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Genetic Testing Summary

Enclosed are the genetic testing results for

CB 956-B

No amount of genetic testing can guarantee that a child will not be affected with a genetic condition. Genetic testing can inform you of the likelihood of passing on the genetic conditions that are tested for, but it cannot eliminate the risk of passing on any genetic condition.

The genetic conditions Cryobio tests for are inherited in an autosomal recessive manner. This means that the child would have to inherit a genetic mutation from both the sperm source and the egg source to be affected with the condition. When both the sperm source and the egg source have undergone genetic carrier screening and the test results are negative, the risk of a child being affected with the conditions tested for is significantly reduced, but it cannot be completely eliminated.

All recipients should discuss both or their own risk for passing on genetic conditions and whether would benefit from genetic counseling and testing with their health care provider. Before using a donor that is a carrier for a specific recessive genetic condition or conditions, we strongly recommend that the recipient (or egg source, if different) consider genetic counseling and testing to determine if they are a carrier for the same genetic condition or conditions as the donor.

Screening and testing have changed dramatically over the years, and so the screening and testing done on each donor may very depending on the testing that was in place when he was actively in Cryobio's donor program. Earlier donors may not have had as extensive testing as later donors. Screening and testing may change again in the future, so please review the results each time before ordering as both the testing done and the results may change.

Patient Information
Name: Cb 956-B
Date of Birth: [redacted]
Sema4 ID: [redacted]
Client ID: CRYBIO-S488212792
Indication: Carrier Screening

Specimen Information
Specimen Type: Blood
Date Collected: 09/08/2022
Date Received: 09/09/2022
Final Report: 09/24/2022

Referring Provider
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Expanded Carrier Screen (502 genes)

with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
Carrier of Cartilage-Hair Hypoplasia (AR) Associated gene(s): *RMRP* Variant(s) Detected: n.-18_-17insACCTACTC, Likely Pathogenic, Heterozygous (one copy) **Carrier of Congenital Disorder of Glycosylation, Type Ia (AR)** Associated gene(s): *PMM2* Variant(s) Detected: c 422G>A, p.R141H, Pathogenic, Heterozygous (one copy) **Carrier of Congenital Dyserythropoietic Anemia, Type Ia (AR)** Associated gene(s): *CDAN1* Variant(s) Detected: c.2868+1G>A, Likely Pathogenic, Heterozygous (one copy)	**Negative for all other genes tested** To view a full list of genes and diseases tested please see Table 1 in this report

AR=Autosomal recessive; XL=X-linked

Recommendations

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

Cartilage-Hair Hypoplasia (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic promoter variant, n.-18_-17insACCTACTC, was detected in the *RMRP* gene (NR_003051.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for cartilage-hair hypoplasia. Therefore, this individual is expected to be at least a carrier for cartilage-hair hypoplasia. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Cartilage-Hair Hypoplasia?

Cartilage-hair hypoplasia is an autosomal recessive disorder caused by pathogenic variants in the gene *RMRP*. It has the highest prevalence in the Old Order Amish and Finnish populations. All patients have disproportionately short limbs and stature, and most present with skeletal deformities, joint hypermobility, autoimmune deficiency, and anemia. Rarer symptoms include lymphomas, Hirschsprung disease (characterized by bowel dysmotility), and intestinal malabsorption. Skeletal abnormalities will typically occur prenatally, while patients may develop anemia, immunodeficiencies, or Hirschsprung disease within the first few years of life. The incidence of death in childhood is increased due to autoimmune deficiencies and cancer development, but many patients live into adulthood. There have been no reported genotype-phenotype correlations. As clinical symptoms can vary within a family, it is difficult to predict the severity of the disease based on the inherited variants.

Congenital Disorder of Glycosylation, Type Ia (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.422G>A, p.R141H, was detected in the *PMM2* gene (NM_000303.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for congenital disorder of glycosylation, type Ia. Therefore, this individual is expected to be at least a carrier for congenital disorder of glycosylation, type Ia. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Congenital Disorder of Glycosylation, Type Ia?

Congenital disorder of glycosylation, type Ia is an autosomal recessive syndrome caused by pathogenic variants in the gene *PMM2*. While patients have been reported from multiple ethnicities, this disease is more common in the Ashkenazi Jewish and Caucasian populations. This disease may present in infancy, childhood or adolescence, and the clinical manifestations are highly variable. In infants, the disease may present as failure to thrive as a result of feeding problems; later, the disease may manifest as encephalopathy, hypotonia, delayed language and motor development, intellectual disability, stroke-like episodes, and retinitis pigmentosa. Severely affected individuals may die in early childhood, but more mildly affected individuals may survive into adulthood with variable intellectual disability, spinal abnormalities, endocrine dysfunction and coagulopathy. Several specific variants have been associated with milder or more severe disease, and therefore the disease severity may be predicted in some patients.

Congenital Dyserythropoietic Anemia, Type Ia (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic splice site variant, c.2868+1G>A, was detected in the *CDAN1* gene (NM_138477.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for congenital dyserythropoietic anemia, type Ia. Therefore, this individual is expected to be at least a carrier for congenital dyserythropoietic anemia, type Ia. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Congenital Dyserythropoietic Anemia, Type Ia?

