



Donor 6754

Genetic Testing Summary

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

Last Updated: 07/12/22

Donor Reported Ancestry: Nepalese

Jewish Ancestry: No

Genetic Test*	Result	Comments/Donor's Residual Risk**
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Cystic Fibrosis (CF) carrier screening	Negative by gene sequencing in the CFTR gene	1/800
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 and gene sequencing in the SMN1 gene	1/757
Expanded Genetic Disease Carrier Screening Panel attached- 283 diseases by gene sequencing	<p>Carrier: Leber Congenital Amaurosis 5 (LCA5)</p> <p>Carrier: Mucopolysaccharidosis Type IIIB (NAGLU)</p> <p>Carrier: Nephrotic Syndrome (NPHS1-Related) / Congenital Finnish Nephrosis (NPHS1)</p> <p>Carrier: Niemann-Pick Disease, Type C (NPC1-Related)</p> <p>Negative for other genes sequenced</p>	Partner testing recommended before using this donor.

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy. **Donor residual risk is the chance the donor is still a carrier after testing negative.

Patient Information

Name: Donor 6754
 Date of Birth: [REDACTED]
 Sema4 ID: [REDACTED]
 Client ID: [REDACTED]
 Indication: Carrier Screening

Specimen Information

Specimen Type: Blood
 Date Collected: 11/12/2021
 Date Received: 11/13/2021
 Final Report: 11/30/2021

Referring Provider

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

Expanded Carrier Screen Minus TSE (283 genes)
 with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
<p>Carrier of Leber Congenital Amaurosis 5 (AR) Associated gene(s): <i>LCA5</i> Variant(s) Detected: c.838C>T, p.R280X, Pathogenic, Heterozygous (one copy)</p> <p>Carrier of Mucopolysaccharidosis Type IIIB (AR) Associated gene(s): <i>NAGLU</i> Variant(s) Detected: c.1073C>T, p.P358L, Likely Pathogenic, Heterozygous (one copy)</p> <p>Carrier of Nephrotic Syndrome (NPHS1-Related) / Congenital Finnish Nephrosis (AR) Associated gene(s): <i>NPHS1</i> Variant(s) Detected: c.1096A>C, p.S366R, Pathogenic, Heterozygous (one copy)</p> <p>Carrier of Niemann-Pick Disease, Type C (NPC1-Related) (AR) Associated gene(s): <i>NPC1</i> Variant(s) Detected: c.2780C>T, p.A927V, Pathogenic, Heterozygous (one copy)</p>	<p>Negative for all other genes tested To view a full list of genes and diseases tested please see Table 1 in this report</p>

AR=Autosomal recessive; XL=X-linked

Recommendations

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

Interpretation of positive results

Leber Congenital Amaurosis 5 (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic premature stop codon, c.838C>T, p.R280X, was detected in the *LCA5* gene (NM_181714.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Leber congenital amaurosis 5. Therefore, this individual is expected to be at least a carrier for Leber congenital amaurosis 5. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Leber Congenital Amaurosis 5?

Leber congenital amaurosis 5 is an autosomal recessive, pan-ethnic disease that is caused by pathogenic variants in the gene *LCA5*. Clinical features include uncontrollable eye movements and loss of vision that begins during infancy. Patients develop a profound loss of vision at an early age. Life expectancy is not decreased, and no genotype-phenotype correlation has been noted.

Mucopolysaccharidosis Type IIIB (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic missense variant, c.1073C>T, p.P358L, was detected in the *NAGLU* gene (NM_000263.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for mucopolysaccharidosis type IIIB. Therefore, this individual is expected to be at least a carrier for mucopolysaccharidosis type IIIB. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Mucopolysaccharidosis Type IIIB?

