000
Salla Disease	<i>SLC17A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
Salt and Pepper Developmental Regression Syndrome	<i>ST3GAL5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Sandhoff Disease	<i>HEXB</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Schimke Immunoosseous Dysplasia	<i>SMARCA1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
Seckel Syndrome 5 / Microcephaly 9	<i>CEP152</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 740
Segawa Syndrome	<i>TH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,100
Sepiapterin Reductase Deficiency	<i>SPR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 49,000
Severe Combined Immunodeficiency ( <i>IL7R</i> -Related)	<i>IL7R</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 51,000
Severe Combined Immunodeficiency ( <i>JAK3</i> -Related)	<i>JAK3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100
Severe Combined Immunodeficiency ( <i>PTPRC</i> -Related)	<i>PTPRC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,500
Severe Congenital Neutropenia 4	<i>G6PC3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,200
Severe Neonatal Hyperparathyroidism	<i>CASR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 5,000
Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis	<i>POC1A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 256,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 700
Shwachman-Diamond Syndrome	<i>SBDS</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,200
Sialidosis, Type I and Type II	<i>NEU1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,400
Sjogren-Larsson Syndrome	<i>ALDH3A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
Smith-Lemli-Opitz Syndrome	<i>DHCR7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,100
Spastic Paraplegia 15	<i>ZFYVE26</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 85,000
Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly	<i>SLC1A4</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 385,000
Spherocytosis, Type 5	<i>EPB42</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,200
Spinal Muscular Atrophy	<i>SMN1</i>	AR	Reduced Risk	SMN1 copy number: 2 SMN2 copy number: 2 c.3*80T>G: Negative SMN1 Sequencing: Negative <b>Personalized Residual Risk:</b> 1 in 757
Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S	<i>IGHMBP2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 880
Spinocerebellar Ataxia with Axonal Neuropathy 3	<i>COA7</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 12,000
Spondylocostal Dysostosis 1	<i>DLL3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,200
Spondylometaphyseal Dysplasia ( <i>DDR2</i> -Related)	<i>DDR2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 220,000

<b>Spondylothoracic Dysostosis</b>	<i>MESP2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 306,000
<b>Steel Syndrome</b>	<i>COL27A1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 513,000
<b>Stuve-Wiedemann Syndrome</b>	<i>LIFR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,000
<b>Sulfate Transporter-Related Osteochondrodysplasia</b>	<i>SLC26A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,800
<b>Tay-Sachs Disease</b>	<i>HEXA</i>	AR	Reduced Risk	Tay-Sachs disease enzyme: Non-carrier  White blood cells: Non-carrier  <ul style="list-style-type: none"> <li>Hex A%: 62.1% (Non-carrier : 55.0 - 72.0%; Carrier: &lt;50%)</li> <li>Total hexosaminidase activity: 1810 nmol/hr/mg</li> </ul> Plasma: Non-carrier  <ul style="list-style-type: none"> <li>Hex A%: 61.8 (Non-carrier : 58.0 - 72.0%; Carrier: &lt;54%)</li> <li>Total hexosaminidase activity: 787 nmol/hr/ml</li> </ul> HEXA Sequencing: Negative <b>Personalized Residual Risk:</b> 1 in 400
<b>Thiamine-Responsive Megaloblastic Anemia Syndrome</b>	<i>SLC19A2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000
<b>Thyroid Dysmorphogenesis 1</b>	<i>SLC5A5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 63,000
<b>Thyroid Dysmorphogenesis 2A</b>	<i>TPO</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
<b>Thyroid Dysmorphogenesis 3</b>	<i>TG</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 850
<b>Thyroid Dysmorphogenesis 4</b>	<i>IYD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,800
<b>Thyroid Dysmorphogenesis 5</b>	<i>DUOXA2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 28,000
<b>Thyroid Dysmorphogenesis 6</b>	<i>DUOX2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 190
<b>Trichohepatoenteric Syndrome 1</b>	<i>TTC37</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,100
<b>Tyrosinemia, Type I</b>	<i>FAH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,900
<b>Tyrosinemia, Type II</b>	<i>TAT</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 6,300
<b>Tyrosinemia, Type III</b>	<i>HPD</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 103,000
<b>Usher Syndrome, Type IB</b>	<i>MYO7A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,200
<b>Usher Syndrome, Type IC</b>	<i>USH1C</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 930
<b>Usher Syndrome, Type ID</b>	<i>CDH23</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 640
<b>Usher Syndrome, Type IF</b>	<i>PCDH15</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,600
<b>Usher Syndrome, Type IIA</b>	<i>USH2A</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 190
<b>Usher Syndrome, Type III</b>	<i>CLRN1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,400
<b>Very Long Chain Acyl-CoA Dehydrogenase Deficiency</b>	<i>ACADVL</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,300
<b>Vitamin D-Dependent Rickets, Type I</b>	<i>CYP27B1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 14,000
<b>Vitamin D-Resistant Rickets, Type IIA</b>	<i>VDR</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 15,000
<b>Walker-Warburg Syndrome and Other FKTN-Related Dystrophies</b>	<i>FKTN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 8,300
<b>Werner Syndrome</b>	<i>WRN</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,500
<b>Wilson Disease</b>	<i>ATP7B</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 200
<b>Wiskott-Aldrich Syndrome (WAS-Related)</b>	<i>WAS</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 1,203,000
<b>Wolcott-Rallison Syndrome</b>	<i>EIF2AK3</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 22,000
<b>Wolman Disease / Cholesteryl Ester Storage Disease</b>	<i>LIPA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 3,200
<b>Woodhouse-Sakati Syndrome</b>	<i>DCAF17</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 249,000
<b>X-Linked Juvenile Retinoschisis</b>	<i>RS1</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 40,000
<b>X-Linked Severe Combined Immunodeficiency</b>	<i>IL2RG</i>	XL	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 250,000
<b>Xeroderma Pigmentosum (POLH-Related)</b>	<i>POLH</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 24,000
<b>Xeroderma Pigmentosum, Group A</b>	<i>XPA</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 11,000

