Patient Name	DOB	Sex	MRN	Invitae #
Jane Doe		Female		
Clinical Team	**Report Date**	**Sample Type**	**Sample Collection Date**	**Sample Accession Date**
		Blood		

Test Performed
Sequence analysis and deletion/duplication testing of the 288 genes listed in the results section below.

- Invitae Comprehensive Carrier Screen

Reason for Testing
Patient/partner is pregnant (Est. due date: 07.21.2019)

INVITAE COMPREHENSIVE CARRIER SCREEN RESULTS

About this test

This carrier test evaluated 288 genes for genetic changes (variants) that are associated with an increased risk of having a child with a genetic disorder. Knowledge of carrier status for one of these disorders may provide information that can be used to assist with family planning and/or preparation.

Result

POSITIVE

Summary

This test shows the presence of clinically significant genetic change(s) in this individual in the gene(s) indicated below. No other clinically significant changes were identified in the remaining genes evaluated with this test.

Results	Gene	Variant(s)	Inheritance	Partner testing recommended
CARRIER: Alpha-thalassemia	HBA1/ HBA2	HBA1: Deletion (Entire coding sequence)	Autosomal recessive	Yes
CARRIER: Bardet-Biedl syndrome (BBS10-related)	BBS10	c.850C>T (p.Gln284*)	Autosomal recessive	Yes
CARRIER: Gaucher disease	GBA	c.1448T>C (p.Leu483Pro)	Autosomal recessive	Yes

Next steps

- See the table above for recommendations regarding testing of this individual's reproductive partner.
- Even for genes that have a negative test result, there is always a small risk that an individual could still be a carrier. This is called "residual risk." See the table below for residual risks, which presumes a negative family history of the disorders listed.
- Genetic counseling is recommended to further explain the implications of this test result and assess family health history, which may point to health information that merits additional consideration.
- All patients, regardless of result, may wish to consider additional screening for hemoglobinopathies by complete blood count (CBC) and hemoglobin electrophoresis, if this has not already been completed.
- Individuals can register their tests at https://www.invitae.com/patients/ to access online results, educational resources, and next steps.

Laboratory Director Tina Hambuch, Ph.D., FACMG
NY Laboratory Director Swaroop Aradhya, Ph.D., FACMG
Invitae 1400 16th Street, San Francisco, CA 94103
E: clientservices@invitae.com P: 415.374.7782 or 800.436.3037

Clinical summary

CARRIER: Alpha-thalassemia

A single Pathogenic variant, HBA1: Deletion (Entire coding sequence), was identified. This individual is expected to be a "silent" carrier of alpha-thalassemia (aa/a-).

What is alpha-thalassemia?

Alpha-thalassemia is a blood disorder in which the body does not produce enough hemoglobin, a protein in red blood cells that carries oxygen throughout the body. Carriers of one copy (aa/a-, also called "silent" carrier) or two copies (a-/a- or aa/--, also called alpha-thalassemia trait) of certain changes in the HBA1 or HBA2 gene(s) typically have few or no health problems, though some may have other symptoms— usually mild— such as anemia or other blood problems. Another form of alpha-thalassemia, HbH disease (a-/--), occurs in patients who have three copies of certain changes in the HBA1 or HBA2 genes. HbH typically causes mild to moderate anemia, hepatosplenomegaly, and yellowing of the eyes and skin (jaundice). Some affected individuals also have bone changes such as overgrowth of the upper jaw or an unusually prominent forehead. HbH usually presents in early childhood, and with treatment, affected individuals typically live into adulthood. A more severe form, HbH/Constant Spring, can present with similar features, however life threatening anemia can occur during fevers. The most severe form of alpha-thalassemia, Hb Bart syndrome (--/--), occurs in patients who have certain changes in both of their HBA1 genes and both of their HBA2 genes. In Hb Bart, excess fluid builds up in the body of affected fetuses before birth; newborns have severe symptoms, including red blood cells that don't bring enough oxygen to the body's tissues (anemia), an enlarged liver and spleen (hepatosplenomegaly), heart defects, and abnormalities of the urinary system or genitalia. Most babies with Hb Bart are stillborn or die soon after birth; however, fetal blood transfusions have been shown to increase chances of survival.

Next steps

Carrier testing for the reproductive partner is recommended.

If your partner tests positive:

Alpha-thalassemia inheritance involves both the HBA1 and HBA2 genes. Individuals typically have two copies of each of these genes, for a total of four copies of HBA1 and HBA2. Individuals who are carriers for alpha-thalassemia have certain changes in either one copy ("silent" carrier) or two copies (alpha-thalassemia trait) of their HBA1 or HBA2 genes, and are at increased risk for having a child with forms of alpha-thalassemia known as HbH disease (3 copies of certain HBA1 and HBA2 changes) or Hb Bart syndrome (4 copies of certain HBA1 and HBA2 changes). The chance of having a child with either of these conditions is dependent upon the carrier status of the individual's partner, and which combination of HBA1 and HBA2 changes each individual carries.

If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for alpha-thalassemia. The values provided assume a negative family history and the absence of symptoms and are based on the detection rate for the disorder as tested at Invitae.

Disease (Inheritance)	Gene	Ethnicity	Carrier Frequency	Carrier Residual Risk
Alpha-thalassemia (AR) NM_000558.4, NM_000517.4	HBA1/HBA2*	African-American Asian Caucasian Pan-ethnic	1 in 30 1 in 20 ≤1 in 500 1 in 25	1 in 291 1 in 191 Reduced 1 in 241

CARRIER: Bardet-Biedl syndrome (BBS10-related)

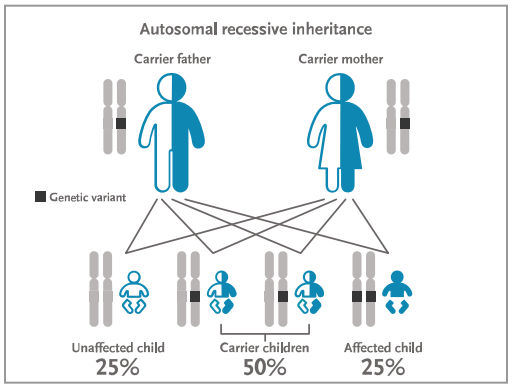
A single Pathogenic variant, c.850C>T (p.Gln284*), was identified in BBS10.

What is Bardet-Biedl syndrome (BBS10-related)?

Bardet-Biedl syndrome (BBS) is a multisystem disorder that involves defects in the microscopic, finger-like projections (cilia) that are located on the surface of cells and that are involved in cell movement and signaling. Symptoms of BBS generally include vision loss that gradually worsens, potentially life-threatening kidney problems, intellectual disability, and genital abnormalities. Patients are commonly obese and have extra fingers and toes. Symptoms can vary widely, even within the same family. Some patients may not have obvious symptoms ("incomplete penetrance"). BBS can result from changes in many different genes. There is no known cure for BBS, and treatment is focused on managing symptoms.

Next steps

Carrier testing for the reproductive partner is recommended.



If your partner tests positive:

Bardet-Biedl syndrome (BBS10-related) is inherited in an autosomal recessive fashion. In order for an individual to be affected with an autosomal recessive disorder, they must have two disease-causing genetic changes, one in each copy of the BBS10 gene. Carriers of the disorder, who have only one disease-causing genetic change, typically do not have symptoms. When both reproductive partners are carriers of an autosomal recessive disorder, there is a 25% chance for each child to have the disorder.

If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for Bardet-Biedl syndrome (BBS10-related). The values provided assume a negative family history and the absence of symptoms and are based on the detection rate for the disorder as tested at Invitae.