Mucopolysaccharidosis type IIIB, also known as Sanfilippo syndrome type B, is a pan-ethnic, autosomal recessive disease caused by pathogenic variants in the gene *NAGLU*. This disease is characterized by severe behavioral disturbances, including hyperactivity, sleep disturbances and destructive behavior. The age of onset is usually around 3 to 4 years of age. Other features include intellectual disability, enlarged liver and spleen, stiffness of the joints, hearing loss and seizures. No treatment is known. Life expectancy is generally reported to be into adolescence or early adulthood, but may be variable. No clear genotype-phenotype correlation is known.

Nephrotic Syndrome (*NPHS1*-Related) / Congenital Finnish Nephrosis (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.1096A>C, p.S366R, was detected in the *NPHS1* gene (NM_004646.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for nephrotic syndrome (*NPHS1*-related). Therefore, this individual is expected to be at least a carrier for nephrotic syndrome (*NPHS1*-related). Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Nephrotic Syndrome (*NPHS1*-Related) / Congenital Finnish Nephrosis?

Nephrotic syndrome (*NPHS1*-related), also known as congenital Finnish nephrosis, is an autosomal recessive disorder caused by pathogenic variants in the gene *NPHS1*. Although it has been reported in ethnicities around the world, it is particularly common in the Finnish population, as well as individuals from certain Amish communities. Onset is during the prenatal period, where affected individuals lose large amounts of protein in their urine. Babies are born small and premature with large placentas. Without a kidney transplant, there will be rapid progression to end-stage kidney failure and death. Many patients are cured after kidney transplant, but some will relapse. Rarely, patients have been identified with a milder phenotype that does not require transplantation. The common Finnish variants cause the severe, infantile-onset disease.

Niemann-Pick Disease, Type C (*NPC1*-Related) (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.2780C>T, p.A927V, was detected in the *NPC1* gene (NM_000271.4). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Niemann-Pick disease, type C (*NPC1*-related). Therefore, this individual is expected to be at least a carrier for Niemann-Pick disease, type C (*NPC1*-related). Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Niemann-Pick Disease, Type C (*NPC1*-Related)?

Niemann-Pick disease, type C (*NPC1*-related) is an autosomal recessive, pan-ethnic neurodegenerative disorder that is caused by pathogenic variants in the gene *NPC1*. The classic presentation includes spastic ataxia and seizures that begin between the ages of 2 and 4, often after a period of normal development. Progressive deterioration leads to the loss of previously learned speech, dystonia that eventually prevents oral feeding, and dementia. Most patients die in adolescence. Some patients may present in infancy with liver and lung problems, many of whom die in infancy. Occasionally, patients can present in adolescence or adulthood with neurologic manifestations. Several specific variants may be associated with the development of either the severe infantile or typical juvenile form, but some variants may not be associated with a known genotype-phenotype correlation.

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.



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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				
Leber Congenital Amaurosis 5	LCA5	AR	Carrier	c.838C>T, p.R280X, Pathogenic, Heterozygous (one copy)
Mucopolysaccharidosis Type IIIB	NAGLU	AR	Carrier	c.1073C>T, p.P358L, Likely Pathogenic, Heterozygous (one copy)
Nephrotic Syndrome (NPHS1-Related) / Congenital Finnish Nephrosis	NPHS1	AR	Carrier	c.1096A>C, p.S366R, Pathogenic, Heterozygous (one copy)
Niemann-Pick Disease, Type C (NPC1-Related)	NPC1	AR	Carrier	c.2780C>T, p.A927V, Pathogenic, Heterozygous (one copy)
Negative				
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	HSD3B2	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,200
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 1,000
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 7,400
6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	PTS	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Abetalipoproteinemia	MTTP	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Achromatopsia (CNGB3-related)	CNGB3	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Acrodermatitis Enteropathica	SLC39A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 55,000
Acute Infantile Liver Failure	TRMU	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Acyl-CoA Oxidase I Deficiency	ACOX1	AR	Reduced Risk	Personalized Residual Risk: 1 in 192,000
Adenosine Deaminase Deficiency	ADA	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100
Adrenoleukodystrophy, X-Linked	ABCD1	XL	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Aicardi-Goutieres Syndrome (SAMHD1-Related)	SAMHD1	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Alpha-Mannosidosis	MAN2B1	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
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 380
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 3,500
Alport Syndrome (COL4A4-Related)	COL4A4	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,700
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 3,400
Andermann Syndrome	SLC12A6	AR	Reduced Risk	Personalized Residual Risk: 1 in 256,000
Argininosuccinic Aciduria	ASL	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Aromatase Deficiency	CYP19A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,200
Arthrogryposis, Mental Retardation, and Seizures	SLC35A3	AR	Reduced Risk	Personalized Residual Risk: 1 in 399,000

