

Donor 6098

Genetic Testing Summary

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

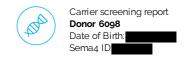
Last Updated: 09/19/22

Donor Reported Ancestry: German, Polish, Russian, Ukrainian Jewish Ancestry: Yes

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	1/1200
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 in the SMN1 gene	1/4800
Expanded Genetic Disease Carrier Screening Panel attached- 283 diseases by gene sequencing	Carrier: Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (CYP21A2) Non-classic variant Carrier: Congenital Amegakaryocytic Thrombocytopenia (MPL) Carrier: Glycogen Storage Disease, Type II (GAA) Carrier: Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies (CEP290) Carrier: Non-Syndromic Hearing Loss (GJB2-Related) Negative for other genes sequenced	Partner testing recommended before using this donor.
Special Testing	regaine for other genes sequenced	
Genes: AP1S1, ACADS	Negative by gene sequencing	See attached results for residual risks

^{*}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 6098

Date of Birth:
Sema4 ID:

Client ID Indication: Carrier Testing

Specimen Information

Specimen Type: Blood
Date Collected: 09/14/2020
Date Received: 09/15/2020
Final Report: 09/29/2020

Referring Provider

Fairfax Cryobank, Inc.



Expanded Carrier Screen (283) Minus TSE

Number of genes tested: 283

SUMMARY OF RESULTS AND RECOMMENDATIONS

① Positive	○ Negative
Carrier of Congenital Adrenal Hyperplasia due to 21-Hydroxylase	
Deficiency (AR)	Negative for all other genes tested
Associated gene(s): CYP21A2	To view a full list of genes and diseases tested
Variant(s) Detected: c.841G>T, p.V281L, Pathogenic, Heterozygous	please see Table 1 in this report
(one copy)	
Carrier of Congenital Amegakaryocytic Thrombocytopenia (AR)	
Associated gene(s): MPL	
Variant(s) Detected: c.79+2T>A, Pathogenic, Heterozygous (one copy)	
Carrier of Glycogen Storage Disease, Type II (AR)	
Associated gene(s): GAA	
Variant(s) Detected: c32-13T>G, Pathogenic, Heterozygous (one	
сору)	
Carrier of Leber Congenital Amaurosis 10 and Other CEP290-	
Related Ciliopathies (AR)	
Associated gene(s): CEP290	
Variant(s) Detected: c.4882C>T, p.Q1628X, Pathogenic, Heterozygous	
(one copy)	
Carrier of Non-Syndromic Hearing Loss (<i>GJB2</i> -Related) (AR)	
Associated gene(s): GJB2	
Variant(s) Detected: c.101T>C, p.M34T, Pathogenic, Heterozygous	
(one copy)	

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

Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (AR)

Results and Interpretation

CYP21A2 copy number: 2

No pathogenic copy number variants detected

CYP21A2 sequencing: c.841G>T, p.V281L, Pathogenic, Heterozygous (one copy)

Genes analyzed: CYP21A2 (NM_000500.6)

Inheritance: Autosomal Recessive

A heterozygous (one copy) pathogenic missense variant, c.841G>T, p.V281L, was detected in the *CYP21A2* gene (NM_000500.6). Please note that this variant is typically causative for the non-classic form of congenital adrenal hyperplasia (PMID: 29450859). Variants associated with the non-classic form usually cause non-classic congenital adrenal hyperplasia when found in trans with a pathogenic allele, regardless of whether the second variant is associated with classic or non-classic disease (PMID: 29450859). Therefore, this individual is expected to be at least a carrier for non-classic congenital adrenal hyperplasia. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is congenital adrenal hyperplasia (due to 21-hydroxylase deficiency)?

Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders resulting from deficiency in the enzymes involved in cortisol biosynthesis. The majority (95%) of CAH cases are due to 21-hydroxylase deficiency (21-OHD CAH), which is caused by homozygous or compound heterozygous pathogenic variants in the gene *CYP21A2*. Approximately 20% of mutant alleles have deletions of 30 kb that have been generated by unequal meiotic crossing-over between the two genes. Another 75% of mutant alleles are due to gene conversion events, where an inactivating mutation from the *CYP21A1P* pseudogene is introduced into one copy of the *CYP21A2* gene, thus making the gene nonfunctional. Three different forms of 21-OHD CAH have been reported: a classic salt wasting form, a classic simple virilizing form, and a nonclassic form.

- The classic salt wasting form results from a nonfunctional enzyme and is the most severe. The phenotype includes prenatal onset of virilization and inadequate adrenal aldosterone secretion that can result in fatal salt-wasting crises.
- The classic simple virilizing form results from low levels of functional enzyme and involves prenatal virilization but no salt-wasting.
- The non-classic form, which results from a mild enzyme deficiency, occurs postnatally and involves phenotypes associated with hyperandrogenism, such as hirsutism, delayed menarche, and infertility.

Treatment for the classic forms of the disorder include glucocorticoid and mineralocorticoid replacement therapy, as well as the possibility of feminizing genitoplasty, while patients with the non-classic form usually do not require treatment. The life expectancy for this disorder can be normal with treatment, however the occurrence of salt-wasting crises can be fatal.

Congenital Amegakaryocytic Thrombocytopenia (AR)

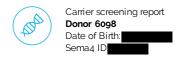
Results and Interpretation

A heterozygous (one copy) pathogenic splice site variant, c.79+2T>A, was detected in the *MPL* gene (NM_005373.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for congenital amegakaryocytic thrombocytopenia. Therefore, this individual is expected to be at least a carrier for congenital amegakaryocytic thrombocytopenia. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Congenital Amegakaryocytic Thrombocytopenia?

Congenital amegakaryocytic thrombocytopenia is an autosomal recessive syndrome caused by pathogenic variants in the gene *MPL*. This disease is predominantly observed in the Ashkenazi Jewish population due to a founder mutation, although it has also been reported in non-Jewish populations. Clinical features include a congenital reduction of platelets and absence of megakaryocytes in the bone marrow, resulting in bone marrow failure and pancytopenia in childhood. Hematopoietic stem cell transplantation is currently the only curative therapy; however, 50% of patients will die before receiving a transplant or due to transplant complications. No genotype-phenotype correlation has been observed.