Disease (Inheritance)	Gene	Ethnicity	Carrier Frequency	Carrier Residual Risk
Bardet-Biedl syndrome (BBS10-related) (AR) NM_024685.3	BBS10	Pan-ethnic	1 in 354	1 in 35300

CARRIER: Gaucher disease

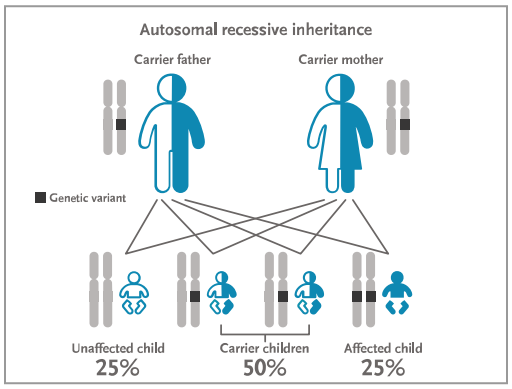
A single Pathogenic variant, c.1448T>C (p.Leu483Pro), was identified in GBA.

What is Gaucher disease?

Gaucher disease (GD) is a disorder in which the body is missing beta-glucocerebroside, an enzyme that breaks down a certain large molecule, glucocerebroside, into a sugar and a fat. Without an adequate amount of this enzyme, damage is caused to the liver, spleen, bone marrow, and sometimes the lungs and brain. In the most common form of GD, type 1, symptoms range from mild to severe and may appear at any time from childhood to adulthood. Symptoms include an enlargement of the liver and spleen (hepatosplenomegaly), a low number of red blood cells (anemia), easy bruising caused by a decrease in blood platelets (thrombocytopenia), lung and heart disease, and bone abnormalities such as bone pain, fractures, and arthritis. Patients are treated using enzyme replacement therapy (ERT), in which they are given the missing beta-glucocerebroside. In GD type 2, which is the most severe form of GD, onset can occur in utero (hydrops) or at birth and presents with seizures, brain damage, and enlarged liver and spleen (hepatosplenomegaly). GD type 2 is fatal. ERT is not effective for GD type 2. GD type 3 also affects the nervous system. Individuals who carry a single gene change in GBA are at an increased risk after the age of 50 of developing neurologic symptoms consistent with a movement disorder (Parkinson disease or Lewy body dementia). Clinical evaluation for symptoms of GBA-related disorders may be warranted.

Next steps

Carrier testing for the reproductive partner is recommended.



If your partner tests positive:

Gaucher disease is inherited in an autosomal recessive fashion. In order for an individual to be affected with an autosomal recessive disorder, they must have two disease-causing genetic changes, one in each copy of the GBA gene. Carriers of the disorder, who have only one disease-causing genetic change, typically do not have symptoms. When both reproductive partners are carriers of an autosomal recessive disorder, there is a 25% chance for each child to have the disorder.

If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for Gaucher disease. The values provided assume a negative family history and the absence of symptoms and are based on the detection rate for the disorder as tested at Invitae.

Disease (Inheritance)	Gene	Ethnicity	Carrier Frequency	Carrier Residual Risk
Gaucher disease (AR) NM_001005741.2	GBA*	Ashkenazi Jewish Pan-ethnic	1 in 15 1 in 158	1 in 234 1 in 561

Results to note

Pseudodeficiency allele

Benign change, c.2065G>A (p.Glu689Lys), known to be a pseudodeficiency allele, identified in the GAA gene. Pseudodeficiency alleles are not known to be associated with disease, including glycogen storage disease type II (Pompe disease).

The presence of a pseudodeficiency allele does not impact this individual's risk to be a carrier. Individuals with pseudodeficiency alleles may exhibit false positive results on related biochemical tests, including newborn screening; however, pseudodeficiency alleles are not known to cause disease, including glycogen storage disease type II (Pompe disease). Carrier testing for the reproductive partner is not indicated.

Variant details

BBS10, Exon 2, c.850C>T (p.Gln284*), heterozygous, PATHOGENIC

- This sequence change results in a premature translational stop signal in the BBS10 gene (p.Gln284*). While this is not anticipated to result in nonsense mediated decay, it is expected to disrupt the last 440 amino acids of the BBS10 protein.
- This variant is present in population databases (rs758732081, ExAC 0.01%).
- This variant has been observed in an individual affected with Bardet-Biedl syndrome (PMID: 24611592). ClinVar contains an entry for this variant (Variation ID: 551120).
- Experimental studies and prediction algorithms are not available for this variant, and the functional significance of the affected amino acid(s) is currently unknown.
- This variant disrupts the C-terminus of the BBS10 protein. Other variant(s) that disrupt this region (p.Val707*) have been determined to be pathogenic (PMID: 25982971, 22773737, 27486776, 20472660). This suggests that variants that disrupt this region of the protein are likely to be causative of disease.
- For these reasons, this variant has been classified as Pathogenic.

GBA, Exon 11, c.1448T>C (p.Leu483Pro), heterozygous, PATHOGENIC

- This sequence change replaces leucine with proline at codon 483 of the GBA protein (p.Leu483Pro). The leucine residue is highly conserved and there is a moderate physicochemical difference between leucine and proline.
- The frequency data for this variant in the population databases (rs421016, ExAC) is considered unreliable due to the presence of homologous sequence, such as pseudogenes or paralogs, in the genome.
- This variant has been observed in several individuals affected with Gaucher disease (PMID: 26096741, 8929950, 22713811), Parkinson's disease (PMID: 25249066, 27094865, 20816920, 25535748, 18987351, 23676350), and dementia with Lewy bodies (PMID: 23588557). ClinVar contains an entry for this variant (Variation ID: 4288, 4297). This variant is also known as p.Leu444Pro in the literature.
- Experimental studies have shown that this missense change impairs GBA enzyme activity (PMID: 8294487, 15146461, 24020503).
- The observation of one or more missense substitutions downstream of this variant (p.Leu483Pro, p.Leu483Arg) in affected individuals suggests that this may be a clinically significant region of the GBA protein (PMID: 7981693).
- For these reasons, this variant has been classified as Pathogenic.

HBA1, Deletion (Entire coding sequence), heterozygous, PATHOGENIC

- A gross deletion of the genomic region encompassing the full coding sequence of the HBA1 gene has been identified.
- Although HBA1 is associated with autosomal recessive disease, a closely related gene called HBA2, when present, can compensate for the loss of HBA1. Disruption of 1 or 2 of the 4 copies of the HBA1 and HBA2 genes is typically associated with no symptoms or very mild symptoms, while disruption of at least 3 of the 4 copies is associated with overt disease (PMID: 19618088, 21381239). Consistent with this, single gene deletions of HBA1 have been observed on the opposite chromosome (in trans) from deletions encompassing both HBA1 and HBA2 in individuals with HbH disease (PMID: 16370493, 1951330, 24826793). Deletions encompassing both HBA1 and HBA2, sometimes along with other nearby genes, have been reported in many individuals affected with alpha-thalassemia and related diseases (PMID: 1520607, 7734346, 12393486, 27492767).
- Loss-of-function variants in HBA1 are known to be pathogenic (PMID: 12393486, 27199182).
- For these reasons, this variant has been classified as Pathogenic.

Residual risk

This table displays residual risks after a negative result for each of the genes and corresponding disorders. The values provided assume a negative family history and the absence of symptoms for each disorder. Residual risk values are provided for disorders when carrier frequency is equal to, or greater than, 1 in 500. For disorders with carrier frequency less than 1 in 500, residual risk is considered to be reduced substantially. When provided, residual risk values are inferred from published carrier frequencies, and estimated detection rates are based on testing technologies used at Invitae. Residual risks are provided only as a guide for assessing approximate risk given a negative result; values will vary based on the exact ethnic background of an individual. With individuals of mixed ethnicity, it is recommended to use the highest residual risk estimate. For any genes marked with an asterisk*, refer to the Limitations section below for detailed coverage information. In the case of a sample-specific limitation, "N/A" indicates that an accurate residual risk value could not be calculated. AR = autosomal recessive, XL = X-linked, AD = autosomal dominant.