Asparagine Synthetase Deficiency	ASNS	AR	Reduced Risk	Personalized Residual Risk: 1 in 307,000
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 240,000
Ataxia-Telangiectasia	ATM	AR	Reduced Risk	Personalized Residual Risk: 1 in 900
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	SACS	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Bardet-Biedl Syndrome (BBS10-Related)	BBS10	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Bardet-Biedl Syndrome (BBS12-Related)	BBS12	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,900
Bardet-Biedl Syndrome (BBS1-Related)	BBS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,400
Bardet-Biedl Syndrome (BBS2-Related)	BBS2	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Bare Lymphocyte Syndrome, Type II	CIITA	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Bartter Syndrome, Type 4A	BSND	AR	Reduced Risk	Personalized Residual Risk: 1 in 73,000
Bernard-Soulier Syndrome, Type A1	GP1BA	AR	Reduced Risk	Personalized Residual Risk: 1 in 66,000
Bernard-Soulier Syndrome, Type C	GP9	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Beta-Globin-Related Hemoglobinopathies	HBB	AR	Reduced Risk	Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies): 1 in 980 Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant): 1 in 81,000 Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant): 1 in 42,000
Beta-Ketothiolase Deficiency	ACAT1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,400
Bilateral Frontoparietal Polymicrogyria	GPR56	AR	Reduced Risk	Personalized Residual Risk: 1 in 64,000
Biotinidase Deficiency	BTBD	AR	Reduced Risk	Personalized Residual Risk: 1 in 370
Bloom Syndrome	BLM	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Canavan Disease	ASPA	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Carbamoylphosphate Synthetase I Deficiency	CPS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Carnitine Palmitoyltransferase IA Deficiency	CPT1A	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
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 28,000
Cartilage-Hair Hypoplasia	RMRP	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
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 7800
Cerebrotendinous Xanthomatosis	CYP27A1	AR	Reduced Risk	Personalized Residual Risk: 1 in 960
Charcot-Marie-Tooth Disease, Type 4D	NDRG1	AR	Reduced Risk	Personalized Residual Risk: 1 in 479,000
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	PRRS1	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
Choreoacanthocytosis	VPS13A	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,900
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 4,800
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 3,600
Citrullinemia, Type 1	ASS1	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Cohen Syndrome	VPS13B	AR	Reduced Risk	Personalized Residual Risk: 1 in 16,000
Combined Malonic and Methylmalonic Aciduria	ACSF3	AR	Reduced Risk	Personalized Residual Risk: 1 in 340
Combined Oxidative Phosphorylation Deficiency 1	GFM1	AR	Reduced Risk	Personalized Residual Risk: 1 in 77,000
Combined Oxidative Phosphorylation Deficiency 3	TSM	AR	Reduced Risk	Personalized Residual Risk: 1 in 21,000
Combined Pituitary Hormone Deficiency 2	PROP1	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
Combined Pituitary Hormone Deficiency 3	LHX3	AR	Reduced Risk	Personalized Residual Risk: 1 in 197,000
Combined SAP Deficiency	PSAP	AR	Reduced Risk	Personalized Residual Risk: 1 in 78,000

Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	<i>CYP17A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,000 <i>CYP21A2</i> copy number: 2 <i>CYP21A2</i> sequencing: Negative
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	<i>CYP21A2</i>	AR	Reduced Risk	Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)): 1 in 300 Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)): 1 in 1,200
Congenital Amegakaryocytic Thrombocytopenia	<i>MPL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,100
Congenital Disorder of Glycosylation, Type Ia	<i>PMM2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,000
Congenital Disorder of Glycosylation, Type Ib	<i>MPI</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Congenital Disorder of Glycosylation, Type Ic	<i>ALG6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Congenital Insensitivity to Pain with Anhidrosis	<i>NTRK1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Congenital Myasthenic Syndrome (CHRNE-Related)	<i>CHRNE</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Congenital Myasthenic Syndrome (RAPSN-Related)	<i>RAPSN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Congenital Neutropenia (HAX1-Related)	<i>HAX1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 82,000
Congenital Neutropenia (VPS45-Related)	<i>VPS45</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 170,000
Corneal Dystrophy and Perceptive Deafness	<i>SLC4A11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Corticosterone Methyloxidase Deficiency	<i>CYP11B2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
Cystic Fibrosis	<i>CFTR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 800
Cystinosis	<i>CTNS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,900
D-Bifunctional Protein Deficiency	<i>HSD17B4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,200
Deafness, Autosomal Recessive 77	<i>LOXHD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 35,000
Duchenne Muscular Dystrophy / Becker Muscular Dystrophy	<i>DMD</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Dyskeratosis Congenita (RTEL1-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 980
Ehlers-Danlos Syndrome, Type VIIC	<i>ADAMTS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 380,000
Ellis-van Creveld Syndrome (EVC-Related)	<i>EVC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,500
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 2,100
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 XI Deficiency	<i>F11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Familial Autosomal Recessive Hypercholesterolemia	<i>LDLRAP1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 192,000
Familial Dysautonomia	<i>IKBKAP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 85,000
Familial Hypercholesterolemia	<i>LDLR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 270
Familial Hyperinsulinism (ABCC8-Related)	<i>ABCC8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Familial Hyperinsulinism (KCNJ11-Related)	<i>KCNJ11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Familial Mediterranean Fever	<i>MEFV</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
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 128,000
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 17,000
Fumarase Deficiency	<i>FH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900

GRACILE Syndrome and Other <i>BCS1L</i> -Related Disorders	<i>BCS1L</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,800
Galactokinase Deficiency	<i>GALK1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Galactosemia	<i>GALT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Gaucher Disease	<i>GBA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Gitelman Syndrome	<i>SLC12A3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 460
Glutaric Acidemia, Type I	<i>GCDH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,400
Glutaric Acidemia, Type IIa	<i>ETFA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,700
Glutaric Acidemia, Type IIc	<i>ETFDH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Glycine Encephalopathy (<i>AMT</i> -Related)	<i>AMT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,700
Glycine Encephalopathy (<i>GLDC</i> -Related)	<i>GLDC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Glycogen Storage Disease, Type II	<i>GAA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,500
Glycogen Storage Disease, Type III	<i>AGL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	<i>GBE1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Glycogen Storage Disease, Type Ia	<i>G6PC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Glycogen Storage Disease, Type Ib	<i>SLC37A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Glycogen Storage Disease, Type V	<i>PYGM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,600
Glycogen Storage Disease, Type VII	<i>PFKM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
HMG-CoA Lyase Deficiency	<i>HMGCL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,700
Hemochromatosis, Type 2A	<i>HFE2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,800
Hemochromatosis, Type 3	<i>TFR2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Hereditary Fructose Intolerance	<i>ALDOB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,700
Hereditary Spastic Paraparesis 49	<i>TECPR2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 112,000
Hermansky-Pudlak Syndrome, Type 1	<i>HPS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
Hermansky-Pudlak Syndrome, Type 3	<i>HPS3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Holocarboxylase Synthetase Deficiency	<i>HLCS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,500
Homocystinuria (<i>CBS</i> -Related)	<i>CBS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
Homocystinuria due to <i>MTHFR</i> Deficiency	<i>MTHFR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,700
Homocystinuria, <i>cbLE</i> Type	<i>MTRR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,600
Hydrolethalus Syndrome	<i>HYLS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 220,000
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	<i>SLC25A15</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Hypohidrotic Ectodermal Dysplasia 1	<i>EDA</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 22,000
Hypophosphatasia	<i>ALPL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Inclusion Body Myopathy 2	<i>GNE</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,600
Infantile Cerebral and Cerebellar Atrophy	<i>MED17</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 308,000
Isovaleric Acidemia	<i>IVD</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,000
Joubert Syndrome 2	<i>TMEM216</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 353,000
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	<i>RPGRIPL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,800
Junctional Epidermolysis Bullosa (<i>LAMA3</i> -Related)	<i>LAMA3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 81,000
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 171,000
Krabbe Disease	<i>GALC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 390
Lamellar Ichthyosis, Type 1	<i>TGM1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,600
Leber Congenital Amaurosis 10 and Other <i>CEP290</i> -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 1,000
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	<i>RPE65</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 490

Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	<i>CRB1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Leigh Syndrome, French-Canadian Type	<i>LRPPRC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 76,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogyrosis with Anterior Horn Cell Disease	<i>GLE1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Leukoencephalopathy with Vanishing White Matter	<i>EIF2B5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,600
Limb-Girdle Muscular Dystrophy, Type 2A	<i>CAPN3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Limb-Girdle Muscular Dystrophy, Type 2B	<i>DYSF</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 930
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 5,000
Limb-Girdle Muscular Dystrophy, Type 2E	<i>SGCB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 19,000
Limb-Girdle Muscular Dystrophy, Type 2I	<i>FKRP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,000
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 7,400
Lipoprotein Lipase Deficiency	<i>LPL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 900
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	<i>HADHA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,900
Lysinuric Protein Intolerance	<i>SLC7A7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
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
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	<i>MKS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Medium Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADM</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 550
Megalencephalic Leukoencephalopathy with Subcortical Cysts	<i>MLC1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,300
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 2,100
Methylmalonic Acidemia (MMAA-Related)	<i>MMAA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Methylmalonic Acidemia (MMAB-Related)	<i>MMAB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Methylmalonic Acidemia (MUT-Related)	<i>MUT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	<i>MMACHC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	<i>MMADHC</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 128,000
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 2,500
Mitochondrial Complex I Deficiency (NDUFAF5-Related)	<i>NDUFAF5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 118,000
Mitochondrial Complex I Deficiency (NDUFS6-Related)	<i>NDUFS6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 216,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	<i>MPV17</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Mitochondrial Myopathy and Sideroblastic Anemia 1	<i>PUS1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 513,000
Mucopolipidosis II / IIIA	<i>GNPTAB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Mucopolipidosis III Gamma	<i>GNPTG</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,400
Mucopolipidosis IV	<i>MCOLN1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Mucopolysaccharidosis Type I	<i>IDUA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,300
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 1,100
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 201,000
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	<i>GLB1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200