Congenital dyserythropoietic anemia, type Ia is an autosomal recessive disorder caused by pathogenic variants in the gene *CDAN1*. This disorder is characterized by moderate to severe anemia that typically is diagnosed in childhood. Rarely the disorder can be detected before birth, where it presents as hydrops fetalis. Individuals typically present with lifelong anemia, jaundice, and hepatosplenomegaly. Rarely individuals are born with limb abnormalities and heart defects. Excess iron absorption can damage tissues and lead to arrhythmia, congestive heart failure, liver cirrhosis, and diabetes. Without proper treatment, complications from iron overload can cause early death. No clear genotype-phenotype correlation has been established.

Test description

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

Alice K Tanner

Alice Tanner, Ph.D., M.S., CGC, FACMG, Laboratory Director
Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D

Genes and diseases tested

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

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

	Disease	Gene	Inheritance Pattern	Status	Detailed Summary
⊕	**Positive**				
	Cartilage-Hair Hypoplasia	*RMRP*	AR	Carrier	n.-18_-17insACCTACTC, Likely Pathogenic, Heterozygous (one copy)
	Congenital Disorder of Glycosylation, Type Ia	*PMM2*	AR	Carrier	c.422G>A, p.R141H, Pathogenic, Heterozygous (one copy)
	Congenital Dyserythropoietic Anemia, Type Ia	*CDAN1*	AR	Carrier	c.2868+1G>A, Likely Pathogenic, Heterozygous (one copy)
⊖	**Negative**				
	2-Methylbutyrylglycinuria	*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 540
	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 29,000
	3-Phosphoglycerate Dehydrogenase Deficiency	*PHGDH*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,600
	6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	*PTS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,800
	***CD59*-Mediated Hemolytic Anemia**	*CD59*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 415,000
	Abetalipoproteinemia	*MTTP*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,200
	Achalasia-Addisonianism-Alacrimia Syndrome	*AAAS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,500
	Achromatopsia (*CNGA3*-Related)	*CNGA3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 410
	Achromatopsia (*CNGB3*-related)	*CNGB3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,300
	Acrodermatitis Enteropathica	*SLC39A4*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 12,000
	Acute Infantile Liver Failure	*TRMU*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,500
	Acyl-CoA Oxidase I Deficiency	*ACOX1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 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 1,200
	Adrenocorticotropic Hormone Deficiency	*TBX19*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,200
	Adrenoleukodystrophy, X-Linked	*ABCD1*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 19,000
	Agammaglobulinemia	*BTK*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 250,000
	Agenesis of the Corpus Callosum	*FRMD4A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 348,000
	Aicardi-Goutieres Syndrome (*RNASEH2C*-Related)	*RNASEH2C*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 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 590
Alpha-Thalassemia Intellectual Disability Syndrome	*ATRX*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 48,000
Alport Syndrome (*COL4A3*-Related)	*COL4A3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,800
Alport Syndrome (*COL4A4*-Related)	*COL4A4*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,500
Alport Syndrome (*COL4A5*-Related)	*COL4A5*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 150,000
Alstrom Syndrome	*ALMS1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,300
Andermann Syndrome	*SLC12A6*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 151,000
Antley-Bixler Syndrome (*POR*-Related)	*POR*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,000
Argininemia	*ARG1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,200
Argininosuccinic Aciduria	*ASL*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
Aromatase Deficiency	*CYP19A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,200
Arthrogryposis, Intellectual Disability, and Seizures	*SLC35A3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 454,000
Asparagine Synthetase Deficiency	*ASNS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 84,000
Aspartylglycosaminuria	*AGA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 13,000
Ataxia With Isolated Vitamin E Deficiency	*TTPA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 32,000
Ataxia-Telangiectasia	*ATM*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,300
Ataxia-Telangiectasia-Like Disorder 1	*MRE11*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,500
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	*SACS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,600
Bardet-Biedl Syndrome (*ARL6*-Related)	*ARL6*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 20,000
Bardet-Biedl Syndrome (*BBS10*-Related)	*BBS10*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,700
Bardet-Biedl Syndrome (*BBS12*-Related)	*BBS12*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,100
Bardet-Biedl Syndrome (*BBS1*-Related)	*BBS1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,400
Bardet-Biedl Syndrome (*BBS2*-Related)	*BBS2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
Bardet-Biedl Syndrome (*BBS4*-Related)	*BBS4*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,700
Bare Lymphocyte Syndrome, Type II	*CIITA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 35,000
Barth Syndrome	*TAZ*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 183,000
Bartter Syndrome, Type 3	*CLCNKB*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 340
Bartter Syndrome, Type 4A	*BSND*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,400
Bernard-Soulier Syndrome, Type A1	*GP1BA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 42,000
Bernard-Soulier Syndrome, Type C	*GP9*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 400
Beta-Globin-Related Hemoglobinopathies	*HBB*	AR	Reduced Risk	**Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies)**: 1 in 1,200 **Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant)**: 1 in 1,000 **Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant)**: 1 in 3,700
Beta-Ketothiolase Deficiency	*ACAT1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,400
Beta-Mannosidosis	*MANBA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,100
BH4-Deficient Hyperphenylalaninemia C	*QDPR*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,100
BH4-Deficient Hyperphenylalaninemia D	*PCBD1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,000
Bilateral Frontoparietal Polymicrogyria	*GPR56*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 92,000
Biotinidase Deficiency	*BTD*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 500
Bloom Syndrome	*BLM*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,400
Canavan Disease	*ASPA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,000
Carbamoylphosphate Synthetase I Deficiency	*CPS1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,100