Glycogen Storage Disease, Type II (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic intronic variant, c.-32-13T>G, was detected in the *GAA* gene (NM_000152.3). Individuals with this variant tend to have a later onset of the disease, slower progression and longer lifespan. While the age of onset can vary between infancy to more than 50 years of age, no patients with this variant have been reported to develop the classic infantile form of Pompe disease. Homozygotes for this variant are not expected to be affected with infantile Pompe disease, unless this variant is present as part of a complex allele. When this variant is present in trans with a pathogenic variant, it is considered to be causative for glycogen storage disease, type II. Therefore, this individual is expected to be at least a carrier for glycogen storage disease, type II. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Glycogen Storage Disease, Type II?

Glycogen storage disease type II, also known as Pompe disease, is an autosomal recessive disorder that is caused by pathogenic variants in the gene *GAA*. While it is found in populations worldwide, it is most prevalent in individuals of Ashkenazi Jewish or African descent. Symptoms can manifest in infancy or later in life. There are two main forms of the disease.

- Infantile-onset disease is characterized by poor feeding and failure to thrive, hypotonia, and an enlarged heart. If untreated, the cardiac manifestations usually cause death in the first year of life. A variant form of the infantile-onset disease has a slower progression, with death in occurring in childhood. Enzyme replacement therapy may slow the disease progression.
- Late-onset disease can begin any time after infancy. These patients do not usually have cardiac problems, but have muscle weakness and difficulty breathing. Patients may reach adulthood, but life expectancy is reduced.

Specific variants have been associated with the infantile-onset or late-onset forms; however, the correlation is not always absolute, and some variants do not have a known genotype-phenotype correlation.

Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic premature stop codon, c.4882C>T, p.Q1628X, was detected in the *CEP290* gene (NM_025114.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for a *CEP290* -related ciliopathy. Therefore, this individual is expected to be at least a carrier for a *CEP290* -related ciliopathy. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies?

CEP290 - related ciliopathies include four different overlapping disorders, known as Leber congenital amaurosis, Bardet-Biedl syndrome, Joubert syndrome and Meckel syndrome. All diseases are inherited in an autosomal recessive manner and are can be caused by pathogenic variants in the gene CEP290. Leber congenital amaurosis manifests with vision loss at birth or in early infancy. Patients have profound loss of vision at an early age, and some have been reported to have intellectual disability. Bardet-Biedl syndrome is characterized by obesity, intellectual disability, kidney disease, and loss of vision beginning with loss of night vision and progression to tunnel vision and blindness. Clinical features of Joubert syndrome include intellectual disability, brain malformations, ocular problems including uncontrollable eye movements and loss of vision, and kidney cysts leading to end-stage renal disease. Meckel syndrome often manifests before birth and is characterized by occipital encephalocele, brain malformations, facial dysmorphism, renal agenesis, and extra digits. Life expectancy varies according to the phenotype; it is not reduced in patients with Leber congenital amaurosis, but death in infancy is expected in patients with Meckel syndrome. Currently, it is not possible to predict which phenotype a patient will have based on the variants inherited.

Non-Syndromic Hearing Loss (GJB2-Related) (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.101T>C, p.M34T, was detected in the *GJB2* gene (NM_004004.5). Please note that this variant has been reported to have a variable penetrance, and some individuals with a pathogenic variant on the opposite allele may not have hearing loss. When this variant is present in trans with a pathogenic variant, it is considered to be causative for non-syndromic hearing loss (*GJB2*-related). Therefore, this individual is expected to be at least a carrier for non-syndromic hearing loss (*GJB2*-related). Heterozygous





carriers are not expected to exhibit symptoms of this disease.

What is Non-Syndromic Hearing Loss (GJB2-Related)?

Non-syndromic hearing loss (*GJB2*-related) is an autosomal recessive disorder that is caused by pathogenic variants in the gene *GJB2*. It is found in individuals of many different ethnicities, but it more prevalent in individuals of Ashkenazi Jewish descent, as well as Caucasians and Asians. Patients with this form of hearing loss do not experience any other disease manifestations. Hearing loss is usually present from birth and does not progress in severity over time. The level of hearing loss can vary between patients from mild to profound. Patients with two inactivating variants are more likely to have profound hearing loss, whereas patients with two non-inactivating variants are more likely to have mild hearing loss. However, the variability that exists between patients means that it may not be possible to predict the severity of an individual's hearing loss based on their genotype. Life expectancy is not reduced.

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, and **go.sema4.com/residualrisk** for specific detection rates and residual risk by ethnicity. With individuals of mixed ethnicity, it is recommended to use the highest residual risk estimate. Only variants determined to be pathogenic or likely pathogenic are reported in this carrier screening test.



Ashley Birch, Ph.D., DABMGG, FCCMG, Laboratory Director

Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D.

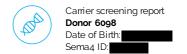
Genes and diseases tested

For specific detection rates and residual risk by ethnicity, please visit **go.sema4.com/residualrisk**

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

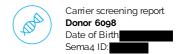
	Disease	Gene	Inheritance Pattern	Status	Detailed Summary
(+)	Positive				
	Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	CYP21A2	AR	Carrier	CYP21A2 copy number: 2 No pathogenic copy number variants detected CYP21A2 sequencing: c.841G>T, p.V281L,
	Congonital Amongology (eq. tip Thyomb on top onic	MPL	AR	Carrier	Pathogenic, Heterozygous (one copy) c.79+2T>A, Pathogenic, Heterozygous (one copy)
-	Congenital Amegakaryocytic Thrombocytopenia Glycogen Storage Disease, Type II	GAA	AR	Carrier	c32-13T>G, Pathogenic, Heterozygous (one copy)
	Leber Congenital Amaurosis 10 and Other CEP290- Related Ciliopathies	CEP290	AR	Carrier	c.4882C>T, p.Q1628X, Pathogenic, Heterozygous (one copy)
	Non-Syndromic Hearing Loss (GJB2-Related)	GJB2	AR	Carrier	c.101T>C, p.M34T, Pathogenic, Heterozygous (one copy)
Θ	Negative				
	3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	HSD3B2	AR	Reduced Risk	
	3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1- Related)	MCCC1	AR	Reduced Risk	





