

**Patient Information**

Name: Donor N4010  
 Date of Birth: [REDACTED]  
 Sema4 ID: 22192200  
 Client ID: SEATSB-S452699990  
 Indication: Carrier Screening

**Specimen Information**

Specimen Type: Blood  
 Date Collected: 09/23/2022  
 Date Received: 09/24/2022  
 Final Report: 10/11/2022

**Referring Provider**

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

### SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
<p><b>Carrier of Limb-Girdle Muscular Dystrophy, Type 2A (AR)</b>            Associated gene(s): <i>CAPN3</i>            Variant(s) Detected: c.1800+2T&gt;C, Likely Pathogenic,            Heterozygous (one copy)</p> <p><b>Carrier of Neuronal Ceroid-Lipofuscinosis (CLN3-Related) (AR)</b>            Associated gene(s): <i>CLN3</i>            Variant(s) Detected: c.461-280_677+382del966, Pathogenic,            Heterozygous (one copy)</p>	<p style="text-align: center;"><b>Negative for all other genes tested</b></p> <p style="text-align: center;">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

**Limb-Girdle Muscular Dystrophy, Type 2A (AR)**

**Results and Interpretation**

A heterozygous (one copy) likely pathogenic splice site variant, c.1800+2T>C, was detected in the *CAPN3* gene (NM\_000070.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for limb-girdle muscular dystrophy, type 2A. Therefore, this individual is expected to be at least a carrier for limb-girdle muscular dystrophy, type 2A. Heterozygous carriers are not expected to exhibit symptoms of this disease.

### What is Limb-Girdle Muscular Dystrophy, Type 2A?

Limb-girdle muscular dystrophy, type 2A is an autosomal recessive, pan-ethnic disorder that is caused by pathogenic variants in the gene *CAPN3*. This form of muscular dystrophy presents with weakness of the pelvic girdle and legs, and eventually progresses to the upper limbs. Sometimes it presents with weakness of the upper limbs and progresses to the lower limbs. Onset is usually in childhood or early adolescence, although variability exists. Patients usually lose the ability to walk independently about 20 years after diagnosis, and death usually occurs in middle age. Some patients also experience weakness of the facial muscles or contractures of the joints. Patients with at least one missense variant may experience a slightly slower rate of progression than those with two null variants, but the severity of the disease appears to be the same.

### Neuronal Ceroid-Lipofuscinosis (*CLN3*-Related) (AR)

#### Results and Interpretation

A heterozygous (one copy) pathogenic deletion, c.461-280\_677+382delg66, was detected in the *CLN3* gene (NM\_000086.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for neuronal ceroid-lipofuscinosis (*CLN3*-related). Therefore, this individual is expected to be at least a carrier for neuronal ceroid-lipofuscinosis (*CLN3*-related). Heterozygous carriers are not expected to exhibit symptoms of this disease.

### What is Neuronal Ceroid-Lipofuscinosis (*CLN3*-Related)?

Neuronal ceroid-lipofuscinosis (*CLN3*-related) is an autosomal recessive neurodegenerative disorder that is caused by pathogenic variants in the gene *CLN3*. It has been reported in patients from different ethnicities around the world. Most *CLN3*-caused neuronal ceroid-lipofuscinosis results in the juvenile form, in which symptoms begin between 4 and 10 years of age. Clinical features include progressive visual loss which proceeds to blindness in childhood. Neurologic and psychiatric symptoms include seizures, difficulty speaking, intellectual disability, psychosis or dementia, and ataxia leading to an inability to walk. Affected individuals often die between the ages of 20 and 40. Some patients have a milder form with less neurologic involvement. It is not currently possible to predict the severity of disease based on the patient's genotype.

## Test description

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



Juliette J. Kahle, Ph.D., FACMG, 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>				
Limb-Girdle Muscular Dystrophy, Type 2A	CAPN3	AR	Carrier	c.1800>2T>C, Likely Pathogenic, Heterozygous (one copy)
Neuronal Ceroid-Lipofuscinosis (CLN3-Related)	CLN3	AR	Carrier	c.461-280_677>382del966, Pathogenic, Heterozygous (one copy)
<b>Negative</b>				
2-Methylbutyrylglucosuria	ACADSB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	HSD3B2	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related)	MCCC1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)	MCCC2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
3-Methylglutaconic Aciduria, Type III	OPA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 50,000
3-Phosphoglycerate Dehydrogenase Deficiency	PHGDH	AR	Reduced Risk	Personalized Residual Risk: 1 in 63,000
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 415,000
Abetalipoproteinemia	MTPP	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Achalasia-Addisonianism-Alacrimia Syndrome	AAAS	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,500
Achromatopsia (CNGA3-Related)	CNGA3	AR	Reduced Risk	Personalized Residual Risk: 1 in 830
Achromatopsia (CNGB3-related)	CNGB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,600
Acrodermatitis Enteropathica	SLC39A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Acute Infantile Liver Failure	TRMU	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,400
Acyl-CoA Oxidase I Deficiency	ACOX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 39,000
Adams-Oliver Syndrome 4	EOGT	AR	Reduced Risk	Personalized Residual Risk: 1 in 44,000
Adenosine Deaminase Deficiency	ADA	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,100
Adrenocorticotropic Hormone Deficiency	TBX19	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Adrenoleukodystrophy, X-Linked	ABCD1	XL	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Agammaglobulinemia	BTK	XL	Reduced Risk	Personalized Residual Risk: 1 in 250,000
Agenesis of the Corpus Callosum	FRMD4A	AR	Reduced Risk	Personalized Residual Risk: 1 in 124,000
Aicardi-Goutieres Syndrome (RNASEH2C-Related)	RNASEH2C	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
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 3,200
Albinism, Oculocutaneous, Type III	TYRP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Alkaptonuria	HGD	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Alpha-Mannosidosis	MAN2B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,200
Alpha-Thalassemia	HBA1/HBA2	AR	Reduced Risk	HBA1 Copy Number: 2 HBA2 Copy Number: 2 No pathogenic copy number variants detected HBA1/HBA2 Sequencing: Negative Personalized Residual Risk: 1 in 490