Carnitine Acylcarnitine Translocase Deficiency	*SLC25A20*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,900
Carnitine Palmitoyltransferase IA Deficiency	*CPT1A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 24,000
Carnitine Palmitoyltransferase II Deficiency	*CPT2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 670
Carpenter Syndrome	*RAB23*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 21,000
Catecholaminergic Polymorphic Ventricular Tachycardia	*CASQ2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,900
Central Hypothyroidism and Testicular Enlargement	*IGSF1*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 781,000
Cerebral Creatine Deficiency Syndrome 1	*SLC6A8*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 208,000
Cerebral Creatine Deficiency Syndrome 2	*GAMT*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,100
Cerebral Creatine Deficiency Syndrome 3	*GATM*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,900
Cerebral Dysgenesis, Neuropathy, Ichthyosis, and Palmoplantar Keratoderma Syndrome	*SNAP29*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 383,000
Cerebrotendinous Xanthomatosis	*CYP27A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,900
Charcot Marie Tooth Disease, Type 4D	*NDRG1*	AR	Reduced Risk	**Personalized Residual Risk** 1 in 730,000
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	*PRPS1*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 114,000
Charcot-Marie-Tooth Disease, X-Linked	*GJB1*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 11,000
Chediak-Higashi Syndrome	*LYST*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,100
Chondrodysplasia Punctata	*ARSE*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 862,000
Choreoacanthocytosis	*VPS13A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,100
Choroideremia	*CHM*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 125,000
Chronic Granulomatous Disease (*CYBA*-Related)	*CYBA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,600
Chronic Granulomatous Disease (*CYBB*-Related)	*CYBB*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 294,000
Citrin Deficiency	*SLC25A13*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,700
Citrullinemia, Type 1	*ASS1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,500
Cockayne Syndrome, Type A	*ERCC8*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,900
Cockayne Syndrome, Type B and other *ERCC6*-Related Disorders	*ERCC6*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,800
Cohen Syndrome	*VPS13B*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,500
Combined Factor V and VIII Deficiency	*LMAN1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,900
Combined Malonic and Methylmalonic Aciduria	*ACSF3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,400
Combined Oxidative Phosphorylation Deficiency 1	*GFM1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 13,000
Combined Oxidative Phosphorylation Deficiency 3	*TSFM*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 27,000
Combined Pituitary Hormone Deficiency 1	*POU1F1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,900
Combined Pituitary Hormone Deficiency 2	*PROP1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,800
Combined Pituitary Hormone Deficiency 3	*LHX3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 140,000
Combined SAP Deficiency	*PSAP*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 44,000
Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1	*GUCY2D*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 400
Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency	*CYP11B1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 520
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	*CYP17A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,800
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	*CYP21A2*	AR	Reduced Risk	*CYP21A2* copy number: 2 *CYP21A2* sequencing: Negative **Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic))**: 1 in 200 **Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic))**: 1 in 1,300
Congenital Adrenal Hypoplasia (*NR0B1*-Related)	*NR0B1*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 353,000
Congenital Adrenal Insufficiency (*CYP11A1*-Related)	*CYP11A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,100

Congenital Amegakaryocytic Thrombocytopenia	*MPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,100
Congenital Bile Acid Synthesis Defect (*AKR1D1*-Related)	*AKR1D1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,900
Congenital Bile Acid Synthesis Defect (*HSD3B7*-Related)	*HSD3B7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,900
Congenital Disorder of Deglycosylation	*NGLY1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,200
Congenital Disorder of Glycosylation, Type Ib	*MPI*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Congenital Disorder of Glycosylation, Type Ic	*ALG6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Congenital Disorder of Glycosylation, Type Im	*DOLK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 134,000
Congenital Dyserythropoietic Anemia Type 2	*SEC23B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Congenital Ichthyosis 4A and 4B	*ABCA12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Congenital Insensitivity to Pain with Anhidrosis	*NTRK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Congenital Muscular Dystrophy (*LAMA2*-Related)	*LAMA2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 640
Congenital Myasthenic Syndrome (*CHAT*-Related)	*CHAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Congenital Myasthenic Syndrome (*CHRNE*-Related)	*CHRNE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Congenital Myasthenic Syndrome (*DOK7*-Related)	*DOK7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Congenital Myasthenic Syndrome (*RAPSN*-Related)	*RAPSN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
Congenital Neutropenia (*HAX1*-Related)	*HAX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Congenital Neutropenia (*VPS45*-Related)	*VPS45*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 112,000
Congenital Nongoitrous Hypothyroidism 1	*TSHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Congenital Nongoitrous Hypothyroidism 4	*TSHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 118,000
Congenital Secretory Chloride Diarrhea 1	*SLC26A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Corneal Dystrophy and Perceptive Deafness	*SLC4A11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Corticosterone Methyloxidase Deficiency	*CYP11B2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 940
Cystic Fibrosis	*CFTR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 440
Cystinosis	*CTNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
Cystinuria (*SLC3A1*-Related)	*SLC3A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 590
Cytochrome C Oxidase Deficiency / Leigh Syndrome (*COX15*-Related)	*COX15*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,300
D-Bifunctional Protein Deficiency	*HSD17B4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Deafness, Autosomal Recessive 3	*MYO15A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240
Deafness, Autosomal Recessive 59	*PJVK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 57,000
Deafness, Autosomal Recessive 7	*TMC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Deafness, Autosomal Recessive 76	*SYNE4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 43,000
Deafness, Autosomal Recessive 77	*LOXHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Deafness, Autosomal Recessive 8/10	*TMPRSS3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 510
Deafness, Autosomal Recessive 9	*OTOF*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 580
Desbuquois Dysplasia 1	*CANT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 24,000
Desmosterolosis	*DHCR24*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 27,000
Diaphanospondylodysostosis	*BMPER*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 18,000
Distal Renal Tubular Acidosis and other *SLC4A1*-related Disorders	*SLC4A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,300
Duchenne Muscular Dystrophy / Becker Muscular Dystrophy	*DMD*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Dyskeratosis Congenita (*DKC1*-related)	*DKC1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 9,259,000
Dyskeratosis Congenita (*RTEL1*-Related)	*RTEL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,800
Dystrophic Epidermolysis Bullosa	*COL7A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 690
Ehlers-Danlos Syndrome, Type VI	*PLOD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Ehlers-Danlos Syndrome, Type VIIC	*ADAMTS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 142,000