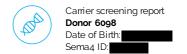
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)	MCCC2	AR	Reduced Risk	
(MCCC2-Related) 3-Methylglutaconic Aciduria, Type III	OPA3	AR	Reduced Risk	
3-Phosphoglycerate Dehydrogenase Deficiency	PHGDH	AR	Reduced Risk	
6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	PTS	AR	Reduced Risk	
Abetalipoproteinemia	MTTP	AR	Reduced Risk	
<u>' '</u>	CNGB3	AR	Reduced Risk	
Achromatopsia (<i>CNGB3</i> -related) Acrodermatitis Enteropathica		AR	Reduced Risk	
Acrode matris Enteropatrica Acute Infantile Liver Failure	SLC39A4 TRMU	AR	Reduced Risk	
		AR	Reduced Risk	
Advancing Descriptions Deficiency	ACOX1			
Adenosine Deaminase Deficiency	ADA	AR	Reduced Risk	
Adrenoleukodystrophy, X-Linked	ABCD1	XL	Reduced Risk	
Aicardi-Goutieres Syndrome (SAMHD1-Related)	SAMHD1	AR	Reduced Risk	
Alpha-Mannosidosis	MAN2B1	AR	Reduced Risk	
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
Alpha-Thalassemia Mental Retardation Syndrome	ATRX	XL	Reduced Risk	
Alport Syndrome (<i>COL4A3</i> -Related)	COL4A3	AR	Reduced Risk	
Alport Syndrome (<i>COL4A4</i> -Related)	COL4A4	AR	Reduced Risk	
Alport Syndrome (COL4A5-Related)	COL4A5	XL	Reduced Risk	
Alstrom Syndrome	ALMS1	AR	Reduced Risk	
Andermann Syndrome	SLC12A6	AR	Reduced Risk	
Argininosuccinic Aciduria	ASL	AR	Reduced Risk	
Aromatase Deficiency	CYP19A1	AR	Reduced Risk	
Arthrogryposis, Mental Retardation, and Seizures	SLC35A3	AR	Reduced Risk	
Asparagine Synthetase Deficiency	ASNS	AR	Reduced Risk	
Aspartylglycosaminuria	AGA	AR	Reduced Risk	
Ataxia With Isolated Vitamin E Deficiency	TTPA	AR	Reduced Risk	
Ataxia-Telangiectasia	ATM	AR	Reduced Risk	
Autosomal Recessive Spastic Ataxia of Charlevoix- Saguenay	SACS	AR	Reduced Risk	
Bardet-Biedl Syndrome (<i>BBS10</i> -Related)	BBS10	AR	Reduced Risk	
Bardet-Biedl Syndrome (<i>BBS12</i> -Related)	BBS12	AR	Reduced Risk	
Bardet-Biedl Syndrome (BBS1-Related)	BBS1	AR	Reduced Risk	
Bardet-Biedl Syndrome (BBS2-Related)	BBS2	AR	Reduced Risk	
Bare Lymphocyte Syndrome, Type II	CIITA	AR	Reduced Risk	
· · · · · · · · · · · · · · · · · · ·	BSND	AR	Reduced Risk	
Bartter Syndrome, Type 4A	GP1BA			
Bernard-Soulier Syndrome, Type A1		AR	Reduced Risk	
Bernard-Soulier Syndrome, Type C	GP9	AR	Reduced Risk	
Beta-Globin-Related Hemoglobinopathies	HBB	AR	Reduced Risk	
Beta-Ketothiolase Deficiency	ACAT1	AR	Reduced Risk	
Bilateral Frontoparietal Polymicrogyria	GPR56	AR	Reduced Risk	
Biotinidase Deficiency	BTD	AR	Reduced Risk	
Bloom Syndrome	BLM	AR	Reduced Risk	
Canavan Disease	ASPA	AR	Reduced Risk	
Carbamoylphosphate Synthetase I Deficiency	CPS1	AR	Reduced Risk	
Carnitine Palmitoyltransferase IA Deficiency	CPT1A	AR	Reduced Risk	
Carnitine Palmitoyltransferase II Deficiency	CPT2	AR	Reduced Risk	
Carpenter Syndrome	RAB23	AR	Reduced Risk	
Cartilage-Hair Hypoplasia	RMRP	AR	Reduced Risk	
Cerebral Creatine Deficiency Syndrome 1	SLC6A8	XL	Reduced Risk	
Cerebral Creatine Deficiency Syndrome 2	GAMT	AR	Reduced Risk	
Cerebrotendinous Xanthomatosis	CYP27A1	AR	Reduced Risk	
Charcot-Marie-Tooth Disease, Type 4D	NDRG1	AR	Reduced Risk	
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	PRPS1	XL	Reduced Risk	
Charcot-Marie-Tooth Disease, X-Linked	GJB1	XL	Reduced Risk	
			D 1 10:1	
Choreoacanthocytosis	VPS13A	AR	Reduced Risk	