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
3-beta-hydroxysteroid dehydrogenase type II deficiency (congenital adrenal hyperplasia) (AR)	HSD3B2	Pan-ethnic	≤1 in 500	Reduced
3-hydroxy-3-methylglutarayl-CoA lyase deficiency (AR)	HMGCL	Pan-ethnic Portuguese	≤1 in 500 1 in 160	Reduced 1 in 15900
3-methylglutaconic aciduria type III (Costeff optic atrophy) (AR)	OPA3	Pan-ethnic Sephardic Jewish (Iraqi)	≤1 in 500 1 in 10	Reduced 1 in 900
11-beta-hydroxylase-deficient congenital adrenal hyperplasia (AR)	CYP11B1	Pan-ethnic Sephardic Jewish (Moroccan)	1 in 194 1 in 40	1 in 19300 1 in 3900
17-alpha-hydroxylase-deficient congenital adrenal hyperplasia (AR)	CYP17A1	Pan-ethnic	≤1 in 500	Reduced
Abetalipoproteinemia (AR)	MTTP	Ashkenazi Jewish Pan-ethnic	1 in 131 ≤1 in 500	1 in 13000 Reduced
ACAD9 deficiency (AR)	ACAD9	Pan-ethnic	≤1 in 500	Reduced
Achromatopsia (CNGB3-related) (AR)	CNGB3	Pan-ethnic	1 in 93	1 in 9200
Acrodermatitis enteropathica (AR)	SLC39A4	Pan-ethnic	1 in 354	1 in 35300
Adenosine deaminase deficiency (AR)	ADA	Pan-ethnic	1 in 224	1 in 2788
Aicardi-Goutières syndrome (SAMHD1-related) (AR)	SAMHD1	Pan-ethnic	≤1 in 500	Reduced
Aldosterone synthase deficiency (AR)	CYP11B2	Pan-ethnic Sephardic Jewish (Iranian)	≤1 in 500 1 in 30	Reduced 1 in 2900
Alpha-mannosidosis (AR)	MAN2B1	Pan-ethnic	1 in 354	1 in 35300
Alpha-thalassemia X-linked intellectual disability syndrome (XL)	ATRX	Pan-ethnic	≤1 in 500	Reduced
Alport syndrome (COL4A3-related) (AR)	COL4A3	Ashkenazi Jewish Caucasian Pan-ethnic	1 in 192 1 in 284 1 in 354	1 in 19100 1 in 28300 1 in 35300
Alport syndrome (COL4A4-related) (AR)	COL4A4	Pan-ethnic	1 in 353	1 in 35200
Alport syndrome, X-linked (COL4A5-related) (XL)	COL4A5 *	Pan-ethnic	≤1 in 500	Reduced
Alstrom syndrome (AR)	ALMS1	Pan-ethnic	≤1 in 500	Reduced
Andermann syndrome (AR)	SLC12A6	French Canadian (Saguenay-Lac-St-Jean) Pan-ethnic	1 in 23 ≤1 in 500	1 in 2200 Reduced
Arginase deficiency (AR)	ARG1	Pan-ethnic	1 in 274	1 in 27300
Argininosuccinic aciduria (AR)	ASL	Pan-ethnic	1 in 133	1 in 1321

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
Aromatase deficiency (AR)	CYP19A1	Pan-ethnic	≤1 in 500	Reduced
Asparagine synthetase deficiency (AR)	ASNS	Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish (Iranian)	1 in 80	1 in 7900
Aspartylglucosaminuria (AR)	AGA	Finnish	1 in 69	1 in 6800
		Pan-ethnic	≤1 in 500	Reduced
Ataxia telangiectasia (AR)	ATM	Pan-ethnic	1 in 100	1 in 9900
		Sephardic Jewish	1 in 69	1 in 6800
Ataxia with Vitamin E deficiency (AR)	TTPA	Italian	1 in 274	1 in 2731
		Pan-ethnic	≤1 in 500	Reduced
Autoimmune polyendocrinopathy with candidiasis and ectodermal dysplasia (AR)	AIRE	Finnish	1 in 79	1 in 7800
		Pan-ethnic	1 in 150	1 in 14900
		Sardinian	1 in 60	1 in 5900
		Sephardic Jewish (Iranian)	1 in 48	1 in 4700
Autosomal recessive deafness 77 (AR)	LOXHD1	Ashkenazi Jewish	1 in 180	1 in 17900
		Pan-ethnic	≤1 in 500	Reduced
Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) (AR)	SACS	French Canadian (Saguenay-Lac-St-Jean)	1 in 21	1 in 2000
		Pan-ethnic	≤1 in 500	Reduced
Bardet-Biedl syndrome (BBS1-related) (AR)	BBS1	Faroese	1 in 30	1 in 2900
		Pan-ethnic	1 in 330	1 in 32900
Bardet-Biedl syndrome (BBS2-related) (AR)	BBS2	Ashkenazi Jewish	1 in 140	1 in 13900
		Pan-ethnic	1 in 560	Reduced
Bardet-Biedl syndrome (BBS12-related) (AR)	BBS12	Pan-ethnic	1 in 708	Reduced
Bartter syndrome type IV (BSND-related) (AR)	BSND	Pan-ethnic	≤1 in 500	Reduced
Beta-ketothiolase deficiency (AR)	ACAT1	Caucasian	1 in 354	1 in 35300
		Pan-ethnic	≤1 in 500	Reduced
Bloom syndrome (AR)	BLM	Ashkenazi Jewish	1 in 100	1 in 9900
		Pan-ethnic	≤1 in 500	Reduced
Canavan disease (AR)	ASPA	Ashkenazi Jewish	1 in 57	1 in 5600
		Pan-ethnic	1 in 159	1 in 15800
Carbamoylphosphate synthetase I deficiency (AR)	CPS1	Pan-ethnic	≤1 in 500	Reduced
Carnitine palmitoyltransferase I deficiency (AR)	CPT1A	Hutterite	1 in 16	1 in 1500
		Pan-ethnic	≤1 in 500	Reduced
Carnitine palmitoyltransferase II deficiency (AR)	CPT2	Ashkenazi Jewish	1 in 45	1 in 4400
		Pan-ethnic	1 in 182	1 in 18100
Carpenter syndrome (RAB23-related) (AR)	RAB23	Pan-ethnic	≤1 in 500	Reduced
Cartilage-hair hypoplasia-anauxetic dysplasia spectrum disorders (AR)	RMRP	Amish	1 in 10	1 in 900
		Finnish	1 in 76	1 in 7500
		Pan-ethnic	≤1 in 500	Reduced
Cerebrotendinous xanthomatosis (AR)	CYP27A1	Pan-ethnic	1 in 112	1 in 5550
		Sephardic Jewish	1 in 76	1 in 3750