Alpha-Thalassemia Intellectual Disability Syndrome	<i>ATRX</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 48,000
Alport Syndrome ( <i>COL4A3</i> -Related)	<i>COL4A3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Alport Syndrome ( <i>COL4A4</i> -Related)	<i>COL4A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Alport Syndrome ( <i>COL4A5</i> -Related)	<i>COL4A5</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 150,000
Alstrom Syndrome	<i>ALMS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Andermann Syndrome	<i>SLC12A6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 151,000
Antley-Bixler Syndrome ( <i>POR</i> -Related)	<i>POR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Argininemia	<i>ARG1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,500
Argininosuccinic Aciduria	<i>ASL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Aromatase Deficiency	<i>CYP19A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Arthrogryposis, Intellectual Disability, and Seizures	<i>SLC35A3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 454,000
Asparagine Synthetase Deficiency	<i>ASNS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 202,000
Aspartylglycosaminuria	<i>AGA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Ataxia With Isolated Vitamin E Deficiency	<i>TTPA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 61,000
Ataxia-Telangiectasia	<i>ATM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Ataxia-Telangiectasia-Like Disorder 1	<i>MRE11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	<i>SACS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Bardet-Biedl Syndrome ( <i>ARL6</i> -Related)	<i>ARL6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000
Bardet-Biedl Syndrome ( <i>BBS10</i> -Related)	<i>BBS10</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Bardet-Biedl Syndrome ( <i>BBS12</i> -Related)	<i>BBS12</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,900
Bardet-Biedl Syndrome ( <i>BBS1</i> -Related)	<i>BBS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Bardet-Biedl Syndrome ( <i>BBS2</i> -Related)	<i>BBS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Bardet-Biedl Syndrome ( <i>BBS4</i> -Related)	<i>BBS4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 22,000
Bare Lymphocyte Syndrome, Type II	<i>CIITA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Barth Syndrome	<i>TAZ</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 183,000
Bartter Syndrome, Type 3	<i>CLCNKB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 740
Bartter Syndrome, Type 4A	<i>BSND</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 91,000
Bernard-Soulier Syndrome, Type A1	<i>GP1BA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 42,000
Bernard-Soulier Syndrome, Type C	<i>GP9</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Beta-Globin-Related Hemoglobinopathies	<i>HBB</i>	AR	Reduced Risk	Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies): 1 in 2,000 Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant): 1 in 11,000 Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant): 1 in 42,000
Beta-Ketothiolase Deficiency	<i>ACAT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Beta-Mannosidosis	<i>MANBA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,100
BH4-Deficient Hyperphenylalaninemia C	<i>QDPR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
BH4-Deficient Hyperphenylalaninemia D	<i>PCBD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,000
Bilateral Frontoparietal Polymicrogyria	<i>GPR56</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 203,000
Biotinidase Deficiency	<i>BTD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 500
Bloom Syndrome	<i>BLM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
Canavan Disease	<i>ASPA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Carbamoylphosphate Synthetase I Deficiency	<i>CPS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Carnitine Acylcarnitine Translocase Deficiency	<i>SLC25A20</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,100
Carnitine Palmitoyltransferase IA Deficiency	<i>CPT1A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 24,000
Carnitine Palmitoyltransferase II Deficiency	<i>CPT2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 670
Carpenter Syndrome	<i>RAB23</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000

Cartilage-Hair Hypoplasia	<i>RMRP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 960
Catecholaminergic Polymorphic Ventricular Tachycardia	<i>CASQ2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Central Hypothyroidism and Testicular Enlargement	<i>IGSF1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 781,000
Cerebral Creatine Deficiency Syndrome 1	<i>SLC6A8</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 208,000
Cerebral Creatine Deficiency Syndrome 2	<i>GAMT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Cerebral Creatine Deficiency Syndrome 3	<i>GATM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,900
Cerebral Dysgenesis, Neuropathy, Ichthyosis, and Palmoplantar Keratoderma Syndrome	<i>SNAP29</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,730,000
Cerebrotendinous Xanthomatosis	<i>CYP27A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,900
Charcot-Marie-Tooth Disease, Type 4D	<i>NDRG1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 730,000
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	<i>PRPS1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 114,000
Charcot-Marie-Tooth Disease, X-Linked	<i>GJB1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Chediak-Higashi Syndrome	<i>LYST</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,100
Chondrodysplasia Punctata	<i>ARSE</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 862,000
Choreoacanthocytosis	<i>VPS13A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Choroideremia	<i>CHM</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 125,000
Chronic Granulomatous Disease (CYBA-Related)	<i>CYBA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Chronic Granulomatous Disease (CYBB-Related)	<i>CYBB</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 294,000
Citrin Deficiency	<i>SLC25A13</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Citrullinemia, Type 1	<i>ASS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Cockayne Syndrome, Type A	<i>ERCC8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,900
Cockayne Syndrome, Type B and other ERCC6-Related Disorders	<i>ERCC6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,100
Cohen Syndrome	<i>VPS13B</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Combined Factor V and VIII Deficiency	<i>LMAN1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 102,000
Combined Malonic and Methylmalonic Aciduria	<i>ACSF3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Combined Oxidative Phosphorylation Deficiency 1	<i>GFM1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Combined Oxidative Phosphorylation Deficiency 3	<i>TSMF</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Combined Pituitary Hormone Deficiency 1	<i>POU1F1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,900
Combined Pituitary Hormone Deficiency 2	<i>PROP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Combined Pituitary Hormone Deficiency 3	<i>LHX3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 140,000
Combined SAP Deficiency	<i>PSAP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 44,000
Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1	<i>GUCY2D</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency	<i>CYP11B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 520
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	<i>CYP17A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
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 200 <b>Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)):</b> 1 in 1,300
Congenital Adrenal Hypoplasia (NR0B1-Related)	<i>NR0B1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 353,000
Congenital Adrenal Insufficiency (CYP11A1-Related)	<i>CYP11A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,100
Congenital Amegakaryocytic Thrombocytopenia	<i>MPL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
Congenital Bile Acid Synthesis Defect (AKR1D1-Related)	<i>AKR1D1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,900