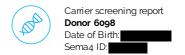
Chronic Granulomatous Disease (CYBA-Related)	CYBA	AR	Reduced Risk	
Chronic Granulomatous Disease (CYBB-Related)	CYBB	XL	Reduced Risk	
Citrin Deficiency	SLC25A13	AR	Reduced Risk	
Citrullinemia, Type 1	ASS1	AR	Reduced Risk	
Cohen Syndrome	VPS13B	AR	Reduced Risk	
Combined Malonic and Methylmalonic Aciduria	ACSF3	AR	Reduced Risk	
Combined Oxidative Phosphorylation Deficiency 1	GFM1	AR	Reduced Risk	
Combined Oxidative Phosphorylation Deficiency 3	TSFM	AR	Reduced Risk	
Combined Pituitary Hormone Deficiency 2	PROP1	AR	Reduced Risk	
Combined Pituitary Hormone Deficiency 3	LHX3	AR	Reduced Risk	
Combined SAP Deficiency	PSAP	AR	Reduced Risk	
Congenital Adrenal Hyperplasia due to 17-Alpha- Hydroxylase Deficiency	CYP17A1	AR	Reduced Risk	
Congenital Disorder of Glycosylation, Type Ia	PMM2	AR	Reduced Risk	
Congenital Disorder of Glycosylation, Type Ib	MPI	AR	Reduced Risk	
Congenital Disorder of Glycosylation, Type Ic	ALG6	AR	Reduced Risk	
Congenitat Discrete or drycosylation, hyperc	NTRK1	AR	Reduced Risk	
·	CHRNE	AR		
Congenital Myasthenic Syndrome (CHRNE-Related)			Reduced Risk	
Congenital Myasthenic Syndrome (<i>RAPSN</i> -Related)	RAPSN	AR	Reduced Risk	
Congenital Neutropenia (HAX1-Related)	HAX1	AR	Reduced Risk	
Congenital Neutropenia (VPS45-Related)	VPS45	AR	Reduced Risk	
Corneal Dystrophy and Perceptive Deafness	SLC4A11	AR	Reduced Risk	
Corticosterone Methyloxidase Deficiency	CYP11B2	AR	Reduced Risk	
Cystic Fibrosis	CFTR	AR	Reduced Risk	
Cystinosis	CTNS	AR	Reduced Risk	
D-Bifunctional Protein Deficiency	HSD17B4	AR	Reduced Risk	
Deafness, Autosomal Recessive 77	LOXHD1	AR	Reduced Risk	
Duchenne Muscular Dystrophy / Becker Muscular Dystrophy	DMD	XL	Reduced Risk	
Dyskeratosis Congenita (RTEL1-Related)	RTEL1	AR	Reduced Risk	
Dystrophic Epidermolysis Bullosa	COL7A1	AR	Reduced Risk	
Ehlers-Danlos Syndrome, Type VIIC	ADAMTS2	AR	Reduced Risk	
Ellis-van Creveld Syndrome (EVC-Related)	EVC	AR	Reduced Risk	
Emery-Dreifuss Myopathy 1	EMD	XL	Reduced Risk	
Enhanced S-Cone Syndrome	NR2E3	AR	Reduced Risk	
	ETHE1	AR	Reduced Risk	
Ethylmalonic Encephalopathy			Reduced Risk	
Fabry Disease	GLA	XL		
Factor IX Deficiency	F9	XL	Reduced Risk	
Factor XI Deficiency	F11	AR	Reduced Risk	
Familial Autosomal Recessive Hypercholesterolemia	LDLRAP1	AR	Reduced Risk	
Familial Dysautonomia	IKBKAP	AR	Reduced Risk	
Familial Hypercholesterolemia	LDLR	AR	Reduced Risk	
Familial Hyperinsulinism (ABCC8-Related)	ABCC8	AR	Reduced Risk	
Familial Hyperinsulinism (KCNJ11-Related)	KCNJ11	AR	Reduced Risk	
Familial Mediterranean Fever	MEFV	AR	Reduced Risk	
Fanconi Anemia, Group A	<i>FANCA</i>	AR	Reduced Risk	
Fanconi Anemia, Group C	FANCC	AR	Reduced Risk	
Fanconi Anemia, Group G	FANCG	AR	Reduced Risk	
				FMR1 CGG repeat sizes: Not Performed
Fragile X Syndrome	FMR1	XL	Reduced Risk	FMR1 Sequencing: Negative Fragile X CGG triplet repeat expansion testing v not performed at this time, as the patient has ei been previously tested or is a male.
			Reduced Risk Reduced Risk	Fragile X CGG triplet repeat expansion testing not performed at this time, as the patient has e
Fumarase Deficiency GRACILE Syndrome and Other BCS1L-Related	FMR1 FH BCS1L	XL AR AR		Fragile X CGG triplet repeat expansion testing not performed at this time, as the patient has e
Fumarase Deficiency GRACILE Syndrome and Other BCS1L-Related Disorders	FH BCS1L	AR AR	Reduced Risk Reduced Risk	Fragile X CGG triplet repeat expansion testing not performed at this time, as the patient has e
Furnarase Deficiency GRACILE Syndrome and Other BCS1L-Related Disorders Galactokinase Deficiency	FH BCS1L GALK1	AR AR AR	Reduced Risk Reduced Risk Reduced Risk	Fragile X CGG triplet repeat expansion testing not performed at this time, as the patient has e
Fumarase Deficiency GRACILE Syndrome and Other BCS1L-Related Disorders	FH BCS1L	AR AR	Reduced Risk Reduced Risk	Fragile X CGG triplet repeat expansion testing not performed at this time, as the patient has eight