Mucopolysaccharidosis type IX	<i>HYAL1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 128,000
Mucopolysaccharidosis type VI	<i>ARSB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Multiple Sulfatase Deficiency	<i>SUMF1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Muscle-Eye-Brain Disease and Other <i>POMGNT1</i> -Related Congenital Muscular Dystrophy-Dystroglycanopathies	<i>POMGNT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,300
Myoneurogastrointestinal Encephalopathy	<i>TYMP</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 5,000
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 7,300
Nemaline Myopathy 2	<i>NEB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,200
Nephrogenic Diabetes Insipidus, Type II	<i>AQP2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,600
Nephrotic Syndrome (<i>NPHS2</i> -Related) / Steroid-Resistant Nephrotic Syndrome	<i>NPHS2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,000
Neuronal Ceroid-Lipofuscinosis (<i>CLN3</i> -Related)	<i>CLN3</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 9,200
Neuronal Ceroid-Lipofuscinosis (<i>CLN5</i> -Related)	<i>CLN5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Neuronal Ceroid-Lipofuscinosis (<i>CLN6</i> -Related)	<i>CLN6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 13,000
Neuronal Ceroid-Lipofuscinosis (<i>CLN8</i> -Related)	<i>CLN8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,500
Neuronal Ceroid-Lipofuscinosis (<i>MFSD8</i> -Related)	<i>MFSD8</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,700
Neuronal Ceroid-Lipofuscinosis (<i>PPT1</i> -Related)	<i>PPT1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
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 1,300
Niemann-Pick Disease, Type C (<i>NPC2</i> -Related)	<i>NPC2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 12,000
Nijmegen Breakage Syndrome	<i>NBN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Non-Syndromic Hearing Loss (<i>GJB2</i> -Related)	<i>GJB2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 970
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	<i>WNT10A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,400
Omenn Syndrome (<i>RAG2</i> -Related)	<i>RAG2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 96,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	<i>DCLRE1C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,900
Ornithine Aminotransferase Deficiency	<i>OAT</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,700
Ornithine Transcarbamylase Deficiency	<i>OTC</i>	XL	Reduced Risk	Personalized Residual Risk: 1 in 103,000
Osteopetrosis 1	<i>TCIRG1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,500
Pendred Syndrome	<i>SLC26A4</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 430
Phenylalanine Hydroxylase Deficiency	<i>PAH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 640
Polycystic Kidney Disease, Autosomal Recessive	<i>PKHD1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Polyglandular Autoimmune Syndrome, Type 1	<i>AIRE</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,000
Pontocerebellar Hypoplasia, Type 1A	<i>VRK1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 47,000
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 1,300
Primary Ciliary Dyskinesia (<i>DNAH5</i> -Related)	<i>DNAH5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,500
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 67,000
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 7,000
Progressive Cerebello-Cerebral Atrophy	<i>SEPSECS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Progressive Familial Intrahepatic Cholestasis, Type 2	<i>ABCB11</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,500
Propionic Acidemia (<i>PCCA</i> -Related)	<i>PCCA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,300
Propionic Acidemia (<i>PCCB</i> -Related)	<i>PCCB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,400
Pycnodysostosis	<i>CTSK</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 450

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 600
Retinitis Pigmentosa 26	<i>CERKL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Retinitis Pigmentosa 28	<i>FAM161A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 79,000
Retinitis Pigmentosa 59	<i>DHDDS</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 201,000
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 1,024,000
Roberts Syndrome	<i>ESCO2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 138,000
Salla Disease	<i>SLC17A5</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 15,000
Sandhoff Disease	<i>HEXB</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Schimke Immunoosseous Dysplasia	<i>SMARCAL1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,800
Segawa Syndrome	<i>TH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,100
Sjogren-Larsson Syndrome	<i>ALDH3A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 14,000
Smith-Lemli-Opitz Syndrome	<i>DHCR7</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,100
Spinal Muscular Atrophy	<i>SMN1</i>	AR	Reduced Risk	SMN1 copy number: 2 SMN2 copy number: 2 c.*3+80T>G: Negative SMN1 Sequencing: Negative Personalized Residual Risk: 1 in 757
Spondylothoracic Dysostosis	<i>MESP2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 306,000
Steel Syndrome	<i>COL27A1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 513,000
Stuve-Wiedemann Syndrome	<i>LIFR</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 6,000
Sulfate Transporter-Related Osteochondrodysplasia	<i>SLC26A2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,800
Tay-Sachs Disease	<i>HEXA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 400
Tyrosinemia, Type I	<i>FAH</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,900
Usher Syndrome, Type IB	<i>MYO7A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,200
Usher Syndrome, Type IC	<i>USH1C</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 930
Usher Syndrome, Type ID	<i>CDH23</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 640
Usher Syndrome, Type IF	<i>PCDH15</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 4,600
Usher Syndrome, Type IIA	<i>USH2A</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 190
Usher Syndrome, Type III	<i>CLRN1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,400
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	<i>ACADVL</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 1,300
Walker-Warburg Syndrome and Other <i>FKTN</i> -Related Dystrophies	<i>FKTN</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 8,300
Wilson Disease	<i>ATP7B</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 200
Wolman Disease / Cholesteryl Ester Storage Disease	<i>LIPA</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 3,200
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
Zellweger Syndrome Spectrum (<i>PEX10</i> -Related)	<i>PEX10</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 7,100
Zellweger Syndrome Spectrum (<i>PEX1</i> -Related)	<i>PEX1</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 10,000
Zellweger Syndrome Spectrum (<i>PEX2</i> -Related)	<i>PEX2</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 96,000
Zellweger Syndrome Spectrum (<i>PEX6</i> -Related)	<i>PEX6</i>	AR	Reduced Risk	Personalized Residual Risk: 1 in 2,100