Congenital Bile Acid Synthesis Defect ( <i>HSD3B7</i> -Related)	<i>HSD3B7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,900
Congenital Disorder of Deglycosylation	<i>NGLY1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Congenital Disorder of Glycosylation, Type Ia	<i>PMM2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 540
Congenital Disorder of Glycosylation, Type Ib	<i>MPI</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,600
Congenital Disorder of Glycosylation, Type Ic	<i>ALG6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,100
Congenital Disorder of Glycosylation, Type Im	<i>DOLK</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 134,000
Congenital Dyserythropoietic Anemia Type 2	<i>SEC23B</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Congenital Dyserythropoietic Anemia, Type Ia	<i>CDAN1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 470
Congenital Ichthyosis 4A and 4B	<i>ABCA12</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,100
Congenital Insensitivity to Pain with Anhidrosis	<i>NTRK1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,700
Congenital Muscular Dystrophy ( <i>LAMA2</i> -Related)	<i>LAMA2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 640
Congenital Myasthenic Syndrome ( <i>CHAT</i> -Related)	<i>CHAT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
Congenital Myasthenic Syndrome ( <i>CHRNE</i> -Related)	<i>CHRNE</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,100
Congenital Myasthenic Syndrome ( <i>DOK7</i> -Related)	<i>DOK7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Congenital Myasthenic Syndrome ( <i>RAPSN</i> -Related)	<i>RAPSN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Congenital Neutropenia ( <i>HAX1</i> -Related)	<i>HAX1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 82,000
Congenital Neutropenia ( <i>VPS45</i> -Related)	<i>VPS45</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Congenital Nongoitrous Hypothyroidism 1	<i>TSHR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Congenital Nongoitrous Hypothyroidism 4	<i>TSHB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 118,000
Congenital Secretory Chloride Diarrhea 1	<i>SLC26A3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Corneal Dystrophy and Perceptive Deafness	<i>SLC4A11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,600
Corticosterone Methyloxidase Deficiency	<i>CYP11B2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Cystic Fibrosis	<i>CFTR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 440
Cystinosis	<i>CTNS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,700
Cystinuria ( <i>SLC3A1</i> -Related)	<i>SLC3A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 590
Cytochrome C Oxidase Deficiency / Leigh Syndrome ( <i>COX15</i> -Related)	<i>COX15</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
D-Bifunctional Protein Deficiency	<i>HSD17B4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Deafness, Autosomal Recessive 3	<i>MYO15A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 240
Deafness, Autosomal Recessive 59	<i>PJVK</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 57,000
Deafness, Autosomal Recessive 7	<i>TMC1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Deafness, Autosomal Recessive 76	<i>SYNE4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 43,000
Deafness, Autosomal Recessive 77	<i>LOXHD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,700
Deafness, Autosomal Recessive 8/10	<i>TMPRSS3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 510
Deafness, Autosomal Recessive 9	<i>OTOF</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Desbuquois Dysplasia 1	<i>CANT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 24,000
Desmosterolosis	<i>DHCR24</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 27,000
Diaphanospondylodysostosis	<i>BMPER</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 18,000
Distal Renal Tubular Acidosis and other <i>SLC4A1</i> -related Disorders	<i>SLC4A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Duchenne Muscular Dystrophy / Becker Muscular Dystrophy	<i>DMD</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Dyskeratosis Congenita ( <i>DKC1</i> -related)	<i>DKC1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 9,259,000
Dyskeratosis Congenita ( <i>RTEL1</i> -Related)	<i>RTEL1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,800
Dystrophic Epidermolysis Bullosa	<i>COL7A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 900
Ehlers-Danlos Syndrome, Type VI	<i>PLOD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Ehlers-Danlos Syndrome, Type VIIC	<i>ADAMTS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 243,000
Ellis-Van Creveld Syndrome ( <i>EVC2</i> -Related)	<i>EVC2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,300