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
CFTR-related disorders (AR)	CFTR	African-American - classic CF	1 in 61	1 in 6000
		Ashkenazi Jewish - classic CF	1 in 29	1 in 2800
		Asian - classic CF	1 in 88	1 in 8700
		Caucasian - classic CF	1 in 28	1 in 2700
		Pan-ethnic - classic CF	1 in 45	1 in 4400
		Pan-ethnic - classic CF and CFTR-related disorders	1 in 9	1 in 800
Charcot-Marie-Tooth disease (NDRG1-related) (AR)	NDRG1	Roma	1 in 22	1 in 2100
Charcot-Marie-Tooth disease, X-linked (GJB1-related) (XL)	GJB1	Pan-ethnic	≤1 in 500	Reduced
Chorea-acanthocytosis (AR)	VPS13A *	Pan-ethnic	≤1 in 500	Reduced
Choroideremia (XL)	CHM	Pan-ethnic	≤1 in 500	Reduced
Chronic granulomatous disease (CYBA-related) (AR)	CYBA	Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish (Moroccan)	1 in 13	1 in 1200
Chronic granulomatous disease (CYBB-related) (XL)	CYBB	Pan-ethnic	≤1 in 500	Reduced
Citrin deficiency (AR)	SLC25A13	Chinese	1 in 65	1 in 6400
		Japanese	1 in 65	1 in 6400
		Korean	1 in 112	1 in 11100
		Southern Chinese and Taiwanese	1 in 48	1 in 4700
Citrullinemia type 1 (AR)	ASS1	Pan-ethnic	1 in 120	1 in 2975
Cockayne syndrome type A (AR)	ERCC8	Pan-ethnic	1 in 514	Reduced
Cockayne syndrome type B (AR)	ERCC6	Pan-ethnic	1 in 377	1 in 37600
Cohen syndrome (AR)	VPS13B	Amish (Ohio)	1 in 12	1 in 1100
		Pan-ethnic	≤1 in 500	Reduced
Combined malonic and methylmalonic aciduria (ACSF3-related) (AR)	ACSF3	Pan-ethnic	1 in 87	1 in 8600
Combined oxidative phosphorylation deficiency (GFM1-related) (AR)	GFM1	Pan-ethnic	≤1 in 500	Reduced
Combined oxidative phosphorylation deficiency (TSFM-related) (AR)	TSFM *	Finnish	1 in 80	1 in 1129
		Pan-ethnic	≤1 in 500	Reduced
Combined pituitary hormone deficiency (LHX3-related) (AR)	LHX3	Pan-ethnic	≤1 in 500	Reduced
Combined pituitary hormone deficiency (PROP1-related) (AR)	PROP1	Pan-ethnic	1 in 45	1 in 2200
Combined SAP deficiency (AR)	PSAP	Pan-ethnic	≤1 in 500	Reduced
Congenital amegakaryocytic thrombocytopenia (AR)	MPL	Ashkenazi Jewish	1 in 57	1 in 5600
		Pan-ethnic	≤1 in 500	Reduced
Congenital disorder of glycosylation (ALG6-related) (AR)	ALG6 *	Pan-ethnic	≤1 in 500	Reduced
Congenital disorder of glycosylation (MPI-related) (AR)	MPI	Pan-ethnic	≤1 in 500	Reduced
Congenital disorder of glycosylation (PMM2-related) (AR)	PMM2	Ashkenazi Jewish	1 in 61	1 in 6000
		Caucasian	1 in 60	1 in 5900
		Pan-ethnic	1 in 190	1 in 18900
Congenital ichthyosis (TGM1-related) (AR)	TGM1	Norwegian	1 in 151	1 in 3000
		Pan-ethnic	1 in 224	1 in 4460

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
Congenital insensitivity to pain with anhidrosis (AR)	NTRK1	Pan-ethnic	≤1 in 500	Reduced
Congenital myasthenic syndrome (CHRNE-related) (AR)	CHRNE	European Roma Pan-ethnic	1 in 25 1 in 200	1 in 2400 1 in 19900
Congenital myasthenic syndrome (RAPSN-related) (AR)	RAPSN	Pan-ethnic	1 in 283	1 in 28200
Congenital neutropenia (HAX1-related) (AR)	HAX1	Pan-ethnic	≤1 in 500	Reduced
Corneal dystrophy and perceptive deafness (AR)	SLC4A11	Pan-ethnic	≤1 in 500	Reduced
Cystinosis (AR)	CTNS	French Canadian (Saguenay-Lac-St-Jean) Pan-ethnic Sephardic Jewish (Moroccan)	1 in 39 1 in 158 1 in 100	1 in 3800 1 in 15700 1 in 9900
D-bifunctional protein deficiency (AR)	HSD17B4	Pan-ethnic	1 in 158	1 in 15700
DHDDS-related disorders (AR)	DHDDS	Ashkenazi Jewish	1 in 117	1 in 11600
Dihydrolipoamide dehydrogenase deficiency (AR)	DLD	Ashkenazi Jewish Pan-ethnic	1 in 107 ≤1 in 500	1 in 5300 Reduced
DMD-related dystrophinopathy (XL)	DMD	Pan-ethnic	1 in 667	Reduced
Dystrophic epidermolysis bullosa (COL7A1-related) (AR)	COL7A1	Pan-ethnic	1 in 370	1 in 12300
Ehlers-Danlos syndrome, dermatosparaxis type (AR)	ADAMTS2	Ashkenazi Jewish Pan-ethnic	1 in 187 ≤1 in 500	1 in 18600 Reduced
Ellis-van Creveld syndrome (EVC2-related) (AR)	EVC2	Pan-ethnic	1 in 199	1 in 19800
Ellis-van Creveld syndrome (EVC-related) (AR)	EVC	Amish Pan-ethnic	1 in 8 1 in 220	1 in 700 1 in 21900
Emery-Dreifuss muscular dystrophy (EMD-related) (XL)	EMD	Pan-ethnic	≤1 in 500	Reduced
Enhanced S-cone syndrome/retinitis pigmentosa 37 (AR)	NR2E3	Pan-ethnic	≤1 in 500	Reduced
Ethylmalonic encephalopathy (AR)	ETHE1	Pan-ethnic	≤1 in 500	Reduced
Fabry disease (XL)	GLA	Pan-ethnic	≤1 in 500	Reduced
Factor IX deficiency (hemophilia B) (XL)	F9	Pan-ethnic	≤1 in 500	Reduced
Familial dysautonomia (AR)	ELP1	Ashkenazi Jewish Pan-ethnic	1 in 36 ≤1 in 500	1 in 3500 Reduced
Familial hypercholesterolemia (LDLR-related) (AD)	LDLR	Afrikaner Ashkenazi Jewish French Canadian Pan-ethnic	1 in 72 1 in 69 1 in 270 1 in 250	1 in 7100 1 in 6800 1 in 26900 1 in 24900
Familial hypercholesterolemia (LDLRAP1-related) (AR)	LDLRAP1	Pan-ethnic Sardinian	≤1 in 500 1 in 143	Reduced 1 in 14200
Familial hyperinsulinism (ABCC8-related) (AR) When the mother is a noncarrier, but the father is a carrier, there is a residual risk for focal disease (1 in 540 for the Ashkenazi Jewish population; undetermined in other ethnic groups)	ABCC8	Ashkenazi Jewish Finnish Pan-ethnic	1 in 52 1 in 100 1 in 177	1 in 5100 1 in 9900 1 in 17600
Familial hyperinsulinism (KCNJ11-related) (AR)	KCNJ11	Pan-ethnic	≤1 in 500	Reduced
Fanconi anemia type A (AR)	FANCA	Afrikaner Pan-ethnic	1 in 83 1 in 345	1 in 8200 1 in 34400