AR=Autosomal recessive; XL=X-linked

Test methods and comments

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

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

PCR amplification using Asuragen, Inc. AmpliX[®] *FMR1* PCR reagents followed by capillary electrophoresis for allele sizing was performed. Samples positive for *FMR1* CGG repeats in the premutation and full mutation size range were further analyzed by Southern blot analysis to assess the size and methylation status of the *FMR1* CGG repeat.

Genotyping (Analytical Detection Rate >99%)

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

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

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

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

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

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

For spinal muscular atrophy (SMA), the copy numbers of the *SMN1* and *SMN2* genes were analyzed. The individual dosage of exons 7 and 8 as well as the combined dosage of exons 1, 4, 6 and 8 of *SMN1* and *SMN2* were assessed. Copy number gains and losses can be detected with this assay. Depending on ethnicity, 6 - 29 % of carriers will not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *SMN1* gene on one chromosome and loss of *SMN1* (deletion) on the other chromosome (silent 20 carrier) or individuals that carry an intragenic mutation in *SMN1*. Please also note that 2% of individuals diagnosed with SMA have a causative *SMN1* variant that occurred *de novo*, and therefore cannot be picked up by carrier screening in the parents. Analysis of *SMN1* is performed in association with short-read sequencing of exons 2a-7, followed by confirmation using long-range PCR (described below).

The presence of the c.*380T>G (chr5:70,247,901T>G) variant allele in an individual with Ashkenazi Jewish or Asian ancestry is typically indicative of a duplication of *SMN1*. When present in an Ashkenazi Jewish or Asian individual with two copies of *SMN1*, c.*380T>G is likely indicative of a silent (20) carrier. In individuals with two copies of *SMN1* with African American, Hispanic or Caucasian ancestry, the presence or absence of c.*380T>G significantly increases or decreases, respectively, the likelihood of being a silent 20 carrier.

MLPA for Gaucher disease (*GBA*), cystic fibrosis (*CFTR*), and non-syndromic hearing loss (*GJB2/GJB6*) will only be performed if indicated for confirmation of detected CNVs. If *GBA* analysis was performed, the copy numbers of exons 1, 3, 4, and 6 - 10 of the *GBA* gene (of 11 exons total) were analyzed. If *CFTR* analysis was performed, the copy numbers of all 27 *CFTR* exons were analyzed. If *GJB2/GJB6* analysis was performed, the copy number of the two *GJB2* exons were analyzed, as well as the presence or absence of the two upstream deletions of the *GJB2* regulatory region, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854).

Next Generation Sequencing (NGS) (Analytical Detection Rate >95%)

NGS was performed on a panel of genes for the purpose of identifying pathogenic or likely pathogenic variants.