Ellis-van Creveld Syndrome (EVC-Related)	<i>EVC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Emery-Dreifuss Myopathy 1	<i>EMD</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 833,000
Enhanced S-Cone Syndrome	<i>NR2E3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Ethylmalonic Encephalopathy	<i>ETHE1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Fabry Disease	<i>GLA</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 7,700
Factor IX Deficiency	<i>F9</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 5,100
Factor VII Deficiency	<i>F7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 450
Factor XI Deficiency	<i>F11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Familial Autosomal Recessive Hypercholesterolemia	<i>LDLRAP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 136,000
Familial Dysautonomia	<i>IKBKAP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 51,000
Familial Hypercholesterolemia	<i>LDLR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 280
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	<i>HADH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,200
Familial Hyperinsulinism (ABCC8-Related)	<i>ABCC8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 450
Familial Hyperinsulinism (KCNJ11-Related)	<i>KCNJ11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Familial Hyperphosphatemic Tumor Calcinosi	<i>GALNT3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7800
Familial Mediterranean Fever	<i>MEFV</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Fanconi Anemia, Group A	<i>FANCA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Fanconi Anemia, Group C	<i>FANCC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Fanconi Anemia, Group G	<i>FANCG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 28,000
Fanconi-Bickel Syndrome	<i>SLC2A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
Fragile X Syndrome	<i>FMR1</i>	XL	Reduced Risk	<i>FMR1</i> CGG repeat sizes: Not Performed <i>FMR1</i> Sequencing: Negative Fragile X CGG triplet repeat expansion testing was not performed at this time, as the patient has either been previously tested or is a male. Personalized Residual Risk: 1 in 19,000
Fructose-1,6-Bisphosphatase Deficiency	<i>FBP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Fucosidosis	<i>FUCA1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,200
Fumarase Deficiency	<i>FH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Fundus Albipunctatus	<i>RDH5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Galactokinase Deficiency	<i>GALK1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Galactose Epimerase Deficiency	<i>GALE</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,600
Galactosemia	<i>GALT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Galactosialidosis	<i>CTSA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,900
Gaucher Disease	<i>GBA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Generalized Thyrotropin-Releasing Hormone Resistance	<i>TRHR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 104,000
Geroderma Osteodysplasticum	<i>GORAB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 70,000
Gitelman Syndrome	<i>SLC12A3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 290
Glanzmann Thrombasthenia (ITGA2B-Related)	<i>ITGA2B</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Glanzmann Thrombasthenia (ITGB3-Related)	<i>ITGB3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Glutaric Acidemia, Type I	<i>GCDH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Glutaric Acidemia, Type IIa	<i>ETFA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,700
Glutaric Acidemia, Type IIb	<i>ETFB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Glutaric Acidemia, Type IIc	<i>ETFDH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Glutathione Synthetase Deficiency	<i>GSS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Glycine Encephalopathy (AMT-Related)	<i>AMT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,700
Glycine Encephalopathy (GLDC-Related)	<i>GLDC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 760
Glycogen Storage Disease, Type 0	<i>GYS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Glycogen Storage Disease, Type Ia	<i>G6PC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Glycogen Storage Disease, Type Ib	<i>SLC37A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,300

Glycogen Storage Disease, Type II	GAA	AR	Reduced Risk	Personalized Residual Risk: 1 in 520
Glycogen Storage Disease, Type III	AGL	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,600
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	GBE1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Glycogen Storage Disease, Type IXb	PHKB	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Glycogen Storage Disease, Type V	PYGM	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Glycogen Storage Disease, Type VI	PYGL	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Glycogen Storage Disease, Type VII	PFKM	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
GRACILE Syndrome and Other BCS1L-Related Disorders	BCS1L	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,900
Gray Platelet Syndrome	NBEAL2	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,800
Growth Hormone Deficiency, Type IB	GHRHR	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,900
Hemochromatosis, Type 2A	HFE2	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Hemochromatosis, Type 3	TFR2	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
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 116,000
Hermansky-Pudlak Syndrome, Type 1	HPS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Hermansky-Pudlak Syndrome, Type 3	HPS3	AR	Reduced Risk	Personalized Residual Risk: 1 in 49,000
Hermansky-Pudlak Syndrome, Type 4	HPS4	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Hermansky-Pudlak Syndrome, Type 6	HPS6	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,400
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 2,000
Holocarboxylase Synthetase Deficiency	HLCS	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Homocystinuria (CBS-Related)	CBS	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Homocystinuria due to MTHFR Deficiency	MTHFR	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
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 2,100
Hydrocephalus	L1CAM	XL	Reduced Risk	Personalized Residual Risk: 1 in 40,000
Hydrolethals Syndrome	HYLS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
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 5,700
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	SARS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 23,000
Hypohidrotic Ectodermal Dysplasia 1	EDA	XL	Reduced Risk	Personalized Residual Risk: 1 in 22,000
Hypomagnesemia 1	TRPM6	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Hypomyelinating Leukodystrophy 3	AIMP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 341,000
Hypomyelinating Leukodystrophy 12	VPS11	AR	Reduced Risk	Personalized Residual Risk: 1 in 72,000
Hypoparathyroidism-Retardation-Dysmorphic Syndrome	TBCE	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Hypophosphatasia	ALPL	AR	Reduced Risk	Personalized Residual Risk: 1 in 790
Hypophosphatemic Rickets with Hypercalciuria	SLC34A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Hypotrichosis 8 / Autosomal Recessive Woolly Hair 1	LPAR6	AR	Reduced Risk	Personalized Residual Risk: 1 in 27,000
Immunodeficiency 18	CD3E	AR	Reduced Risk	Personalized Residual Risk: 1 in 73,000
Immunodeficiency 19	CD3D	AR	Reduced Risk	Personalized Residual Risk: 1 in 46,000
Inclusion Body Myopathy 2	GNE	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Infantile Cerebral and Cerebellar Atrophy	MED17	AR	Reduced Risk	Personalized Residual Risk: 1 in 129,000
Infantile Neuroaxonal Dystrophy 1 and other PLA2G6-Related Disorders	PLA2G6	AR	Reduced Risk	Personalized Residual Risk: 1 in 690
Intellectual Disability, Autosomal Recessive 3	CC2D1A	AR	Reduced Risk	Personalized Residual Risk: 1 in 220,000
Intrahepatic Cholestasis	ATP8B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Isovaleric Acidemia	IVD	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000