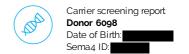
Glutaric Acidemia, Type I	GCDH	AR	Reduced Risk
Glutaric Acidemia, Type Ila	ETFA	AR	Reduced Risk
Glutaric Acidemia, Type IIc	ETFDH	AR	Reduced Risk
Glycine Encephalopathy (AMT-Related)	AMT	AR	Reduced Risk
Glycine Encephalopathy (GLDC-Related)	GLDC	AR	Reduced Risk
Glycogen Storage Disease, Type III	AGL	AR	Reduced Risk
Glycogen Storage Disease, Type IV / Adult	GBE1	AR	Reduced Risk
Polyglucosan Body Disease	GDEI	7111	Neddeca Nisk
Glycogen Storage Disease, Type la	G6PC	AR	Reduced Risk
Glycogen Storage Disease, Type Ib	SLC37A4	AR	Reduced Risk
Glycogen Storage Disease, Type V	PYGM	AR	Reduced Risk
Glycogen Storage Disease, Type VII	PFKM	AR	Reduced Risk
HMG-CoA Lyase Deficiency	HMGCL	AR	Reduced Risk
Hemochromatosis, Type 2A	HFE2	AR	Reduced Risk
Hemochromatosis, Type 3	TFR2	AR	Reduced Risk
Hereditary Fructose Intolerance	ALDOB	AR	Reduced Risk
Hereditary Spastic Paraparesis 49	TECPR2	AR	Reduced Risk
Hermansky-Pudlak Syndrome, Type 1	HPS1	AR	Reduced Risk
Hermansky-Pudlak Syndrome, Type 3	HPS3	AR	Reduced Risk
Holocarboxylase Synthetase Deficiency	HLCS	AR	Reduced Risk
<u> </u>			
Homocystinuria (CBS-Related)	CBS	AR	Reduced Risk
Homocystinuria due to MTHFR Deficiency	MTHFR	AR	Reduced Risk
Homocystinuria, cblEType	MTRR	AR	Reduced Risk
Hydrolethalus Syndrome	HYLS1	AR	Reduced Risk
Hyperornithinemia-Hyperammonemia-	SLC25A15	AR	Reduced Risk
Homocitrullinuria Syndrome			
Hypohidrotic Ectodermal Dysplasia 1	EDA	XL	Reduced Risk
Hypophosphatasia	ALPL	AR	Reduced Risk
Inclusion Body Myopathy 2	GNE	AR	Reduced Risk
Infantile Cerebral and Cerebellar Atrophy	MED17	AR	Reduced Risk
Isovaleric Acidemia	IVD	AR	Reduced Risk
Joubert Syndrome 2	TMEM216	AR	Reduced Risk
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH	RPGRIP1L	AR	Reduced Risk
Syndrome	NI GNII IL	AIX	Neduced Nisk
Junctional Epidermolysis Bullosa (LAMA3-Related)	LAMA3	AR	Reduced Risk
Junctional Epidermolysis Bullosa (<i>LAMB3</i> -Related)	LAMB3	AR	Reduced Risk
Junctional Epidermolysis Bullosa (<i>LAMC2</i> -Related)	LAMC2	AR	Reduced Risk
Krabbe Disease	GALC	AR	Reduced Risk
Lamellar Ichthyosis, Type 1	TGM1	AR	Reduced Risk
Leber Congenital Amaurosis 13	RDH12	AR	Reduced Risk
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	RPE65		
	RPEU5	AR	Reduced Risk
		AR AR	Reduced Risk Reduced Risk
Leber Congenital Amaurosis 5	LCA5	AR	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12			
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	LCA5 CRB1	AR AR	Reduced Risk Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type	LCA5	AR	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal	LCA5 CRB1	AR AR	Reduced Risk Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease	LCA5 CRB1 LRPPRC GLE1	AR AR AR AR	Reduced Risk Reduced Risk Reduced Risk Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter	LCA5 CRB1 LRPPRC GLE1 EIF2B5	AR AR AR AR AR	Reduced Risk Reduced Risk Reduced Risk Reduced Risk Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3	AR AR AR AR AR AR	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Hom Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF	AR AR AR AR AR AR AR AR AR	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B Limb-Girdle Muscular Dystrophy, Type 2C	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG	AR	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B Limb-Girdle Muscular Dystrophy, Type 2C Limb-Girdle Muscular Dystrophy, Type 2D	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG SGCA	AR	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2C Limb-Girdle Muscular Dystrophy, Type 2D Limb-Girdle Muscular Dystrophy, Type 2D	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG SGCA SGCB	AR	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B Limb-Girdle Muscular Dystrophy, Type 2C Limb-Girdle Muscular Dystrophy, Type 2D Limb-Girdle Muscular Dystrophy, Type 2E Limb-Girdle Muscular Dystrophy, Type 2E	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG SGCA SGCB FKRP	AR A	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B Limb-Girdle Muscular Dystrophy, Type 2C Limb-Girdle Muscular Dystrophy, Type 2D Limb-Girdle Muscular Dystrophy, Type 2E Limb-Girdle Muscular Dystrophy, Type 2I Limb-Girdle Muscular Dystrophy, Type 2I	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG SGCA SGCB FKRP DLD	AR A	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B Limb-Girdle Muscular Dystrophy, Type 2C Limb-Girdle Muscular Dystrophy, Type 2D Limb-Girdle Muscular Dystrophy, Type 2E Limb-Girdle Muscular Dystrophy, Type 2I Lipoamide Dehydrogenase Deficiency Lipoid Adrenal Hyperplasia	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG SGCA SGCB FKRP DLD STAR	AR A	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B Limb-Girdle Muscular Dystrophy, Type 2C Limb-Girdle Muscular Dystrophy, Type 2D Limb-Girdle Muscular Dystrophy, Type 2E Limb-Girdle Muscular Dystrophy, Type 2I Limb-Girdle Muscular Dystrophy, Type 2I	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG SGCA SGCB FKRP DLD	AR A	Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B Limb-Girdle Muscular Dystrophy, Type 2C Limb-Girdle Muscular Dystrophy, Type 2D Limb-Girdle Muscular Dystrophy, Type 2E Limb-Girdle Muscular Dystrophy, Type 2I Lipoamide Dehydrogenase Deficiency Lipoid Adrenal Hyperplasia	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG SGCA SGCB FKRP DLD STAR LPL	AR A	Reduced Risk Reduced Risk
Leber Congenital Amaurosis 5 Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy Leigh Syndrome, French-Canadian Type Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease Leukoencephalopathy with Vanishing White Matter Limb-Girdle Muscular Dystrophy, Type 2A Limb-Girdle Muscular Dystrophy, Type 2B Limb-Girdle Muscular Dystrophy, Type 2C Limb-Girdle Muscular Dystrophy, Type 2D Limb-Girdle Muscular Dystrophy, Type 2E Limb-Girdle Muscular Dystrophy, Type 2I Lipoamide Dehydrogenase Deficiency Lipoid Adrenal Hyperplasia Lipoprotein Lipase Deficiency	LCA5 CRB1 LRPPRC GLE1 EIF2B5 CAPN3 DYSF SGCG SGCA SGCB FKRP DLD STAR	AR A	Reduced Risk