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
		Sephardic Jewish	1 in 133	1 in 13200
		Spanish Roma	1 in 64	1 in 6300
Fanconi anemia type C (AR)	FANCC	Ashkenazi Jewish	1 in 89	1 in 8800
		Pan-ethnic	1 in 417	1 in 41600
Fanconi anemia type G (AR)	FANCG	African-American	1 in 100	1 in 9900
		Pan-ethnic	≤1 in 500	Reduced
FKRP-related disorders (AR)	FKRP	Norwegian	1 in 116	1 in 11500
		Pan-ethnic	1 in 158	1 in 15700
FKTN-related disorders (AR)	FKTN	Ashkenazi Jewish	1 in 80	1 in 7900
		Japanese	1 in 188	1 in 18700
		Pan-ethnic	≤1 in 500	Reduced
Fragile X syndrome (XL) CGG repeats observed: 30, 32	FMR1 *	Ashkenazi Jewish	1 in 58	1 in 5700
		Asian	≤1 in 500	Reduced
		Caucasian	1 in 187	1 in 18600
		Hispanic	≤1 in 500	Reduced
		Pan-ethnic	1 in 259	1 in 25800
Fumarate hydratase deficiency (AR)	FH	Pan-ethnic	≤1 in 500	Reduced
Galactokinase deficiency galactosemia (AR)	GALK1	Pan-ethnic	1 in 122	1 in 12100
		Roma	1 in 47	1 in 4600
Galactosemia (GALT-related) (AR)	GALT	African-American	1 in 87	1 in 8600
		Ashkenazi Jewish	1 in 156	1 in 15500
		Irish Traveller	1 in 11	1 in 1000
		Pan-ethnic	1 in 100	1 in 9900
Gitelman syndrome (SLC12A3-related) (AR)	SLC12A3	Pan-ethnic	1 in 100	1 in 9900
GJB2-related DFNB1 nonsyndromic hearing loss and deafness (AR)	GJB2	Ashkenazi Jewish	1 in 13	1 in 1200
		Pan-ethnic	1 in 50	1 in 4900
		Thai	1 in 9	1 in 800
Glutaric acidemia type I (AR)	GCDH	Amish	1 in 9	1 in 800
		Oji-Cree First Nations	1 in 9	1 in 800
		Pan-ethnic	1 in 87	1 in 8600
Glutaric acidemia type II (ETFA-related) (AR)	ETFA	Pan-ethnic	≤1 in 500	Reduced
Glutaric acidemia type II (ETFDH-related) (AR)	ETFDH	Asian	1 in 87	1 in 8600
		Pan-ethnic	1 in 250	1 in 24900
Glycine encephalopathy (AMT-related) (AR)	AMT	Finnish	1 in 142	1 in 14100
		Pan-ethnic	1 in 325	1 in 32400
Glycine encephalopathy (GLDC-related) (AR)	GLDC	Caucasian	1 in 141	1 in 14000
		Pan-ethnic	1 in 165	1 in 16400
Glycogen storage disease type Ia (AR)	G6PC	Ashkenazi Jewish	1 in 71	1 in 1400
		Pan-ethnic	1 in 177	1 in 3520
Glycogen storage disease type Ib (AR)	SLC37A4	Pan-ethnic	1 in 354	1 in 7060
Glycogen storage disease type II (Pompe disease) (AR)	GAA	African-American	1 in 60	1 in 5900

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
		Ashkenazi Jewish	1 in 58	1 in 5700
		Asian	1 in 112	1 in 11100
		Pan-ethnic	1 in 100	1 in 9900
Glycogen storage disease type III (AR)	AGL	Faroese	1 in 28	1 in 540
		Pan-ethnic	1 in 159	1 in 3160
		Sephardic Jewish (Moroccan)	1 in 34	1 in 660
Glycogen storage disease type IV/adult polyglucosan body disease (AR)	GBE1	Ashkenazi Jewish	1 in 68	1 in 6700
		Pan-ethnic	1 in 387	1 in 38600
Glycogen storage disease type V (AR)	PYGM	Caucasian	1 in 158	1 in 15700
		Sephardic Jewish (Kurdish)	1 in 84	1 in 8300
Glycogen storage disease type VII (AR)	PFKM	Ashkenazi Jewish	1 in 250	1 in 24900
		Pan-ethnic	≤1 in 500	Reduced
GRACILE syndrome/BCS1L-related disorders (AR)	BCS1L	Caucasian	1 in 407	1 in 40600
		Finnish	1 in 108	1 in 10700
		Pan-ethnic	≤1 in 500	Reduced
Guanidinoacetate methyltransferase deficiency (AR)	GAMT	Pan-ethnic	≤1 in 500	Reduced
		Portuguese	1 in 125	1 in 12400
HBB-related hemoglobinopathies (AR)	HBB	African-American	1 in 8	1 in 700
		Asian	1 in 54	1 in 5300
		Caucasian	1 in 373	1 in 37200
		Hispanic	1 in 17	1 in 1600
		Mediterranean	1 in 28	1 in 2700
		Pan-ethnic	1 in 49	1 in 4800
Hereditary fructose intolerance (AR)	ALDOB	African-American	1 in 226	1 in 22500
		Middle Eastern	1 in 97	1 in 9600
		Pan-ethnic	1 in 122	1 in 12100
Hereditary hemochromatosis (HJV-related) (AR)	HJV	Pan-ethnic	≤1 in 500	Reduced
Hereditary hemochromatosis (TFR2-related) (AR)	TFR2	Pan-ethnic	≤1 in 500	Reduced
Hermansky-Pudlak syndrome (HPS1-related) (AR)	HPS1	Pan-ethnic	≤1 in 500	Reduced
		Puerto Rican (Northwestern)	1 in 21	1 in 2000
Hermansky-Pudlak syndrome (HPS3-related) (AR)	HPS3	Ashkenazi Jewish	1 in 235	1 in 23400
		Pan-ethnic	≤1 in 500	Reduced
		Puerto Rican (Central)	1 in 63	1 in 6200
Holocarboxylase synthetase deficiency (AR)	HLCS	Faroese	1 in 20	1 in 1900
		Japanese	1 in 158	1 in 15700
		Pan-ethnic	1 in 224	1 in 22300
Homocystinuria (CBS-related) (AR)	CBS	Norwegian	1 in 40	1 in 3900
		Pan-ethnic	1 in 224	1 in 22300
		Qatari	1 in 21	1 in 2000
Homocystinuria due to MTHFR deficiency (AR)	MTHFR *	Sephardic Jewish (Bukharian)	1 in 39	1 in 3800
Homocystinuria, cobalamin E type (AR)	MTRR	Pan-ethnic	≤1 in 500	Reduced

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
Hydrolethalus syndrome type 1 (AR)	HYLS1	Finnish	1 in 40	1 in 3900
		Pan-ethnic	≤1 in 500	Reduced
Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome (AR)	SLC25A15	Metis (Saskatchewan)	1 in 19	1 in 1800
		Pan-ethnic	≤1 in 500	Reduced
Hypohidrotic ectodermal dysplasia (EDA-related) (XL)	EDA	Pan-ethnic	1 in 112	1 in 11100
Hypophosphatasia (AR)	ALPL	Mennonite	1 in 25	1 in 480
		Pan-ethnic	1 in 150	1 in 2980
Inclusion body myopathy 2 (AR)	GNE	Pan-ethnic	1 in 179	1 in 17800
		Sephardic Jewish (Iranian)	1 in 10	1 in 900
Isovaleric acidemia (AR)	IVD	Pan-ethnic	1 in 250	1 in 24900
Joubert syndrome 2/TMEM216-related disorders (AR)	TMEM216	Ashkenazi Jewish	1 in 92	1 in 9100
		Pan-ethnic	≤1 in 500	Reduced
Junctional epidermolysis bullosa (LAMA3-related) (AR)	LAMA3	Pan-ethnic	≤1 in 500	Reduced
Junctional epidermolysis bullosa (LAMB3-related) (AR)	LAMB3	Pan-ethnic	1 in 317	1 in 31600
Junctional epidermolysis bullosa (LAMC2-related) (AR)	LAMC2	Pan-ethnic	≤1 in 500	Reduced
Krabbe disease (AR)	GALC	Druze	1 in 6	1 in 500
		Pan-ethnic	1 in 158	1 in 15700
LAMA2-related muscular dystrophy (AR)	LAMA2	Pan-ethnic	1 in 87	1 in 8600
Leber congenital amaurosis 2 (AR)	RPE65	Pan-ethnic	1 in 228	1 in 22700
		Sephardic Jewish	1 in 90	1 in 8900
Leber congenital amaurosis 5 (AR)	LCA5	Pan-ethnic	1 in 645	Reduced
Leber congenital amaurosis 8/CRB1-related disorders (AR)	CRB1	Pan-ethnic	1 in 112	1 in 11100
Leber congenital amaurosis 10/CEP290-related disorders (AR)	CEP290	Pan-ethnic	1 in 185	1 in 18400
Leber congenital amaurosis 13 (AR)	RDH12	Pan-ethnic	1 in 460	1 in 45900
Leigh syndrome, French Canadian type (AR)	LRPPRC	French Canadian (Saguenay-Lac-St-Jean)	1 in 23	1 in 2200
		Pan-ethnic	≤1 in 500	Reduced
Lethal congenital contracture syndrome 1/lethal arthrogryposis with anterior horn cell disease (AR)	GLE1	Finnish	1 in 100	1 in 9900
		Pan-ethnic	≤1 in 500	Reduced
Leukoencephalopathy with vanishing white matter (EIF2B5-related) (AR)	EIF2B5	Pan-ethnic	≤1 in 500	Reduced
Limb-girdle muscular dystrophy type 2A (calpainopathy) (AR)	CAPN3	Pan-ethnic	1 in 134	1 in 13300
Limb-girdle muscular dystrophy type 2B (dysferlinopathy) (AR)	DYSF	Pan-ethnic	1 in 311	1 in 31000
		Sephardic Jewish (Libyan)	1 in 10	1 in 900
Limb-girdle muscular dystrophy type 2C (AR)	SGCG	Caucasian	1 in 571	Reduced
		Japanese	1 in 374	1 in 37300
		Moroccan	1 in 250	1 in 24900
		Pan-ethnic	≤1 in 500	Reduced
		Roma	1 in 59	1 in 5800
Limb-girdle muscular dystrophy type 2D (AR)	SGCA	Caucasian	1 in 286	1 in 28500