Joubert Syndrome 2	<i>TMEM216</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 152,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	<i>NPHP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	<i>RPGRIP1L</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 32,000
Junctional Epidermolysis Bullosa ( <i>COL17A1</i> -Related)	<i>COL17A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 25,000
Junctional Epidermolysis Bullosa ( <i>ITGA6</i> -Related)	<i>ITGA6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 125,000
Junctional Epidermolysis Bullosa ( <i>ITGB4</i> -Related)	<i>ITGB4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Junctional Epidermolysis Bullosa ( <i>LAMA3</i> -Related)	<i>LAMA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Junctional Epidermolysis Bullosa ( <i>LAMB3</i> -Related)	<i>LAMB3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Junctional Epidermolysis Bullosa ( <i>LAMC2</i> -Related)	<i>LAMC2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 77,000
Kohlschutter-Tonz Syndrome	<i>ROGDI</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Krabbe Disease	<i>GALC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 860
Lamellar Ichthyosis, Type 1	<i>TGM1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Laron Dwarfism	<i>GHR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,700
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	<i>CEP290</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Leber Congenital Amaurosis 13	<i>RDH12</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	<i>TULP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	<i>RPE65</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Leber Congenital Amaurosis 4	<i>AIPL1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Leber Congenital Amaurosis 5	<i>LCA5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	<i>CRB1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 990
Leigh Syndrome ( <i>NDUFS7</i> -Related)	<i>NDUFS7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 26,000
Leigh Syndrome ( <i>SURF1</i> -Related)	<i>SURF1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,400
Leigh Syndrome, French-Canadian Type	<i>LRPPRC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 32,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogyposis with Anterior Horn Cell Disease	<i>GLE1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Lethal Congenital Contracture Syndrome 2	<i>ERBB3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 96,000
Lethal Congenital Contracture Syndrome 3	<i>PIP5K1C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 318,000
Leukoencephalopathy with Vanishing White Matter	<i>EIF2B5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Limb-Girdle Muscular Dystrophy, Type 2B	<i>DYSF</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Limb-Girdle Muscular Dystrophy, Type 2C	<i>SGCG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,900
Limb-Girdle Muscular Dystrophy, Type 2D	<i>SGCA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Limb-Girdle Muscular Dystrophy, Type 2E	<i>SGCB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 31,000
Limb-Girdle Muscular Dystrophy, Type 2F	<i>SGCD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 52,000
Limb-Girdle Muscular Dystrophy, Type 2H	<i>TRIM32</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Limb-Girdle Muscular Dystrophy, Type 2I	<i>FKRP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Limb-Girdle Muscular Dystrophy, Type 2L	<i>ANO5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 660
Lipoamide Dehydrogenase Deficiency	<i>DLD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Lipoid Adrenal Hyperplasia	<i>STAR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,600
Lipoprotein Lipase Deficiency	<i>LPL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	<i>HADHA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Lowe Syndrome	<i>OCRL</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 1,375,000
Lysinuric Protein Intolerance	<i>SLC7A7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,000