<b>Xeroderma Pigmentosum, Group C</b>	<i>XPC</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 9,600
<b>Xeroderma Pigmentosum, Group G</b>	<i>ERCC5</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 4,700
<b>Zellweger Syndrome Spectrum (PEX10-Related)</b>	<i>PEX10</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 7,100
<b>Zellweger Syndrome Spectrum (PEX1-Related)</b>	<i>PEX1</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 10,000
<b>Zellweger Syndrome Spectrum (PEX2-Related)</b>	<i>PEX2</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 96,000
<b>Zellweger Syndrome Spectrum (PEX6-Related)</b>	<i>PEX6</i>	AR	Reduced Risk	<b>Personalized Residual Risk:</b> 1 in 2,100

AR=Autosomal recessive; XL=X-linked

## Test methods and comments

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

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

PCR amplification using Asuragen, Inc. AmplideX<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™XT Low Input technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Libraries were pooled and sequenced on the Illumina NovaSeq 6000 platform, using paired-end 100 bp reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house.

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

**Exceptions:** *ABCD1* (NM\_000033.3) exons 8 and 9; *ACADSB* (NM\_001609.3) chr10:124,810,695-124,810,707 (partial exon 9); *ADA* (NM\_000022.2) exon 1; *ADAMTS2* (NM\_014244.4) exon 1; *AGPS* (NM\_003659.3) chr2:178,257,512-178,257,649 (partial exon 1); *ALDH7A1* (NM\_001182.4) chr5:125,911,150-125,911,163 (partial exon 7) and chr5:125,896,807-125,896,821 (partial exon 10); *ALMS1* (NM\_015120.4) chr2:73,612,990-73,613,041 (partial exon 1); *APOPT1* (NM\_032374.4) chr14:104,040,437-104,040,455 (partial exon 3); *CDAN1* (NM\_138477.2) exon 2; *CEP152* (NM\_014985.3) chr15:49,061,146-49,061,165 (partial exon 14) and exon 22; *CEP290* (NM\_025114.3) exon 5, exon 7, chr12:88,519,017-88,519,039 (partial exon 13), chr12:88,514,049-88,514,058 (partial exon 15), chr12:88,502,837-88,502,841 (partial exon 23), chr12:88,481,551-88,481,589 (partial exon 32), chr12:88,471,605-88,471,700 (partial exon 40); *CFTR* (NM\_000492.3) exon 10; *COL4A4* (NM\_000092.4) chr2:227,942,604-227,942,619 (partial exon 25); *COX10* (NM\_001303.3) exon 6; *CYP11B1* (NM\_000497.3) exons 3-7; *CYP11B2* (NM\_000498.3) exons 3-7; *DNAI2* (NM\_023036.4) chr17:72,308,136-72,308,147 (partial exon 12); *DOK7* (NM\_173660.4) chr4:3,465,131-3,465,161 (partial exon 1) and exon 2; *DUOX2* (NM\_014080.4) exons 6-8; *EIF2AK3* (NM\_004836.5) exon 8; *EVC* (NM\_153717.2) exon 1; *F5* (NM\_000130.4) chr1:169,551,662-169,551,679 (partial exon 2); *FH* (NM\_000143.3) exon 1; *GAMT* (NM\_000156.5) exon 1; *GLDC* (NM\_000170.2) exon 1; *GNPTAB* (NM\_024312.4) chr17:4,837,000-4,837,400 (partial exon 2); *GNPTG* (NM\_032520.4) exon 1; *GHR* (NM\_000163.4) exon 3; *GYS2* (NM\_021957.3) chr12:21,699,370-21,699,409 (partial exon 