Maple Syrup Urine Disease, Type 1a	BCKDHA	AR	Reduced Risk
Maple Syrup Urine Disease, Type 1b	BCKDHB	AR	Reduced Risk
Meckel 1 / Bardet-Biedl Syndrome 13	MKS1	AR	Reduced Risk
Medium Chain Acyl-CoA Dehydrogenase Deficiency	ACADM	AR	Reduced Risk
Megalencephalic Leukoencephalopathy with	MLC1	AR	Reduced Risk
Subcortical Cysts	MLCI	AR	neduced hisk
Menkes Disease	ATP7A	XL	Reduced Risk
Metachromatic Leukodystrophy	ARSA	AR	Reduced Risk
Methylmalonic Acidemia (MMAA-Related)	MMAA	AR	Reduced Risk
Methylmalonic Acidemia (MMAB-Related)	MMAB	AR	Reduced Risk
Methylmalonic Acidemia (MUT-Related)	MUT	AR	Reduced Risk
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	MMACHC	AR	Reduced Risk
Methylmalonic Aciduria and Homocystinuria, Cobalamin DType	MMADHC	AR	Reduced Risk
Microphthalmia / Anophthalmia	VSX2	AR	Reduced Risk
Mitochondrial Complex I Deficiency (ACADg-Related)	ACAD9	AR	Reduced Risk
Mitochondrial Complex Deficiency (NDUFAF5-Related)	NDUFAF5	AR	Reduced Risk
Mitochondrial Complex Deficiency (NDUFS6-Related)	NDUFS6	AR	Reduced Risk
Mitochondrial DNA Depletion Syndrome 6 / Navajo	7420700	7 11 1	reduced Hor
Neurohepatopathy	MPV17	AR	Reduced Risk
Mitochondrial Myopathy and Sideroblastic Anemia 1	PUS1	AR	Reduced Risk
Mucolipidosis II / IIIA	GNPTAB	AR	Reduced Risk
Mucolipidosis III Gamma	GNPTG	AR	Reduced Risk
Mucolipidosis IV	MCOLN1	AR	Reduced Risk
Mucopolysaccharidosis Type I	IDUA	AR	Reduced Risk
Mucopolysaccharidosis Type II	IDS	XL	Reduced Risk
Mucopolysaccharidosis Type IIIA	SGSH	AR	Reduced Risk
Mucopolysaccharidosis Type IIIB	NAGLU	AR	Reduced Risk
Mucopolysaccharidosis Type IIIC	HGSNAT	AR	Reduced Risk
Mucopolysaccharidosis Type IIID	GNS	AR	Reduced Risk
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	GLB1	AR	Reduced Risk
Mucopolysaccharidosis type IX	HYAL1	AR	Reduced Risk
Mucopolysaccharidosis type VI	ARSB	AR	Reduced Risk
Multiple Sulfatase Deficiency	SUMF1	AR	Reduced Risk
Muscle-Eye-Brain Disease and Other POMGNT1-	3011111	7111	Neddeca Nisk
Related Congenital Muscular Dystrophy- Dystroglycanopathies	POMGNT1	AR	Reduced Risk
Myoneurogastrointestinal Encephalopathy	TYMP	AR	Reduced Risk
Myotubular Myopathy 1	MTM1	XL	Reduced Risk
N-Acetylglutamate Synthase Deficiency	NAGS	AR	Reduced Risk
Nemaline Myopathy 2	NEB	AR	Reduced Risk
Nephrogenic Diabetes Insipidus, Type II	AQP2	AR	Reduced Risk
Nephrotic Syndrome (NPHS1-Related) / Congenital Finnish Nephrosis	NPHS1	AR	Reduced Risk
Nephrotic Syndrome (NPHS2-Related) / Steroid- Resistant Nephrotic Syndrome	NPHS2	AR	Reduced Risk
Neuronal Ceroid-Lipofuscinosis (CLN3-Related)	CLN3	AR	Reduced Risk
Neuronal Ceroid-Lipofuscinosis (CLN5-Related)	CLN3 CLN5	AR	Reduced Risk
Neuronal Ceroid-Lipofuscinosis (CLN6-Related)	CLN6	AR	Reduced Risk
Neuronal Ceroid-Lipofuscinosis (CLN8-Related)	CLN8	AR	Reduced Risk
Neuronal Ceroid-Lipofuscinosis (MFSD8-Related)	MFSD8	AR	Reduced Risk
Neuronal Ceroid-Lipofuscinosis (PPT1-Related)	PPT1	AR	Reduced Risk
Neuronal Ceroid-Lipofuscinosis (TPP1-Related)	TPP1	AR	Reduced Risk
Niemann-Pick Disease (SMPD1-Related)	SMPD1	AR	Reduced Risk
Niemann-Pick Disease, Type C (NPC1-Related)	NPC1	AR	Reduced Risk
Niemann-Pick Disease, Type C (NPC2-Related)	NPC1 NPC2	AR	Reduced Risk
			Reduced Risk
Nijmegen Breakage Syndrome Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-	NBN WNT10A	AR AR	Reduced Risk
Passarge Syndrome			
Omenn Syndrome (<i>RAG2</i> -Related)	RAG2	AR	Reduced Risk