Ellis-Van Creveld Syndrome (*EVC2*-Related)	*EVC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,300
Ellis-van Creveld Syndrome (*EVC*-Related)	*EVC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Emery-Dreifuss Myopathy 1	*EMD*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 833,000
Enhanced S-Cone Syndrome	*NR2E3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Ethylmalonic Encephalopathy	*ETHE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,400
Fabry Disease	*GLA*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 7,700
Factor IX Deficiency	*F9*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
Factor VII Deficiency	*F7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 450
Factor XI Deficiency	*F11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Familial Autosomal Recessive Hypercholesterolemia	*LDLRAP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 136,000
Familial Dysautonomia	*IKBKAP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 41,000
Familial Hypercholesterolemia	*LDLR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 280
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Familial Hyperinsulinism (*ABCC8*-Related)	*ABCC8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 450
Familial Hyperinsulinism (*KCNJ11*-Related)	*KCNJ11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,300
Familial Hyperphosphatemic Tumoral Calcinosis	*GALNT3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,800
Familial Mediterranean Fever	*MEFV*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 870
Fanconi Anemia, Group A	*FANCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Fanconi Anemia, Group C	*FANCC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Fanconi Anemia, Group G	*FANCG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Fanconi-Bickel Syndrome	*SLC2A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Fragile X Syndrome	*FMR1*	XL	Reduced Risk	*FMR1* CGG repeat sizes: Not Performed *FMR1* Sequencing: Negative Fragile X CGG triplet repeat expansion testing was not performed at this time, as the patient has either been previously tested or is a male. **Personalized Residual Risk:** 1 in 19,000
Fructose-1,6-Bisphosphatase Deficiency	*FBP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Fucosidosis	*FUCA1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,200
Fumarase Deficiency	*FH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Fundus Albipunctatus	*RDH5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Galactokinase Deficiency	*GALK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 910
Galactose Epimerase Deficiency	*GALE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,500
Galactosemia	*GALT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Galactosialidosis	*CTSA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,900
Gaucher Disease	*GBA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Generalized Thyrotropin-Releasing Hormone Resistance	*TRHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 104,000
Geroderma Osteodysplasticum	*GORAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 60,000
Gitelman Syndrome	*SLC12A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 290
Glanzmann Thrombasthenia (*ITGA2B*-Related)	*ITGA2B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Glanzmann Thrombasthenia (*ITGB3*-Related)	*ITGB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Glutaric Acidemia, Type I	*GCDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 560
Glutaric Acidemia, Type IIa	*ETFA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
Glutaric Acidemia, Type IIb	*ETFB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Glutaric Acidemia, Type IIc	*ETFDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Glutathione Synthetase Deficiency	*GSS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Glycine Encephalopathy (*AMT*-Related)	*AMT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Glycine Encephalopathy (*GLDC*-Related)	*GLDC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 760
Glycogen Storage Disease, Type 0	*GYS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Glycogen Storage Disease, Type Ia	*G6PC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,300

Glycogen Storage Disease, Type Ib	*SLC37A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,300
Glycogen Storage Disease, Type II	*GAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 380
Glycogen Storage Disease, Type III	*AGL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	*GBE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Glycogen Storage Disease, Type IXb	*PHKB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Glycogen Storage Disease, Type V	*PYGM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 940
Glycogen Storage Disease, Type VI	*PYGL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 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 2,100
Gray Platelet Syndrome	*NBEAL2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Growth Hormone Deficiency, Type IB	*GHRHR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Hemochromatosis, Type 2A	*HFE2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Hemochromatosis, Type 3	*TFR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Hereditary Fructose Intolerance	*ALDOB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Hereditary Spastic Paraparesis 49	*TECPR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 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 62,000
HMG-CoA Lyase Deficiency	*HMGCL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Hmg-CoA Synthase 2 Deficiency	*HMGCS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 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 1,000
Homocystinuria, cblE Type	*MTRR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,600
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	*MTR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Hydrocephalus	*L1CAM*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 40,000
Hydrolethalus Syndrome	*HYLS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 52,000
Hyper-Igm Syndrome	*CD40LG*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 1,167,000
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	*SLC25A15*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,700
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	*SARS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,800
Hypohidrotic Ectodermal Dysplasia 1	*EDA*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Hypomagnesemia 1	*TRPM6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Hypomyelinating Leukodystrophy 3	*AIMP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 273,000
Hypomyelinating Leukodystrophy 12	*VPS11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 51,000
Hypoparathyroidism-Retardation-Dysmorphic Syndrome	*TBCE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 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 820
Infantile Cerebral and Cerebellar Atrophy	*MED17*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 75,000
Infantile Neuroaxonal Dystrophy 1 and other *PLA2G6*-Related Disorders	*PLA2G6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 340
Intellectual Disability, Autosomal Recessive 3	*CC2D1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Intrahepatic Cholestasis	*ATP8B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400