12); *HGSNAT* (NM\_152419.2) exon 1; *IDS* (NM\_000202.6) exon 3; *ITGB4* (NM\_000213.4) chr17:73,749,976-73,750,060 (partial exon 33); *JAK3* (NM\_000215.3) chr19:17,950,462-17,950,483 (partial exon 10); *LIFR* (NM\_002310.5) exon 19; *LMBRD1* (NM\_018368.3) chr6:70,459,226-70,459,257 (partial exon 5), chr6:70,447,828-70,447,836 (partial exon 7) and exon 12; *LYST* (NM\_000081.3) chr1:235,944,158-235,944,176 (partial exon 16) and chr1:235,875,350-235,875,362 (partial exon 43); *MLYCD* (NM\_012213.2) chr16:83,933,242-83,933,282 (partial exon 1); *MTR* (NM\_000254.2) chr1:237,024,418-237,024,439 (partial exon 20) and chr1:237,038,019-237,038,029 (partial exon 24); *NBEAL2* (NM\_015175.2) chr3:47,021,385-47,021,407 (partial exon 1); *NEB* (NM\_001271208.1) exons 82-105; *NPC1* (NM\_000271.4) chr18:21,123,519-21,123,538 (partial exon 14); *NPHP1* (NM\_000272.3) chr2:110,937,251-110,937,263 (partial exon 3); *OCRL* (NM\_000276.3) chrX:128,674,450-128,674,460 (partial exon 1); *PHKB* (NM\_000293.2) exon 1 and chr16:47,732,498-47,732,504 (partial exon 30); *PIGN* (NM\_176787.4) chr18:59,815,547-59,815,576 (partial exon 8); *PIP5K1C* (NM\_012398.2) exon 1 and chr19:3637602-3637616 (partial exon 17); *POU1F1* (NM\_000306.3) exon 5; *PTPRC* (NM\_002838.4) exons 11 and 23; *PUS1* (NM\_025215.5) chr12:132,414,446-132,414,532 (partial exon 2); *RPGRIP1L* (NM\_015272.2) exon 23; *SGSH* (NM\_000199.3) chr17:78,194,022-78,194,072 (partial exon 1); *SLC6A8* (NM\_005629.3) exons 3 and 4; *ST3GAL5* (NM\_003896.3) exon 1; *SURF1* (NM\_003172.3) chr9:136,223,269-136,223,307 (partial exon 1); *TRPM6* (NM\_017662.4) chr9:77,362,800-77,362,811 (partial exon 31); *TSEN54* (NM\_207346.2) exon 1; *TYR* (NM\_000372.4) exon 5; *VWF* (NM\_000552.3) exons 24-26, chr12:6,125,675-6,125,684 (partial exon 30), chr12:6,121,244-6,121,265 (partial exon 33), and exon 34.

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

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

#### Next Generation Sequencing for *SMN1*

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

#### Copy Number Variant 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 ≥98%)**

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

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

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

## **SELECTED REFERENCES**

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### **Fragile X syndrome:**

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### **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	Specimen Information	Client Information
<b>6531, DONOR</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] Gender: M Phone: NG Patient ID: [REDACTED]	Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED]  Collected: 10/21/2022 Received: 10/22/2022 / 20:45 EDT Reported: 10/31/2022 / 18:33 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: Encounter of male for testing for disease carrier status for procrea management