Agilent SureSelect™XT Low Input technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Libraries were pooled and sequenced on the Illumina NovaSeq 9000 platform, using paired-end 100 bp reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house.

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

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

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

Next Generation Sequencing for SMN1

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

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

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

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

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

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

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. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where two copies of a gene are located on the same chromosome in tandem, only the second copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in the tandem allele and this patient is therefore less likely to be a carrier. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to determine the phase (cis/trans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing is required to determine the carrier status.

Residual Risk Calculations

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

Personalized Residual Risk Calculations

Agilent SureSelect™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.

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.

Please note these tests were developed and their performance characteristics were determined by Mount Sinai Genomics, Inc. They have not been cleared or approved by the FDA. These analyses generally provide highly accurate information regarding the patient's carrier or affected status. Despite this high level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, or other rare genetic variants that interfere with analysis. Families should understand that rare diagnostic errors may occur for these reasons.

Exceptions:

Gen	Transcr	Exceptions



e	ipt	
ABC D1	NM_00 00333	Exons 8 and 9
ADA	NM_00 0022.2	Exon 1
ADA MTS 2	NM_01 4244.4	Exon 1
AGP S	NM_00 3659.3	chr2:178,257,512 - 178,257,649 (partial exon 1)
ALM S1	NM_01 5120.4	chr2:73,612,990 - 73,613,041 (partial exon 1)
CEP 290	NM_02 5114.3	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)
CFT R	NM_00 0492.3	Exon 10
COL 4A4	NM_00 0092.4	chr2:227,942,604 - 227,942,619 (partial exon 25)
CYP 11B2	NM_00 0498.3	Exons 3 - 7
DNA I2	NM_02 3036.4	chr17:72,308,136 - 72,308,147 (partial exon 12)
EVC	NM_15 3717.2	Exon 1
FH	NM_00 0143.3	Exon 1
GA MT	NM_00 0156.5	Exon 1
GLD C	NM_00 0170.2	Exon 1
GNP TAB	NM_02 4312.4	chr17:4,837,000 - 4,837,400 (partial exon 2)
GNP TG	NM_03 2520.4	Exon 1
HGS NAT	NM_15 2419.2	Exon 1
IDS	NM_00 0202.6	Exon 3
LIFR	NM_00 2310.5	Exon 19
NEB	NM_00 1271208 .1	Exons 82 - 105
NPC 1	NM_00 0271.4	chr18:21,123,519 - 21,123,538 (partial exon 14)
PUS	NM_02	chr12:132,414,446 - 132,414,532 (partial exon 2)



1	5215.5	
RPG RIP1 L	NM_01 5272.2	Exon 23
SGS H	NM_00 0199.3	chr17:78,194,022 - 78,194,072 (partial exon 1)
SLC 6A8	NM_00 5629.3	<p>Exons 3 and 4</p> <p>SELECTED REFERENCES</p> <p>Carrier Screening Grody W et al. ACMG position statement on prenatal/preconception expanded carrier screening. <i>Genet Med.</i> 2013 15:482-3.</p> <p>Fragile X syndrome: Chen L et al. An information-rich CGG repeat primed PCR that detects the full range of Fragile X expanded alleles and minimizes the need for Southern blot analysis. <i>J Mol Diag</i> 2010 12:589-600.</p> <p>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. <i>Genet Med.</i> 2014 16:149-56.</p> <p>Ashkenazi Jewish Disorders: Scott SA et al. Experience with carrier screening and prenatal diagnosis for sixteen Ashkenazi Jewish Genetic Diseases. <i>Hum. Mutat.</i> 2010 31:1-11.</p> <p>Duchenne Muscular Dystrophy: Flanigan KM et al. Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. <i>Hum Mutat.</i> 2009 30:1657-66.</p> <p>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. <i>Genet Med.</i> 2015 May;17(5):405-24</p> <p>Additional disease-specific references available upon request.</p>