Isovaleric Acidemia	*IVD*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,000
Joubert Syndrome 2	*TMEM216*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 152,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	*NPHP1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,100
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	*RPGRIP1L*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 26,000
Junctional Epidermolysis Bullosa (*COL17A1*-Related)	*COL17A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 14,000
Junctional Epidermolysis Bullosa (*ITGA6*-Related)	*ITGA6*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 125,000
Junctional Epidermolysis Bullosa (*ITGB4*-Related)	*ITGB4*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,400
Junctional Epidermolysis Bullosa (*LAMA3*-Related)	*LAMA3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 21,000
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 77,000
Kohlschutter-Tonz Syndrome	*ROGDI*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,300
Krabbe Disease	*GALC*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 340
Lamellar Ichthyosis, Type 1	*TGM1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 900
Laron Dwarfism	*GHR*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,700
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	*CEP290*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,100
Leber Congenital Amaurosis 13	*RDH12*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,100
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	*TULP1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 380
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	*RPE65*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,500
Leber Congenital Amaurosis 4	*AIPL1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,100
Leber Congenital Amaurosis 5	*LCA5*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,800
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	*CRB1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 990
Leigh Syndrome (*NDUFS7*-Related)	*NDUFS7*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 26,000
Leigh Syndrome (*SURF1*-Related)	*SURF1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,700
Leigh Syndrome, French-Canadian Type	*LRPPRC*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 32,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease	*GLE1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,300
Lethal Congenital Contracture Syndrome 2	*ERBB3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 79,000
Lethal Congenital Contracture Syndrome 3	*PIP5K1C*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 67,000
Leukoencephalopathy with Vanishing White Matter	*EIF2B5*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,300
Limb-Girdle Muscular Dystrophy, Type 2A	*CAPN3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 450
Limb-Girdle Muscular Dystrophy, Type 2B	*DYSF*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 600
Limb-Girdle Muscular Dystrophy, Type 2C	*SGCG*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,900
Limb-Girdle Muscular Dystrophy, Type 2D	*SGCA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,600
Limb-Girdle Muscular Dystrophy, Type 2E	*SGCB*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 31,000
Limb-Girdle Muscular Dystrophy, Type 2F	*SGCD*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 52,000
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 1,400
Limb-Girdle Muscular Dystrophy, Type 2L	*ANO5*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 660
Lipoamide Dehydrogenase Deficiency	*DLD*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 11,000
Lipoid Adrenal Hyperplasia	*STAR*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,600
Lipoprotein Lipase Deficiency	*LPL*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,300
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADHA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,200

Lowe Syndrome	*OCRL*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 1,375,000
Lysinuric Protein Intolerance	*SLC7A7*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,000
Malonyl-CoA Decarboxylase Deficiency	*MLYCD*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,800
Maple Syrup Urine Disease, Type 1a	*BCKDHA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,600
Maple Syrup Urine Disease, Type 1b	*BCKDHB*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,100
Maple Syrup Urine Disease, Type 2	*DBT*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,600
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	*MKS1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,700
Medium Chain Acyl-CoA Dehydrogenase Deficiency	*ACADM*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,000
MEDNIK Syndrome	*AP1S1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 211,000
Megalencephalic Leukoencephalopathy with Subcortical Cysts	*MLC1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,300
Megaloblastic Anemia 1	*AMN*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,300
Menkes Disease	*ATP7A*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 172,000
Metachromatic Leukodystrophy	*ARSA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,000
Methionine Adenosyltransferase I/III Deficiency	*MAT1A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,900
Methylmalonic Acidemia (*MMAA*-Related)	*MMAA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 15,000
Methylmalonic Acidemia (*MMAB*-Related)	*MMAB*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
Methylmalonic Acidemia (*MUT*-Related)	*MUT*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,300
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	*MMACHC*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	*MMADHC*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 219,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	*LMBRD1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,500
Methylmalonyl-CoA Epimerase Deficiency	*MCEE*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 98,000
Microphthalmia / Anophthalmia	*VSX2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,400
Mitochondrial Complex I Deficiency (*ACAD9*-Related)	*ACAD9*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,800
Mitochondrial Complex I Deficiency (*NDUFA11*-Related)	*NDUFA11*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 414,000
Mitochondrial Complex I Deficiency (*NDUFAF5*-Related)	*NDUFAF5*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 98,000
Mitochondrial Complex I Deficiency (*NDUFS6*-Related)	*NDUFS6*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 353,000
Mitochondrial Complex I Deficiency (*NDUFV1*-Related)	*NDUFV1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 870
Mitochondrial Complex I Deficiency / Leigh Syndrome (*FOXRED1*-Related)	*FOXRED1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,800
Mitochondrial Complex I Deficiency / Leigh Syndrome (*NDUFAF2*-Related)	*NDUFAF2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 168,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (*NDUFS4*-Related)	*NDUFS4*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 41,000
Mitochondrial Complex IV Deficiency (*COX20*-related)	*COX20*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 42,000
Mitochondrial Complex IV Deficiency (*COX6B1*-related)	*COX6B1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,116,000
Mitochondrial Complex IV Deficiency (*APOPT1*-Related)	*APOPT1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,200
Mitochondrial Complex IV Deficiency (*PET100*-Related)	*PET100*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 469,000
Mitochondrial Complex IV Deficiency (*SCO1*-related)	*SCO1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 13,000
Mitochondrial Complex IV Deficiency / Leigh Syndrome (*COX10*-Related)	*COX10*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,600
Mitochondrial DNA Depletion Syndrome 2	*TK2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,900
Mitochondrial DNA Depletion Syndrome 3	*DGUOK*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,200
Mitochondrial DNA Depletion Syndrome 4A and 4B and other *POLG*-Related Disorders	*POLG*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 180
Mitochondrial DNA Depletion Syndrome 5	*SUCLA2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 78,000

Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	*MPV17*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	*PUS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 204,000
Mitochondrial Trifunctional Protein Deficiency (*HADHB*-Related)	*HADHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Molybdenum Cofactor Deficiency A	*MOCS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
Mucolipidosis II / IIIA	*GNPTAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Mucolipidosis III Gamma	*GNPTG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 49,000
Mucolipidosis IV	*MCOLN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,400
Mucopolysaccharidosis Type I	*IDUA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,300
Mucopolysaccharidosis Type II	*IDS*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 76,000
Mucopolysaccharidosis Type IIIA	*SGSH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Mucopolysaccharidosis Type IIIB	*NAGLU*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 950
Mucopolysaccharidosis Type IIIC	*HGSNAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Mucopolysaccharidosis Type IIID	*GNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 137,000
Mucopolysaccharidosis Type IVa	*GALNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 690
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	*GLB1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Mucopolysaccharidosis type IX	*HYAL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 149,000
Mucopolysaccharidosis type VI	*ARSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Mucopolysaccharidosis VII	*GUSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Mulibrey Nanism	*TRIM37*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	*PIGN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Multiple Pterygium Syndrome	*CHRNG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,900
Multiple Sulfatase Deficiency	*SUMF1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 40,000
Muscle-Eye-Brain Disease and Other *POMGNT1*-Related Congenital Muscular Dystrophy-Dystroglycanopathies	*POMGNT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Myoneurogastrointestinal Encephalopathy	*TYMP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 920
Myotubular Myopathy 1	*MTM1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 192,000
N-Acetylglutamate Synthase Deficiency	*NAGS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Nemaline Myopathy 2	*NEB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Nephrogenic Diabetes insipidus (*AVPR2*-related)/ Nephrogenic Syndrome of Inappropriate Antidiuresis	*AVPR2*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 471,000
Nephrogenic Diabetes Insipidus, Type II	*AQP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,400
Nephronophthisis 2	*INVS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 26,000
Nephrotic Syndrome (*NPHS1*-Related) / Congenital Finnish Nephrosis	*NPHS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 920
Nephrotic Syndrome (*NPHS2*-Related) / Steroid-Resistant Nephrotic Syndrome	*NPHS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 780
Neurodegeneration due to Cerebral Folate Transport Deficiency	*FOLR1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,400
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	*PLAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 122,000
Neuronal Ceroid-Lipofuscinosis (*CLN3*-Related)	*CLN3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,400
Neuronal Ceroid-Lipofuscinosis (*CLN5*-Related)	*CLN5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Neuronal Ceroid-Lipofuscinosis (*CLN6*-Related)	*CLN6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,300
Neuronal Ceroid-Lipofuscinosis (*CLN8*-Related)	*CLN8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,500
Neuronal Ceroid-Lipofuscinosis (*MFSD8*-Related)	*MFSD8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,200
Neuronal Ceroid-Lipofuscinosis (*PPT1*-Related)	*PPT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,500
Neuronal Ceroid-Lipofuscinosis (*TPP1*-Related)	*TPP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Niemann-Pick Disease (*SMPD1*-Related)	*SMPD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100