**RESULT:**  
 NORMAL MALE KARYOTYPE

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

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

**NOMENCLATURE:**  
 46,XY

**ASSAY INFORMATION:**

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

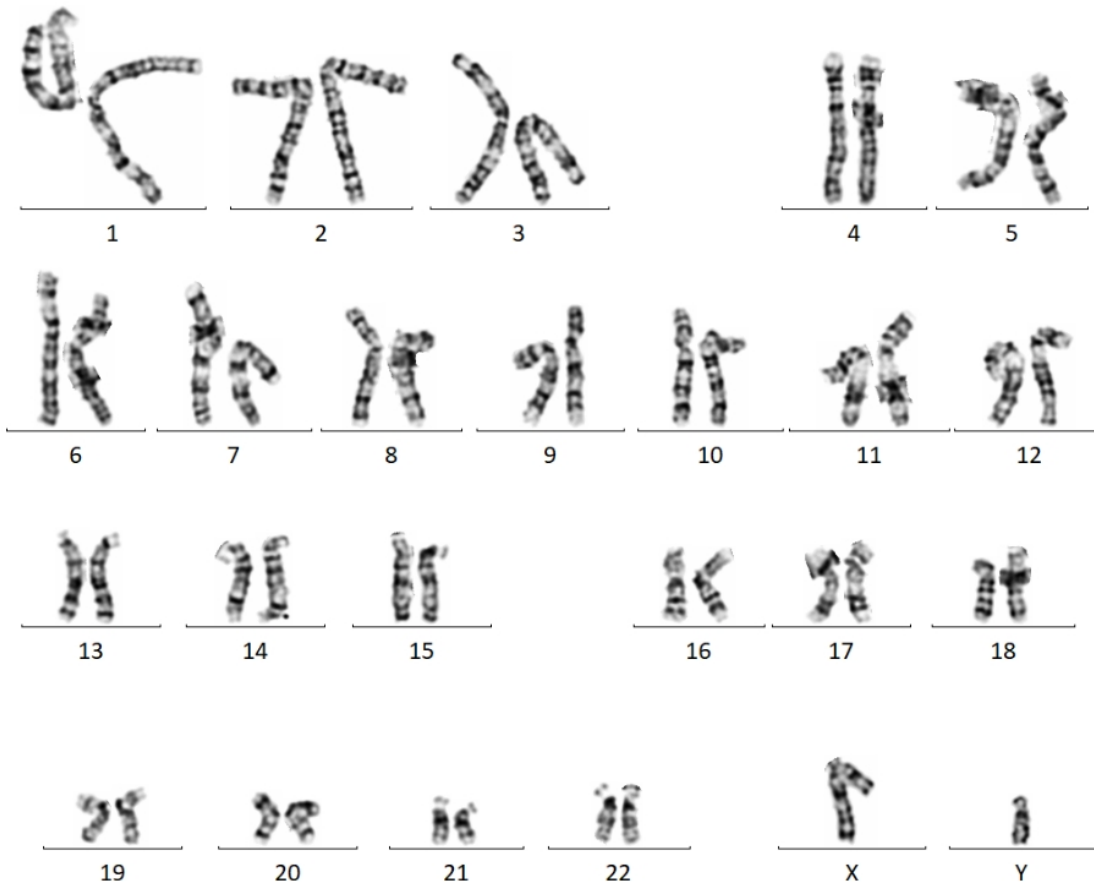
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

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

Electronic Signature:     10/31/2022 5:19 PM



Patient Information	Specimen Information	Client Information
<p><b>6531, DONOR</b></p> <p>DOB: [REDACTED]      AGE: [REDACTED]</p> <p>Gender: M</p> <p>Patient ID: [REDACTED]</p>	<p>Specimen: [REDACTED]</p> <p>Collected: 10/21/2022</p> <p>Received: 10/22/2022 / 20:45 EDT</p> <p>Reported: 10/31/2022 / 18:33 EDT</p>	<p>Client #: 48041578</p> <p>GENOMICS, SEMA4</p>



**PERFORMING SITE:**

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



Patient Information	Specimen Information	Client Information
<b>6531, DONOR</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] Gender: M Phone: NG Patient ID: [REDACTED]	Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED]  Collected: 10/21/2022 Received: 10/22/2022 / 20:44 EDT Reported: 10/26/2022 / 21:27 EDT	Client #: 48041578     NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229

Ward:     FFXCB

Test Name	In Range	Out Of Range	Reference Range	Lab
HEMOGLOBINOPATHY EVALUATION				
RED BLOOD CELL COUNT	4.98		4.20-5.80 Million/uL	Z99
HEMOGLOBIN	15.2		13.2-17.1 g/dL	
HEMATOCRIT	44.2		38.5-50.0 %	
MCV	88.8		80.0-100.0 fL	
MCH	30.5		27.0-33.0 pg	
RDW	12.3		11.0-15.0 %	
HEMOGLOBIN A	97.2		>96.0 %	Z99
HEMOGLOBIN F	<1.0		<2.0 %	
HEMOGLOBIN A2 (QUANT)	2.8		2.2-3.2 %	
INTERPRETATION				
Normal phenotype.				

**PERFORMING SITE:**

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