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
		Finnish	1 in 150	1 in 14900
		Pan-ethnic	≤1 in 500	Reduced
Limb-girdle muscular dystrophy type 2E (AR)	SGCB	Caucasian	1 in 404	1 in 5038
		Pan-ethnic	≤1 in 500	Reduced
Lipoid congenital adrenal hyperplasia (STAR-related) (AR)	STAR	Korean	1 in 170	1 in 16900
		Pan-ethnic	≤1 in 500	Reduced
Lipoprotein lipase deficiency (AR)	LPL	French Canadian (Saguenay-Lac-St-Jean)	1 in 46	1 in 4500
		Pan-ethnic	≤1 in 500	Reduced
Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (AR)	HADHA	Caucasian	1 in 250	1 in 24900
		Finnish	1 in 125	1 in 12400
		Pan-ethnic	1 in 350	1 in 34900
Lysinuric protein intolerance (AR)	SLC7A7	Finnish	1 in 120	1 in 2380
		Japanese	1 in 120	1 in 2380
		Pan-ethnic	≤1 in 500	Reduced
Lysosomal acid lipase deficiency (AR)	LIPA	Caucasian	1 in 112	1 in 1850
		Sephardic Jewish (Iranian)	1 in 33	1 in 534
Major histocompatibility complex class II deficiency (CIITA-related) (AR)	CIITA	Pan-ethnic	≤1 in 500	Reduced
Maple syrup urine disease type 1A (AR)	BCKDHA	Mennonite	1 in 10	1 in 900
		Pan-ethnic	1 in 373	1 in 37200
Maple syrup urine disease type 1B (AR)	BCKDHB	Ashkenazi Jewish	1 in 97	1 in 9600
		Pan-ethnic	1 in 346	1 in 34500
Maple syrup urine disease type 2 (AR)	DBT	Pan-ethnic	≤1 in 500	Reduced
Medium chain acyl-CoA dehydrogenase deficiency (AR)	ACADM	Northern European	1 in 40	1 in 3900
		Pan-ethnic	1 in 66	1 in 6500
Megalencephalic leukoencephalopathy with subcortical cysts type 1 (AR)	MLC1	Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish (Libyan)	1 in 40	1 in 3900
Menkes disease/ATP7A-related disorders (XL)	ATP7A	Pan-ethnic	≤1 in 500	Reduced
Metachromatic leukodystrophy (ARSA-related) (AR)	ARSA	Navajo	1 in 40	1 in 780
		Pan-ethnic	1 in 100	1 in 1980
		Sephardic Jewish	1 in 46	1 in 900
Methylmalonic acidemia (MMAA-related) (AR)	MMAA	Pan-ethnic	1 in 316	1 in 10500
Methylmalonic acidemia (MMAB-related) (AR)	MMAB	Pan-ethnic	1 in 456	1 in 22750
Methylmalonic acidemia (MUT-related) (AR)	MUT	Pan-ethnic	1 in 204	1 in 5075
Methylmalonic acidemia with homocystinuria, cobalamin C type (AR)	MMACHC	Pan-ethnic	1 in 123	1 in 12200
Methylmalonic acidemia with homocystinuria, cobalamin D type (AR)	MMADHC *	Pan-ethnic	≤1 in 500	Reduced
Microphthalmia/clinical anophthalmia (VSX2-related) (AR)	VSX2	Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish	1 in 145	1 in 14400
Mitochondrial complex I deficiency/Leigh syndrome (NDUFAF5-related) (AR)	NDUFAF5	Ashkenazi Jewish	1 in 290	1 in 28900
		Pan-ethnic	≤1 in 500	Reduced

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
Mitochondrial complex I deficiency/Leigh syndrome (NDUFS6-related) (AR)	NDUFS6	Ashkenazi Jewish Caucasus Jewish Pan-ethnic	1 in 290 1 in 24 ≤1 in 500	1 in 28900 1 in 2300 Reduced
Mitochondrial DNA depletion syndrome (MPV17-related) (AR)	MPV17	Navajo Pan-ethnic	1 in 20 ≤1 in 500	1 in 475 Reduced
Mitochondrial myopathy and sideroblastic anemia 1 (AR)	PUS1	Pan-ethnic	≤1 in 500	Reduced
Mitochondrial neurogastrointestinal encephalopathy disease (AR)	TYMP	Pan-ethnic Sephardic Jewish	≤1 in 500 1 in 158	Reduced 1 in 15700
MKS1-related disorders (AR)	MKS1	Finnish Pan-ethnic	1 in 47 1 in 260	1 in 920 1 in 5180
Mucolipidosis type II/III (GNPTAB-related) (AR)	GNPTAB	Irish Traveller Pan-ethnic	1 in 15 1 in 200	1 in 1400 1 in 19900
Mucolipidosis type III (GNPTG-related) (AR)	GNPTG	Pan-ethnic	≤1 in 500	Reduced
Mucolipidosis type IV (AR)	MCOLN1	Ashkenazi Jewish Pan-ethnic	1 in 100 ≤1 in 500	1 in 9900 Reduced
Mucopolysaccharidosis type I (AR)	IDUA	Pan-ethnic	1 in 148	1 in 4900
Mucopolysaccharidosis type II (Hunter syndrome) (XL)	IDS *	Pan-ethnic	≤1 in 500	Reduced
Mucopolysaccharidosis type IIIA (Sanfilippo A syndrome) (AR)	SGSH	Northern European Pan-ethnic Taiwanese	1 in 173 1 in 215 ≤1 in 500	1 in 17200 1 in 21400 Reduced
Mucopolysaccharidosis type IIIB (AR)	NAGLU	Pan-ethnic	1 in 224	1 in 22300
Mucopolysaccharidosis type IIIC (Sanfilippo syndrome)/retinitis pigmentosa 73 (AR)	HGSNAT	Pan-ethnic	≤1 in 500	Reduced
Mucopolysaccharidosis type IIID (Sanfilippo syndrome) (AR)	GNS	Pan-ethnic	≤1 in 500	Reduced
Mucopolysaccharidosis type IVB (Morquio B syndrome)/GM1 gangliosidosis (AR)	GLB1	Pan-ethnic Roma South Brazilian	1 in 158 1 in 50 1 in 58	1 in 15700 1 in 4900 1 in 5700
Mucopolysaccharidosis type IX (AR)	HYAL1	Pan-ethnic	≤1 in 500	Reduced
Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome) (AR)	ARSB	Pan-ethnic	1 in 250	1 in 24900
Multiple sulfatase deficiency (AR)	SUMF1	Pan-ethnic	≤1 in 500	Reduced
N-acetylglutamate synthase deficiency (AR)	NAGS	Pan-ethnic	≤1 in 500	Reduced
Nemaline myopathy 2 (AR)	NEB *	Ashkenazi Jewish Pan-ethnic	1 in 108 1 in 158	1 in 10700 1 in 3140
Nephrogenic diabetes insipidus (AQP2-related) (AR)	AQP2	Pan-ethnic	1 in 1118	Reduced
Nephrotic syndrome/congenital Finnish nephrosis (NPHS1-related) (AR)	NPHS1	Finnish Old Order Mennonite Pan-ethnic	1 in 46 1 in 12 ≤1 in 500	1 in 4500 1 in 1100 Reduced
Nephrotic syndrome/steroid-resistant nephrotic syndrome (NPHS2-related) (AR)	NPHS2	Pan-ethnic	≤1 in 500	Reduced
Neuronal ceroid-lipofuscinosis (CLN3-related) (AR)	CLN3	Pan-ethnic	1 in 230	1 in 22900