Niemann-Pick Disease, Type C (*NPC1*-Related)	*NPC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 690
Niemann-Pick Disease, Type C (*NPC2*-Related)	*NPC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Nijmegen Breakage Syndrome	*NBN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 14,000
Non-Syndromic Hearing Loss (*GJB2*-Related)	*GJB2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 360
Oculocutaneous Albinism, Type IA / IB	*TYR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240
Oculocutaneous Albinism, Type IV	*SLC45A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 830
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	*WNT10A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Omenn Syndrome (*RAG2*-Related)	*RAG2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	*DCLRE1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,500
Omenn Syndrome and other *RAG1*-Related Disorders	*RAG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 850
Ornithine Aminotransferase Deficiency	*OAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,400
Ornithine Transcarbamylase Deficiency	*OTC*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 103,000
Osteogenesis Imperfecta, Type XI	*FKBP10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,500
Osteopetrosis 1	*TCIRG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,300
Osteopetrosis 8	*SNX10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 16,000
Otospondylomegaepiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	*COL11A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Papillon-Lefevre Syndrome	*CTSC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,000
Pendred Syndrome	*SLC26A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 390
Peroxisome Biogenesis Disorder 3A and 3B	*PEX12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Peroxisome Biogenesis Disorder 7A and 7B	*PEX26*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 70,000
Phenylalanine Hydroxylase Deficiency	*PAH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 340
Polycystic Kidney Disease, Autosomal Recessive	*PKHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 320
Polyglandular Autoimmune Syndrome, Type 1	*AIRE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,300
Pontocerebellar Hypoplasia, Type 1A	*VRK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 25,000
Pontocerebellar Hypoplasia, Type 1B	*EXOSC3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Pontocerebellar Hypoplasia, Type 2A and Type 4	*TSEN54*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
Pontocerebellar Hypoplasia, Type 2E	*VPS53*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 94,000
Pontocerebellar Hypoplasia, Type 6	*RARS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,600
Primary Carnitine Deficiency	*SLC22A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Primary Ciliary Dyskinesia (*CCDC103*-Related)	*CCDC103*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 27,000
Primary Ciliary Dyskinesia (*CCDC151*-Related)	*CCDC151*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 59,000
Primary Ciliary Dyskinesia (*CCDC39*-Related)	*CCDC39*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Primary Ciliary Dyskinesia (*DNAH5*-Related)	*DNAH5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Primary Ciliary Dyskinesia (*DNAI1*-Related)	*DNAI1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,000
Primary Ciliary Dyskinesia (*DNAI2*-Related)	*DNAI2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 41,000
Primary Ciliary Dyskinesia (*RSPH9*-Related)	*RSPH9*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 54,000
Primary Coenzyme Q10 Deficiency 7	*COQ4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Primary Congenital Glaucoma 3A	*CYP1B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 880
Primary Hyperoxaluria, Type 1	*AGXT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Primary Hyperoxaluria, Type 2	*GRHPR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Primary Hyperoxaluria, Type 3	*HOGA1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Progressive Cerebello-Cerebral Atrophy	*SEPSECS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,400
Progressive Familial Intrahepatic Cholestasis, Type 2	*ABCB11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 610
Progressive Myoclonic Epilepsy, Type 1B	*PRICKLE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 98,000
Progressive Pseudorheumatoid Dysplasia	*WISP3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,600
Prolidase Deficiency	*PEPD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,300

Propionic Acidemia (*PCCA*-Related)	*PCCA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,400
Propionic Acidemia (*PCCB*-Related)	*PCCB*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,900
Pulmonary Surfactant Dysfunction	*ABCA3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
Pycnodysostosis	*CTSK*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,100
Pyridoxamine 5'-Phosphate Oxidase Deficiency	*PNPO*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 10,000
Pyridoxine-Dependent Epilepsy	*ALDH7A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 860
Pyruvate Carboxylase Deficiency	*PC*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,000
Pyruvate Dehydrogenase E1-Alpha Deficiency	*PDHA1*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 139,000
Pyruvate Dehydrogenase E1-Beta Deficiency	*PDHB*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,700
Renal Tubular Acidosis and Deafness	*ATP6V1B1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,600
Retinitis Pigmentosa 25	*EYS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,800
Retinitis Pigmentosa 26	*CERKL*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 13,000
Retinitis Pigmentosa 28	*FAM161A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 34,000
Retinitis Pigmentosa 36	*PRCD*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 304,000
Retinitis Pigmentosa 59	*DHDDS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 201,000
Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16	*C8ORF37*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 50,000
Rh Deficiency Syndrome	*RHAG*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 46,000
Rhizomelic Chondrodysplasia Punctata, Type 1	*PEX7*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 10,000
Rhizomelic Chondrodysplasia Punctata, Type 3	*AGPS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 620,000
Roberts Syndrome	*ESCO2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 67,000
Salla Disease	*SLC17A5*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,400
Salt and Pepper Developmental Regression Syndrome	*ST3GAL5*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 25,000
Sandhoff Disease	*HEXB*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,300
Schimke Immunoosseous Dysplasia	*SMARCAL1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,800
Seckel Syndrome 5 / Microcephaly 9	*CEP152*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,700
Segawa Syndrome	*TH*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,500
Sepiapterin Reductase Deficiency	*SPR*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 35,000
Severe Combined Immunodeficiency (*IL7R*-Related)	*IL7R*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 17,000
Severe Combined Immunodeficiency (*JAK3*-Related)	*JAK3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,100
Severe Combined Immunodeficiency (*PTPRC*-Related)	*PTPRC*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,500
Severe Congenital Neutropenia 4	*G6PC3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,300
Severe Neonatal Hyperparathyroidism	*CASR*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,600
Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis	*POC1A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 108,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	*ACADS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 530
Shwachman-Diamond Syndrome	*SBDS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 940
Sialidosis, Type I and Type II	*NEU1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,100
Sjogren-Larsson Syndrome	*ALDH3A2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,900
Smith-Lemli-Opitz Syndrome	*DHCR7*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 750
Spastic Paraplegia 15	*ZFYVE26*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 46,000
Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly	*SLC1A4*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 136,000
Spherocytosis, Type 5	*EPB42*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,000