Malonyl-CoA Decarboxylase Deficiency	<i>MLYCD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Maple Syrup Urine Disease, Type 1a	<i>BCKDHA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,100
Maple Syrup Urine Disease, Type 1b	<i>BCKDHB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Maple Syrup Urine Disease, Type 2	<i>DBT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,600
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	<i>MKS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Medium Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
MEDNIK Syndrome	<i>AP1S1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 211,000
Megalencephalic Leukoencephalopathy with Subcortical Cysts	<i>MLC1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Megaloblastic Anemia 1	<i>AMN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,300
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 1,000
Methionine Adenosyltransferase I/III Deficiency	<i>MAT3A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Methylmalonic Acidemia (MMAA-Related)	<i>MMAA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Methylmalonic Acidemia (MMAB-Related)	<i>MMAB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Methylmalonic Acidemia (MUT-Related)	<i>MUT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	<i>MMACHC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,800
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	<i>MMADHC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 219,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	<i>LMBRD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600
Methylmalonyl-CoA Epimerase Deficiency	<i>MCEE</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 98,000
Microphthalmia / Anophthalmia	<i>VSX2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 40,000
Mitochondrial Complex I Deficiency (ACAD9-Related)	<i>ACAD9</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Mitochondrial Complex I Deficiency (NDUFA11-Related)	<i>NDUFA11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 414,000
Mitochondrial Complex I Deficiency (NDUFAF5-Related)	<i>NDUFAF5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,800
Mitochondrial Complex I Deficiency (NDUFS6-Related)	<i>NDUFS6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 353,000
Mitochondrial Complex I Deficiency (NDUFV1-Related)	<i>NDUFV1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 870
Mitochondrial Complex I Deficiency / Leigh Syndrome (FOXRED1-Related)	<i>FOXRED1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFAF2-Related)	<i>NDUFAF2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 168,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (NDUFS4-Related)	<i>NDUFS4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 41,000
Mitochondrial Complex IV Deficiency (COX20-related)	<i>COX20</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 42,000
Mitochondrial Complex IV Deficiency (COX6B1-related)	<i>COX6B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,116,000
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 469,000
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 9,200
Mitochondrial DNA Depletion Syndrome 2	<i>TK2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,900
Mitochondrial DNA Depletion Syndrome 3	<i>DGUOK</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 320
Mitochondrial DNA Depletion Syndrome 5	<i>SUCLA2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 78,000
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 449,000
Mitochondrial Trifunctional Protein Deficiency ( <i>HADHB</i> -Related)	<i>HADHB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,000
Molybdenum Cofactor Deficiency A	<i>MOCS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,700
Mucopolipidosis II / IIIA	<i>GNPTAB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Mucopolipidosis III Gamma	<i>GNPTG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 68,000
Mucopolipidosis IV	<i>MCOLN1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,400
Mucopolysaccharidosis Type I	<i>IDUA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Mucopolysaccharidosis Type II	<i>IDS</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 76,000
Mucopolysaccharidosis Type IIIA	<i>SGSH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Mucopolysaccharidosis Type IIIB	<i>NAGLU</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 950
Mucopolysaccharidosis Type IIIC	<i>HGSNAT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Mucopolysaccharidosis Type IIID	<i>GNS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 137,000
Mucopolysaccharidosis Type IVa	<i>GALNS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 690
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	<i>GLB1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Mucopolysaccharidosis type IX	<i>HYAL1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 149,000
Mucopolysaccharidosis type VI	<i>ARSB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Mucopolysaccharidosis VII	<i>GUSB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Mulibrey Nanism	<i>TRIM37</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	<i>PIGN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,800
Multiple Pterygium Syndrome	<i>CHRNA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,900
Multiple Sulfatase Deficiency	<i>SUMF1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 69,000
Muscle-Eye-Brain Disease and Other Related Congenital Muscular Dystrophy-Dystroglycanopathies	<i>POMGNT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Myoneurogastrointestinal Encephalopathy	<i>TYMP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Myotubular Myopathy 1	<i>MTM1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 192,000
N-Acetylglutamate Synthase Deficiency	<i>NAGS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Nemaline Myopathy 2	<i>NEB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Nephrogenic Diabetes insipidus ( <i>AVPR2</i> -related) / Nephrogenic Syndrome of Inappropriate Antidiuresis	<i>AVPR2</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 471,000
Nephrogenic Diabetes Insipidus, Type II	<i>AQP2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Nephronophthisis 2	<i>INVS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 56,000
Nephrotic Syndrome ( <i>NPHS1</i> -Related) / Congenital Finnish Nephrosis	<i>NPHS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 920
Nephrotic Syndrome ( <i>NPHS2</i> -Related) / Steroid-Resistant Nephrotic Syndrome	<i>NPHS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 780
Neurodegeneration due to Cerebral Folate Transport Deficiency	<i>FOLR1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 630
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	<i>PLAA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 229,000
Neuronal Ceroid-Lipofuscinosis ( <i>CLN5</i> -Related)	<i>CLN5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
Neuronal Ceroid-Lipofuscinosis ( <i>CLN6</i> -Related)	<i>CLN6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,600
Neuronal Ceroid-Lipofuscinosis ( <i>CLN8</i> -Related)	<i>CLN8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
Neuronal Ceroid-Lipofuscinosis ( <i>MFSD8</i> -Related)	<i>MFSD8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,200
Neuronal Ceroid-Lipofuscinosis ( <i>PPT1</i> -Related)	<i>PPT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Neuronal Ceroid-Lipofuscinosis ( <i>TPP1</i> -Related)	<i>TPP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,300
Niemann-Pick Disease ( <i>SMPD1</i> -Related)	<i>SMPD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Niemann-Pick Disease, Type C ( <i>NPC1</i> -Related)	<i>NPC1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 690
Niemann-Pick Disease, Type C ( <i>NPC2</i> -Related)	<i>NPC2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600
Nijmegen Breakage Syndrome	<i>NBN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400

Non-Syndromic Hearing Loss ( <i>GJB2</i> -Related)	<i>GJB2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 600
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 830
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	<i>WNT10A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Omenn Syndrome ( <i>RAG2</i> -Related)	<i>RAG2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 17,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	<i>DCLRE1C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Omenn Syndrome and other <i>RAG1</i> -Related Disorders	<i>RAG1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 850
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 4,700
Osteopetrosis 8	<i>SNX10</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 16,000
Otospondylomegaepiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	<i>COL11A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Papillon-Lefevre Syndrome	<i>CTSC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Pendred Syndrome	<i>SLC26A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 390
Peroxisome Biogenesis Disorder 3A and 3B	<i>PEX12</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 30,000
Peroxisome Biogenesis Disorder 7A and 7B	<i>PEX26</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 70,000
Phenylalanine Hydroxylase Deficiency	<i>PAH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 340
Polycystic Kidney Disease, Autosomal Recessive	<i>PKHD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 450
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 25,000
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 139,000
Pontocerebellar Hypoplasia, Type 6	<i>RARS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,600
Primary Carnitine Deficiency	<i>SLC22A5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Primary Ciliary Dyskinesia ( <i>CCDC103</i> -Related)	<i>CCDC103</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 27,000
Primary Ciliary Dyskinesia ( <i>CCDC151</i> -Related)	<i>CCDC151</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 59,000
Primary Ciliary Dyskinesia ( <i>CCDC39</i> -Related)	<i>CCDC39</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Primary Ciliary Dyskinesia ( <i>DNAH5</i> -Related)	<i>DNAH5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Primary Ciliary Dyskinesia ( <i>DNAI1</i> -Related)	<i>DNAI1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Primary Ciliary Dyskinesia ( <i>DNAI2</i> -Related)	<i>DNAI2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 76,000
Primary Ciliary Dyskinesia ( <i>RSPH9</i> -Related)	<i>RSPH9</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 253,000
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 880
Primary Hyperoxaluria, Type 1	<i>AGXT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Primary Hyperoxaluria, Type 2	<i>GRHPR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Primary Hyperoxaluria, Type 3	<i>HOGA1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Progressive Cerebello-Cerebral Atrophy	<i>SEPSECS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Progressive Familial Intrahepatic Cholestasis, Type 2	<i>ABCB11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 950
Progressive Myoclonic Epilepsy, Type 1B	<i>PRICKLE1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 98,000
Progressive Pseudorheumatoid Dysplasia	<i>WISP3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,600
Prolidase Deficiency	<i>PEPD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 30,000
Propionic Acidemia ( <i>PCCA</i> -Related)	<i>PCCA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Propionic Acidemia ( <i>PCCB</i> -Related)	<i>PCCB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Pulmonary Surfactant Dysfunction	<i>ABCA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200