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
Neuronal ceroid-lipofuscinosis (CLN5-related) (AR)	CLN5	Finnish	1 in 115	1 in 11400
		Pan-ethnic	≤1 in 500	Reduced
Neuronal ceroid-lipofuscinosis (CLN6-related) (AR)	CLN6	Pan-ethnic	≤1 in 500	Reduced
Neuronal ceroid-lipofuscinosis (MFSD8-related) (AR)	MFSD8	Pan-ethnic	≤1 in 500	Reduced
Neuronal ceroid-lipofuscinosis (PPT1-related) (AR)	PPT1	Finnish	1 in 70	1 in 3450
		Pan-ethnic	1 in 199	1 in 9900
Neuronal ceroid-lipofuscinosis (TPP1-related) (AR)	TPP1	Newfoundland	1 in 53	1 in 1734
		Pan-ethnic	1 in 250	1 in 8300
Neuronal ceroid-lipofuscinosis/Northern epilepsy (CLN8-related) (AR)	CLN8	Finnish	1 in 135	1 in 13400
		Pan-ethnic	≤1 in 500	Reduced
Niemann-Pick disease type A/B (AR)	SMPD1	Ashkenazi Jewish	1 in 90	1 in 1780
		Pan-ethnic	1 in 250	1 in 4980
Niemann-Pick disease type C (NPC1-related) (AR)	NPC1	Pan-ethnic	1 in 183	1 in 18200
Niemann-Pick disease type C (NPC2-related) (AR)	NPC2	Pan-ethnic	1 in 871	Reduced
Nijmegen breakage syndrome (AR)	NBN *	Eastern European	1 in 155	1 in 15400
		Pan-ethnic	≤1 in 500	Reduced
Ornithine aminotransferase deficiency (AR)	OAT	Finnish	1 in 126	1 in 12500
		Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish	1 in 177	1 in 17600
Ornithine transcarbamylase deficiency (XL)	OTC	Pan-ethnic	≤1 in 500	Reduced
Osteopetrosis (TCIRG1-related) (AR)	TCIRG1	Ashkenazi Jewish	1 in 350	1 in 34900
		Chuvash	1 in 30	1 in 2900
		Pan-ethnic	1 in 317	1 in 31600
Pendred syndrome (AR)	SLC26A4	Asian	1 in 74	1 in 7300
		Pan-ethnic	1 in 80	1 in 7900
Peroxisomal acyl-CoA oxidase deficiency (AR)	ACOX1	Pan-ethnic	≤1 in 500	Reduced
Phenylalanine hydroxylase deficiency (AR)	PAH	African-American	1 in 111	1 in 11000
		Ashkenazi Jewish	1 in 225	1 in 22400
		East Asian	1 in 50	1 in 1225
		Finnish	1 in 225	1 in 22400
		Irish	1 in 33	1 in 3200
		Japanese	1 in 200	1 in 19900
		Pan-ethnic	1 in 58	1 in 5700
		Turkish	1 in 26	1 in 2500
Phosphoglycerate dehydrogenase deficiency/Neu-Laxova syndrome (AR)	PHGDH	Ashkenazi Jewish	1 in 400	1 in 39900
		Pan-ethnic	≤1 in 500	Reduced
Polycystic kidney disease (PKHD1-related) (AR)	PKHD1	Pan-ethnic	1 in 70	1 in 6900
Polymicrogyria (ADGRG1-related) (AR)	ADGRG1	Pan-ethnic	≤1 in 500	Reduced
POMGNT1-related disorders (AR)	POMGNT1	Finnish	1 in 111	1 in 11000
		Pan-ethnic	≤1 in 500	Reduced

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
Pontocerebellar hypoplasia (RARS2-related) (AR)	RARS2	Pan-ethnic	≤1 in 500	Reduced
Pontocerebellar hypoplasia (SEPSECS-related) (AR)	SEPSECS	Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish (Moroccan and Iraqi)	1 in 43	1 in 4200
Pontocerebellar hypoplasia (VRK1-related) (AR)	VRK1	Ashkenazi Jewish	1 in 225	1 in 22400
		Pan-ethnic	≤1 in 500	Reduced
Postnatal progressive microcephaly with seizures and brain atrophy/infantile cerebral and cerebellar atrophy (MED17-related) (AR)	MED17	Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish	1 in 20	1 in 1900
Primary carnitine deficiency (AR)	SLC22A5	Faroese	1 in 9	1 in 800
		Japanese	1 in 100	1 in 9900
		Pan-ethnic	1 in 71	1 in 7000
Primary ciliary dyskinesia (DNAH5-related) (AR)	DNAH5	Pan-ethnic	1 in 109	1 in 10800
Primary ciliary dyskinesia (DNAI1-related) (AR)	DNAI1	Pan-ethnic	1 in 250	1 in 24900
Primary ciliary dyskinesia (DNAI2-related) (AR)	DNAI2	Ashkenazi Jewish	1 in 200	1 in 19900
		Pan-ethnic	1 in 354	1 in 35300
Primary hyperoxaluria type 1 (AR)	AGXT	Pan-ethnic	1 in 135	1 in 13400
Primary hyperoxaluria type 2 (AR)	GRHPR	Pan-ethnic	≤1 in 500	Reduced
Primary hyperoxaluria type 3 (AR)	HOGA1	Pan-ethnic	1 in 354	1 in 35300
Progressive familial intrahepatic cholestasis type 2 (AR)	ABCB11	Pan-ethnic	1 in 100	1 in 9900
Propionic acidemia (PCCA-related) (AR)	PCCA	Arab	1 in 100	1 in 2475
		Pan-ethnic	1 in 224	1 in 5575
Propionic acidemia (PCCB-related) (AR)	PCCB	Arab	1 in 100	1 in 9900
		Greenlandic Inuit	1 in 20	1 in 1900
		Pan-ethnic	1 in 224	1 in 22300
PRPS1-related disorders (XL)	PRPS1	Pan-ethnic	≤1 in 500	Reduced
Pycnodysostosis (AR)	CTSK	Pan-ethnic	1 in 438	1 in 43700
Pyruvate carboxylase deficiency (AR)	PC	Algonquian Indian	1 in 10	1 in 180
		Pan-ethnic	1 in 250	1 in 4980
Pyruvate dehydrogenase deficiency (PDHA1-related) (XL)	PDHA1	Pan-ethnic	≤1 in 500	Reduced
Pyruvate dehydrogenase deficiency (PDHB-related) (AR)	PDHB	Pan-ethnic	≤1 in 500	Reduced
Renal tubular acidosis with deafness (ATP6V1B1-related) (AR)	ATP6V1B1	Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish	1 in 140	1 in 13900
Retinitis pigmentosa 25 (AR)	EYS	Pan-ethnic	1 in 129	1 in 12800
		Sephardic Jewish	1 in 42	1 in 4100
Retinitis pigmentosa 26 (AR)	CERKL	Pan-ethnic	1 in 137	1 in 13600
		Sephardic Jewish	1 in 24	1 in 2300
Retinitis pigmentosa 28 (AR)	FAM161A	Ashkenazi Jewish	1 in 214	1 in 21300
		Pan-ethnic	1 in 289	1 in 28800
		Sephardic Jewish	1 in 41	1 in 4000
Rhizomelic chondrodysplasia punctata type 1/Refsum disease (PEX7-related) (AR)	PEX7	Pan-ethnic	1 in 157	1 in 15600