Spinal Muscular Atrophy	*SMN1*	AR	Reduced Risk	*SMN1* copy number: >=3 *SMN2* copy number: 1 c.*3+80T>G: Detected *SMN1* Sequencing: Negative **Personalized Residual Risk:** 1 in 618 As additional gene copies are present,the patient's residual risk is expected to be lower than displayed
Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S	*IGHMBP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Spinocerebellar Ataxia with Axonal Neuropathy 3	*COA7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Spondylocostal Dysostosis 1	*DLL3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Spondylometaepiphyseal Dysplasia (*DDR2*-Related)	*DDR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 122,000
Spondylothoracic Dysostosis	*MESP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 225,000
Steel Syndrome	*COL27A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 93,000
Stuve-Wiedemann Syndrome	*LIFR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,000
Sulfate Transporter-Related Osteochondrodysplasia	*SLC26A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Tay-Sachs Disease	*HEXA*	AR	Reduced Risk	Tay-Sachs disease enzyme: Non-carrier White blood cells: Non-carrier • Hex A%: 60.5% (Non-carrier : 55.0 - 72.0%; Carrier: <50%) • Total hexosaminidase activity: 1511 nmol/hr/mg Plasma: Non-carrier • Hex A%: 74.8 (Non-carrier : 58.0 - 72.0%; Carrier: <54%) • Total hexosaminidase activity: 638 nmol/hr/ml *HEXA* Sequencing: Negative **Personalized Residual Risk:** 1 in 400
Thiamine-Responsive Megaloblastic Anemia Syndrome	*SLC19A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Thyroid Dyshormonogenesis 1	*SLC5A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Thyroid Dyshormonogenesis 2A	*TPO*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 400
Thyroid Dyshormonogenesis 3	*TG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 850
Thyroid Dyshormonogenesis 4	*IYD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Thyroid Dyshormonogenesis 5	*DUOXA2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,500
Thyroid Dyshormonogenesis 6	*DUOX2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 190
Trichohepatoenteric Syndrome 1	*TTC37*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Tyrosinemia, Type I	*FAH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Tyrosinemia, Type II	*TAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Tyrosinemia, Type III	*HPD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Usher Syndrome, Type IB	*MYO7A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Usher Syndrome, Type IC	*USH1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Usher Syndrome, Type ID	*CDH23*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 530
Usher Syndrome, Type IF	*PCDH15*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
Usher Syndrome, Type IIA	*USH2A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 290
Usher Syndrome, Type III	*CLRN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	*ACADVL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 600
Vitamin D-Dependent Rickets, Type I	*CYP27B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,500
Vitamin D-Resistant Rickets, Type IIA	*VDR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000

Walker-Warburg Syndrome and Other *FKTN*-Related Dystrophies	*FKTN*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,200
Werner Syndrome	*WRN*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,200
Wilson Disease	*ATP7B*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 350
Wiskott-Aldrich Syndrome (*WAS*-Related)	*WAS*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 1,203,000
Wolcott-Rallison Syndrome	*EIF2AK3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 22,000
Wolman Disease / Cholesteryl Ester Storage Disease	*LIPA*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,200
Woodhouse-Sakati Syndrome	*DCAF17*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 81,000
X-Linked Juvenile Retinoschisis	*RS1*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 40,000
X-Linked Severe Combined Immunodeficiency	*IL2RG*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 250,000
Xeroderma Pigmentosum (*POLH*-Related)	*POLH*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 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 4,300
Zellweger Syndrome Spectrum (*PEX1*-Related)	*PEX1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,000
Zellweger Syndrome Spectrum (*PEX2*-Related)	*PEX2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 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. AmplideX® *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® System were used to identify certain recurrent variants that are complex in nature or are present in low copy repeats. Rare sequence variants may interfere with assay performance.

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

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

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

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

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

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

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^{TM}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_1537172) 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 ΔΔCt formula.

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

Long-range PCR was performed to generate locus-specific amplicons for *CYP21A2*, *HBA1* and *HBA2* and *GBA*. The PCR products were then prepared for short-read NGS sequencing and sequenced. Sequenced reads were mapped back to the original genomic locus and run through the bioinformatics pipeline. If indicated, copy number from MLPA was correlated with the sequencing output to analyze the results. 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^{TM}XT Low-Input technology was utilized in order to create whole-genome libraries for each patient sample. Libraries were then pooled and sequenced on the Illumina NovaSeq platform. Each sequencing lane was multiplexed to achieve 0.4-2x genome coverage, using paired-end 100 bp reads. The sequencing data underwent ancestral analysis using a customized, licensed bioinformatics algorithm that was validated in house. Identified sub-ethnic groupings were binned into one of 7 continental-level groups (African, East Asian, South Asian, Non-Finnish European, Finnish, Native American, and Ashkenazi Jewish) or, for those ethnicities that matched poorly to the continental-level groups, an 8th "unassigned" group, which were then used to select residual risk values for each gene. For individuals belonging to multiple high-level ethnic groupings, a weighting strategy was used to select the most appropriate residual risk. For genes that had insufficient data to calculate ethnic-specific residual risk values, or for sub-ethnic groupings that fell into the "unassigned" group, a "worldwide" residual risk was used. This "worldwide" residual risk was calculated using data from all available continental-level groups.

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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Additional disease-specific references available upon request.