Pycnodysostosis	<i>CTSK</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,100
Pyridoxamine 5'-Phosphate Oxidase Deficiency	<i>PNPO</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Pyridoxine-Dependent Epilepsy	<i>ALDH7A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Pyruvate Carboxylase Deficiency	<i>PC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,000
Pyruvate Dehydrogenase E1-Alpha Deficiency	<i>PDHA1</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 139,000
Pyruvate Dehydrogenase E1-Beta Deficiency	<i>PDHB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Renal Tubular Acidosis and Deafness	<i>ATP6V1B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,600
Retinitis Pigmentosa 25	<i>EYS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Retinitis Pigmentosa 26	<i>CERKL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Retinitis Pigmentosa 28	<i>FAM161A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 34,000
Retinitis Pigmentosa 36	<i>PRCD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 304,000
Retinitis Pigmentosa 59	<i>DHDDS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 601,000
Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16	<i>C8ORF37</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 168,000
Rh Deficiency Syndrome	<i>RHAG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 46,000
Rhizomelic Chondrodysplasia Punctata, Type 1	<i>PEX7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Rhizomelic Chondrodysplasia Punctata, Type 3	<i>AGPS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 620,000
Roberts Syndrome	<i>ESCO2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 139,000
Salla Disease	<i>SLC17A5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
Salt and Pepper Developmental Regression Syndrome	<i>ST3GAL5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 25,000
Sandhoff Disease	<i>HEXB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Schimke Immunoosseous Dysplasia	<i>SMARCA1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Seckel Syndrome 5 / Microcephaly 9	<i>CEP152</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Segawa Syndrome	<i>TH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,100
Sepiapterin Reductase Deficiency	<i>SPR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Severe Combined Immunodeficiency (IL7R-Related)	<i>IL7R</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 20,000
Severe Combined Immunodeficiency (JAK3-Related)	<i>JAK3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Severe Combined Immunodeficiency (PTPRC-Related)	<i>PTPRC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,500
Severe Congenital Neutropenia 4	<i>G6PC3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Severe Neonatal Hyperparathyroidism	<i>CASR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis	<i>POC1A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 108,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 660
Shwachman-Diamond Syndrome	<i>SBDS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Sialidosis, Type I and Type II	<i>NEU1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Sjogren-Larsson Syndrome	<i>ALDH3A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Smith-Lemli-Opitz Syndrome	<i>DHCR7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 750
Spastic Paraplegia 15	<i>ZFYVE26</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 46,000
Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly	<i>SLC1A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 136,000
Spherocytosis, Type 5	<i>EPB42</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Spinal Muscular Atrophy	<i>SMN1</i>	AR	Reduced Risk	SMN1 copy number: 2 SMN2 copy number: 1 c.*3+80T>G: Negative SMN1 Sequencing: Negative Personalized Residual Risk: 1 in 1,107
Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S	<i>IGHMBP2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Spinocerebellar Ataxia with Axonal Neuropathy 3	<i>COA7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000

Spodylocostal Dysostosis 1	<i>DLL3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,200
Spodylometaphyseal Dysplasia (DDR2-Related)	<i>DDR2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 236,000
Spodylothoracic Dysostosis	<i>MESP2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 382,000
Steel Syndrome	<i>COL27A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 93,000
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	<p>Tay-Sachs disease enzyme: Non-carrier</p> <p>White blood cells: Non-carrier</p> <ul style="list-style-type: none"> <li>Hex A%: 69.6% (Non-carrier : 55.0 - 72.0%; Carrier: &lt;50%)</li> <li>Total hexosaminidase activity: 1890 nmol/hr/mg</li> </ul> <p>Plasma: Non-carrier</p> <ul style="list-style-type: none"> <li>Hex A%: 65.1 (Non-carrier : 58.0 - 72.0%; Carrier: &lt;54%)</li> <li>Total hexosaminidase activity: 826 nmol/hr/ml</li> </ul> <p>HEXA Sequencing: Negative</p> <p>Personalized Residual Risk: 1 in 1,400</p>
Thiamine-Responsive Megaloblastic Anemia Syndrome	<i>SLC19A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Thyroid Dysmorphogenesis 1	<i>SLC5A5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 45,000
Thyroid Dysmorphogenesis 2A	<i>TPO</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 910
Thyroid Dysmorphogenesis 3	<i>TG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 850
Thyroid Dysmorphogenesis 4	<i>IYD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Thyroid Dysmorphogenesis 5	<i>DUOXA2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 29,000
Thyroid Dysmorphogenesis 6	<i>DUOX2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 190
Trichohepatoenteric Syndrome 1	<i>TTC37</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Tyrosinemia, Type I	<i>FAH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Tyrosinemia, Type II	<i>TAT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,800
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 1,000
Usher Syndrome, Type IC	<i>USH1C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Usher Syndrome, Type ID	<i>CDH23</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
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 290
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 920
Vitamin D-Dependent Rickets, Type I	<i>CYP27B1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,900
Vitamin D-Resistant Rickets, Type IIA	<i>VDR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 17,000
Walker-Warburg Syndrome and Other FKTN-Related Dystrophies	<i>FKTN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Werner Syndrome	<i>WRN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,200
Wilson Disease	<i>ATP7B</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 350
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 22,000
Wolman Disease / Cholesteryl Ester Storage Disease	<i>LIPA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Woodhouse-Sakati Syndrome	<i>DCAF17</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 81,000
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)	POLH	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Xeroderma Pigmentosum, Group A	XPA	AR	Reduced Risk	Personalized Residual Risk: 1 in 11,000
Xeroderma Pigmentosum, Group C	XPC	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Xeroderma Pigmentosum, Group G	ERCC5	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,000
Zellweger Syndrome Spectrum (PEX10-Related)	PEX10	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,300
Zellweger Syndrome Spectrum (PEX1-Related)	PEX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Zellweger Syndrome Spectrum (PEX2-Related)	PEX2	AR	Reduced Risk	Personalized Residual Risk: 1 in 77,000
Zellweger Syndrome Spectrum (PEX6-Related)	PEX6	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600