Omenn Syndrome / Severe Combined	DCI DE4C	A.D.	Dadwaad Dide	
Immunodeficiency, Athabaskan-Type	DCLRE1C	AR	Reduced Risk	
Ornithine Aminotransferase Deficiency	OAT	AR	Reduced Risk	
Ornithine Transcarbamylase Deficiency	OTC	XL	Reduced Risk	
Osteopetrosis 1	TCIRG1	AR	Reduced Risk	
Pendred Syndrome	SLC26A4	AR	Reduced Risk	
Phenylalanine Hydroxylase Deficiency	PAH	AR	Reduced Risk	
Polycystic Kidney Disease, Autosomal Recessive	PKHD1	AR	Reduced Risk	
Polyglandular Autoimmune Syndrome, Type 1	AIRE	AR	Reduced Risk	
Pontocerebellar Hypoplasia, Type 1A	VRK1	AR	Reduced Risk	
Pontocerebellar Hypoplasia, Type 6	RARS2	AR	Reduced Risk	
Primary Carnitine Deficiency	SLC22A5	AR	Reduced Risk	
Primary Ciliary Dyskinesia (DNAH5-Related)	DNAH5	AR	Reduced Risk	
Primary Ciliary Dyskinesia (DNA/1-Related)	DNAI1	AR	Reduced Risk	
Primary Ciliary Dyskinesia (DNAI2-Related)	DNAI2	AR	Reduced Risk	
Primary Hyperoxaluria, Type 1	AGXT	AR	Reduced Risk	
Primary Hyperoxaluria, Type 2	GRHPR	AR	Reduced Risk	
Primary Hyperoxaluria, Type 3	HOGA1	AR	Reduced Risk	
Progressive Cerebello-Cerebral Atrophy Progressive Typesillal Introduced Chalacteria Type 2	SEPSECS	AR	Reduced Risk	
Progressive Familial Intrahepatic Cholestasis, Type 2 Propionic Acidemia (PCCA-Related)	ABCB11 PCCA	AR AR	Reduced Risk Reduced Risk	
Propionic Acidemia (PCCB-Related)	PCCA	AR	Reduced Risk Reduced Risk	
Pycnodysostosis	CTSK	AR	Reduced Risk	
Pyruvate Dehydrogenase E1-Alpha Deficiency	PDHA1	XL	Reduced Risk	
Pyruvate Dehydrogenase E1-Beta Deficiency	PDHB	AR	Reduced Risk	
Renal Tubular Acidosis and Deafness	ATP6V1B1	AR	Reduced Risk	
Retinitis Pigmentosa 25	EYS	AR	Reduced Risk	
Retinitis Pigmentosa 26	CERKL	AR	Reduced Risk	
Retinitis Pigmentosa 28	FAM161A	AR	Reduced Risk	
Retinitis Pigmentosa 59	DHDDS	AR	Reduced Risk	
Rhizomelic Chondrodysplasia Punctata, Type 1	PEX7	AR	Reduced Risk	
Rhizomelic Chondrodysplasia Punctata, Type 3	AGPS	AR	Reduced Risk	
Roberts Syndrome	ESCO2	AR	Reduced Risk	
Salla Disease	SLC17A5	AR	Reduced Risk	
Sandhoff Disease	HEXB	AR	Reduced Risk	
Schimke Immunoosseous Dysplasia	SMARCAL1	AR	Reduced Risk	
Segawa Syndrome	TH	AR	Reduced Risk	
Sjogren-Larsson Syndrome	ALDH3A2	AR	Reduced Risk	
Smith-Lemli-Opitz Syndrome	DHCR7	AR	Reduced Risk	
				SMN1 copy number: >=3
Spinal Muscular Atrophy	SMN1	AR	Reduced Risk	SMN2 copy number: 1
				c.*3+80T>G: Negative
Spondylothoracic Dysostosis	MESP2	AR	Reduced Risk	
Steel Syndrome	COL27A1	AR	Reduced Risk	
Stuve-Wiedemann Syndrome	LIFR	AR	Reduced Risk	
Sulfate Transporter-Related Osteochondrodysplasia	SLC26A2	AR	Reduced Risk	
Tay-Sachs Disease	HEXA	AR	Reduced Risk	
Tyrosinemia, Type I	FAH	AR	Reduced Risk	
Usher Syndrome, Type IB	MYO7A	AR	Reduced Risk	
Usher Syndrome, Type IC	USH1C	AR	Reduced Risk	
Usher Syndrome, Type ID	CDH23	AR	Reduced Risk	
Usher Syndrome, Type IF	PCDH15	AR	Reduced Risk	
Usher Syndrome, Type IIA	USH2A	AR	Reduced Risk	
Usher Syndrome, Type III	CLRN1	AR	Reduced Risk	
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	ACADVL	AR	Reduced Risk	
Walker-Warburg Syndrome and Other FKTN-Related	FKTN	AR	Reduced Risk	
Dystrophies		45	Deduc ISI	
Wilson Disease	ATP7B	AR	Reduced Risk	_
Wolman Disease / Cholesteryl Ester Storage Disease	LIPA	AR	Reduced Risk	





X-Linked Severe Combined Immunodeficiency	IL2RG	XL	Reduced Risk	
Zellweger Syndrome Spectrum (PEX10-Related)	PEX10	AR	Reduced Risk	
Zellweger Syndrome Spectrum (PEX1-Related)	PEX1	AR	Reduced Risk	
Zellweger Syndrome Spectrum (PEX2-Related)	PEX2	AR	Reduced Risk	
Zellweger Syndrome Spectrum (PEX6-Related)	PEX6	AR	Reduced Risk	

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 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%.

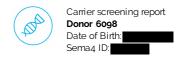
For alpha thalassemia, the copy numbers of the *HBA1* and *HBA2* genes were analyzed. Alpha-globin gene deletions, triplications, and the Constant Spring (CS) mutation are assessed. This test is expected to detect approximately 90% of all alpha-thalassemia mutations, varying by ethnicity. Carriers of 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 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).





The presence of the c.*3+80T>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.*3+80T>G is likely indicative of a silent (2+0) carrier. In individuals with two copies of *SMN1* with African American, Hispanic 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 SureSelectTMXT 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.