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™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.

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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	Specimen Information	Client Information
<b>N4010, DONOR</b>  <b>DOB:</b> ████████ <b>AGE:</b> ██████ Gender: M Phone: NG Patient ID: ████████	Specimen: CF931787F Requisition: 6108713 Lab Ref #: 22816591SPB  Collected: 09/23/2022 Received: 09/24/2022 / 21:29 EDT Reported: 10/05/2022 / 13:42 EDT	Client #: 48041578 NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229

Ward: SEATSB
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**Cytogenetic Report**

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

**CHROMOSOME ANALYSIS, BLOOD**

Order ID: 22-404606  
 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

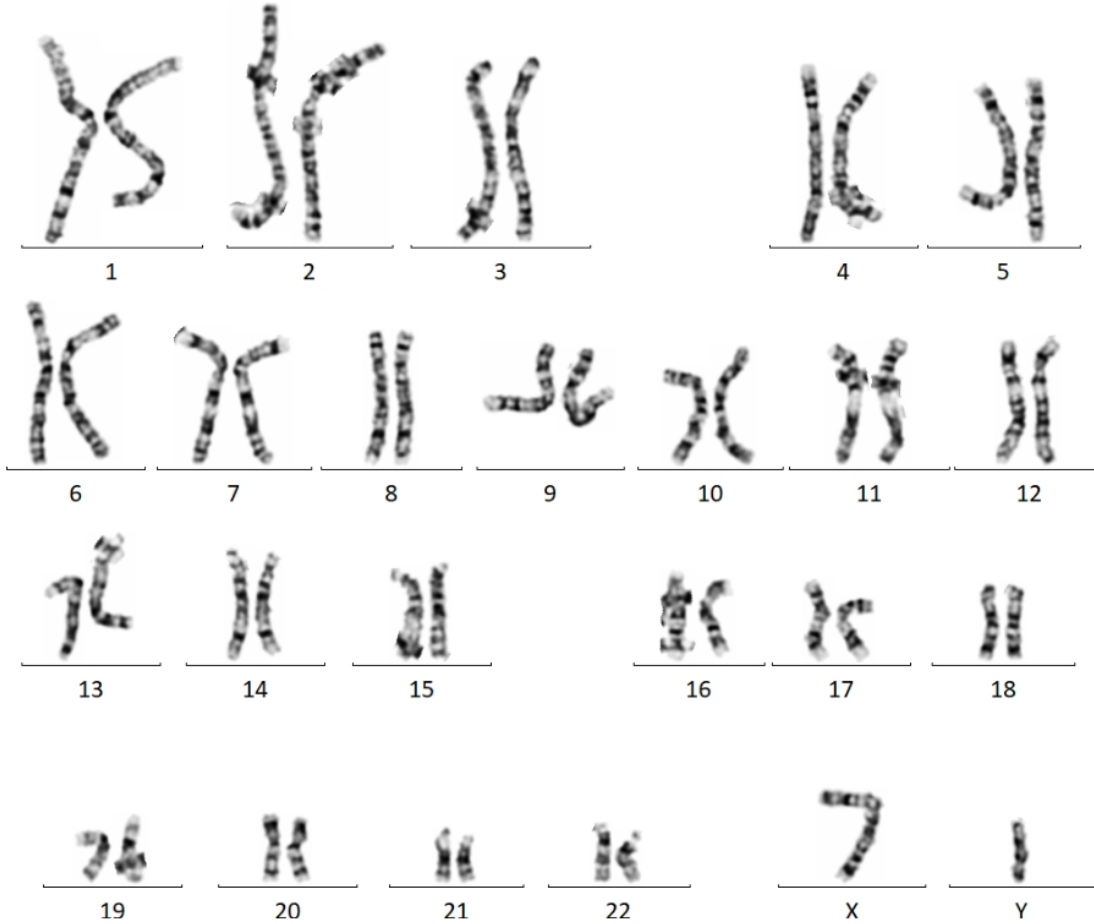
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

Lakshmi J. Nemana, Ph.D., FACMG

Electronic Signature: 10/5/2022 12:25 PM



Patient Information	Specimen Information	Client Information
<b>N4010, DONOR</b>  <b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED] Gender: M Patient ID: [REDACTED]	Specimen: CF931787F Collected: 09/23/2022 Received: 09/24/2022 / 21:29 EDT Reported: 10/05/2022 / 13:42 EDT	Client #: 48041578 GENOMICS, SEMA4



**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