Exceptions: ABCD1 (NM_000033.3) exons 8 and 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); ALMS1 (NM_015120.4) chr2:73,612.990 - 73,613,041 (partial exon 1); 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_00092.4) chr2:227,942,604 - 227,942,619 (partial exon 25); CYP11B2 (NM_000498.3) exons 3 - 7; DNAI2 (NM_023036.4) chr17:72,308.136 - 72,308.147 (partial exon 12); EVC (NM_153717.2) exon 1; 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; HGSNAT (NM_152419.2) exon 1; IDS (NM_000202.6) exon 3; LIFR (NM_002310.5) exon 19; NEB (NM_001271208.1) exons 82 - 105; NPC1 (NM_000271.4) chr18:21,123.519 - 21,123.538 (partial exon 14); 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.

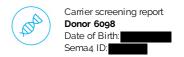
This test will detect variants within the exons and the intron-exon boundaries of the target regions. Variants outside these regions may not be detected, including, but not limited to, UTRs, promoters, and deep intronic areas, or regions that fall into the Exceptions mentioned above. This technology 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.

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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 $\Delta\Delta$ Ct 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.

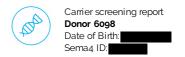
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Carrier frequencies and detection rates for each ethnicity were calculated trough the combination of internal curations of >30,000 variants and genomic frequency data from >138,000 individuals across seven ethnic groups in the gnomAD database. Additional 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.

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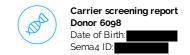
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Additional disease-specific references available upon request.





Patient Information

Name: Donor 6098

Date of Birth:
Sema4 ID:

Client ID:

Indication: Carrier Screening

Specimen Information

Specimen Type: Purified DNA
Date Collected: 07/11/2022
Date Received: 07/14/2022
Final Report: 07/27/2022



Custom Carrier Screen (2 genes)

with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

Negative

Negative for all genes tested: ACADS, and AP1S1

To view a full list of genes and diseases tested please see Table 1 in this report

AR=Autosomal recessive: XL=X-linked

Recommendations

• 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.

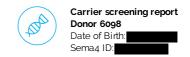
Test description

This patient was tested for the genes listed above using one or more of the following methodologies: target capture and short-read sequencing, long-range PCR followed by short-read sequencing, targeted genotyping, and/or 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 known pathogenic or likely pathogenic variants are reported. This carrier screening test does not report likely benign variants and variants of uncertain significance (VUS). If reporting of likely benign variants and VUS are desired in this patient, please contact the laboratory at 800-298-6470, option 2 to request an amended report.

Anastasia Larmore, Ph.D., Associate 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
Θ	Negative				
	MEDNIK Syndrome	AP1S1	AR	Reduced Risk	Personalized Residual Risk: 1 in 294,000
	Short-Chain Acyl-CoA Dehydrogenase Deficiency	ACADS	AR	Reduced Risk	Personalized Residual Risk: 1 in 660

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 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%)

 $MLPA^{\otimes}$ 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%.

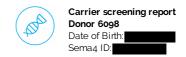
For alpha thalassemia, the copy numbers of the *HBA1* and *HBA2* genes were analyzed. Alpha-globin gene deletions, triplications, and the Constant Spring (CS) mutation are assessed. This test is expected to detect approximately 90% of all alpha-thalassemia mutations, varying by ethnicity. carriers of 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). The presence of the c.*3+80T>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.*3+80T>G is likely indicative of a silent (2+0) carrier. In individuals with two copies of *SMN1* with African American, Hispanic 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 SureSelectTMXT 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.

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); APOPTI (NM_ 032374.4) chr14:104,040,437-104,040,455 (partial exon 3); CDANI (NM_138477.2) exon 2; CEP152 (NM_014985.3) chr15;49,061,146-49,061,165 (partial exon 14) and exon 22; CEP2go (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; DNA/2 (NM_023036.4) chr17;72,308,136-72,308,147 (partial exon 12); DOK7 (NM_173660.4) chr4:3,465,131-3,465,161 (partial exon 1) and exon 2; DUOX2 (NM_014080.4) exons 6-8; EIF2AK3 (NM_004836.5 exon 8; EVC (NM_153717.2) exon 1; F5 (NM_000130.4) chr1:169,551,662-169,551,679 (partial exon 2); FH (NM_000143.3) exon 1; GAMT (NM_000156.5 exon 1; GLDC (NM_000170.2) exon 1; GNPTAB (NM_024312.4) chr17;4,837,000-4,837,400 (partial exon 2); GNPTG (NM_032520.4) exon 1; GHR (NM_000163,4) exon 3; GYS2 (NM_021957,3) chr12:21,699,370-21,699,409 (partial exon 12); HGSNAT (NM_152419,2) exon 1; IDS (NM_000202.6 exon 3; ITGB4 (NM_000213.4) chr17:73,749,976-73,750,060 (partial exon 33); JAK3 (NM_000215.3) chr19:17,950,462-17,950,483 (partial exon 10); LIFR (NM_002310.5 exon 19; LMBRD1 (NM_018368.3) chr6:70,459,226-70,459,257 (partial exon 5), chr6:70,447,828-70,447,836 (partial exon 7) and exon 12; LYST (NM_000081.3) chr1:235,944,158-235,944,176 (partial exon 16) and chr1:235,875,350-235,875,362 (partial exon 43); MLYCD (NM_012213.2) chr16:83,933,242-83,933,282 (partial exon 1); MTR (NM_000254.2) chr1 237,024,418-237,024,439 (partial exon 20) and chr1:237,038,019-237,038,029 (partial exon 24); NBEAL2 (NM_015175.2) chr3 47,021,385-47,021,407 (partial exon 1); NEB (NM_001271208.1 exons 82-105; NPC1 (NM_000271.4) chr18:21,123,519-21,123,538 (partial exon 14); NPHP1 (NM_000272.3) chr2:110,937,251-110,937,253 (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) chrg:136,223,269-136,223,307 (partial exon 1); TRPM6 (NM_017662.4) chrg: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

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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.

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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 these tests were developed and their performance characteristics were determined by Sema4 Opco, 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.

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