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
Rhizomelic chondrodysplasia punctata type 3 (AR)	AGPS	Pan-ethnic	≤1 in 500	Reduced
Roberts syndrome (AR)	ESCO2	Pan-ethnic	≤1 in 500	Reduced
RPGRIP1L-related disorders (AR)	RPGRIP1L *	Pan-ethnic	1 in 259	1 in 5160
RTEL1-related disorders (AR)	RTEL1	Ashkenazi Jewish	1 in 222	1 in 22100
		Pan-ethnic	≤1 in 500	Reduced
Sandhoff disease (AR)	HEXB	Metis (Saskatchewan)	1 in 15	1 in 1400
		Pan-ethnic	1 in 180	1 in 17900
Schimke immuno-osseous dysplasia (AR)	SMARCAL1	Pan-ethnic	≤1 in 500	Reduced
Severe combined immunodeficiency (DCLRE1C-related) (AR)	DCLRE1C	Navajo and Apache	1 in 10	1 in 900
		Pan-ethnic	≤1 in 500	Reduced
Severe combined immunodeficiency/Omenn syndrome (RAG2-related) (AR)	RAG2	Pan-ethnic	≤1 in 500	Reduced
Severe congenital neutropenia (VPS45-related) (AR)	VPS45	Pan-ethnic	≤1 in 500	Reduced
Sialic acid storage disorders (AR)	SLC17A5	Finnish	1 in 100	1 in 9900
		Pan-ethnic	≤1 in 500	Reduced
Sjögren-Larsson syndrome (AR)	ALDH3A2	Pan-ethnic	≤1 in 500	Reduced
		Swedish	1 in 250	1 in 24900
SLC26A2-related disorders (AR)	SLC26A2	Finnish	1 in 75	1 in 1480
		Pan-ethnic	1 in 158	1 in 3140
SLC35A3-related disorder (AR)	SLC35A3	Ashkenazi Jewish	1 in 469	1 in 46800
		Pan-ethnic	≤1 in 500	Reduced
Smith-Lemli-Opitz syndrome (AR)	DHCR7	African-American	1 in 339	1 in 8450
		Ashkenazi Jewish	1 in 41	1 in 1000
		Hispanic	1 in 135	1 in 3350
		Northern European	1 in 50	1 in 1225
		Pan-ethnic	1 in 71	1 in 1750
		Sephardic Jewish	1 in 68	1 in 1675
		Southern European	1 in 83	1 in 2050
Spastic paraplegia type 15 (AR)	ZFYVE26	Pan-ethnic	≤1 in 500	Reduced
Spastic paraplegia type 49 (AR)	TECPR2	Sephardic Jewish - Bukharian	1 in 38	1 in 3700
Spinal muscular atrophy (AR) SMN1: 3 copies Carrier residual risks listed are for 2 copy SMN1 results. Carrier residual risk for >2 copies are 5- to 10-fold lower.	SMN1 *	African-American	1 in 66	1 in 233
		Ashkenazi Jewish	1 in 41	1 in 667
		Asian	1 in 53	1 in 743
		Caucasian	1 in 35	1 in 567
		Hispanic	1 in 117	1 in 1161
Spondylothoracic dysostosis (AR)	MESP2	Pan-ethnic	1 in 224	1 in 22300
		Puerto Rican	1 in 55	1 in 5400
Steel syndrome (AR)	COL27A1 *	Pan-ethnic	≤1 in 500	Reduced
		Puerto Rican	1 in 51	1 in 5000
Stüve-Wiedemann syndrome (AR)	LIFR	Pan-ethnic	≤1 in 500	Reduced
Tay-Sachs disease/hexosaminidase A deficiency (AR)	HEXA	Ashkenazi Jewish	1 in 27	1 in 2600

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
		Asian	1 in 126	1 in 12500
		Caucasian	1 in 182	1 in 18100
		French Canadian	1 in 27	1 in 2600
		Irish	1 in 41	1 in 4000
		Pan-ethnic	1 in 250	1 in 24900
		Sephardic Jewish	1 in 125	1 in 12400
Tetrahydrobiopterin deficiency (PTS-related) (AR)	PTS	Chinese	1 in 122	1 in 12100
		Pan-ethnic	1 in 433	1 in 43200
Transient infantile liver failure (TRMU-related) (AR)	TRMU	Pan-ethnic	≤1 in 500	Reduced
		Sephardic Jewish (Yemenite)	1 in 34	1 in 3300
Tyrosine hydroxylase deficiency (AR)	TH	Caucasian	1 in 224	1 in 22300
		Pan-ethnic	≤1 in 500	Reduced
Tyrosinemia type I (AR)	FAH	Ashkenazi Jewish	1 in 143	1 in 2840
		French Canadian	1 in 66	1 in 1300
		French Canadian (Saguenay-Lac-St-Jean)	1 in 16	1 in 300
		Pan-ethnic	1 in 125	1 in 2480
Tyrosinemia type II (AR)	TAT	Pan-ethnic	1 in 250	1 in 24900
Usher syndrome type IB/MYO7A-related disorders (AR)	MYO7A	Pan-ethnic	1 in 200	1 in 3980
Usher syndrome type IC/USH1C-related disorders (AR)	USH1C	French Canadian/Acadian	1 in 227	1 in 22600
		Pan-ethnic	1 in 353	1 in 3521
		Sephardic Jewish	1 in 125	1 in 1241
Usher syndrome type ID (AR)	CDH23	Pan-ethnic	1 in 202	1 in 4020
Usher syndrome type IF/PCDH15-related disorders (AR)	PCDH15	Ashkenazi Jewish	1 in 78	1 in 7700
		Pan-ethnic	1 in 400	1 in 39900
Usher syndrome type IIA/USH2A-related disorders (AR)	USH2A	Caucasian	1 in 70	1 in 6900
		Pan-ethnic	1 in 112	1 in 11100
		Sephardic Jewish	1 in 36	1 in 3500
Usher syndrome type IIIA (AR)	CLRN1	Ashkenazi Jewish	1 in 120	1 in 11900
		Pan-ethnic	1 in 533	Reduced
Very long-chain acyl-CoA dehydrogenase deficiency (AR)	ACADVL	Pan-ethnic	1 in 100	1 in 9900
Wilson disease (AR)	ATP7B	Ashkenazi Jewish	1 in 67	1 in 3300
		Canary Islander	1 in 25	1 in 1200
		Pan-ethnic	1 in 90	1 in 4450
		Sardinian	1 in 50	1 in 2450
		Sephardic Jewish	1 in 65	1 in 3200
WNT10A-related disorders (AR)	WNT10A	Pan-ethnic	1 in 305	1 in 30400
X-linked adrenoleukodystrophy (XL)	ABCD1	Pan-ethnic	1 in 16800	Reduced
		Sephardic Jewish	≤1 in 500	Reduced
X-linked creatine transporter deficiency (XL)	SLC6A8	Pan-ethnic	≤1 in 500	Reduced
X-linked juvenile retinoschisis (XL)	RS1	Pan-ethnic	≤1 in 500	Reduced
X-linked myotubular myopathy (XL)	MTM1	Pan-ethnic	≤1 in 500	Reduced

Disorder (inheritance)	Gene	Ethnicity	Carrier frequency before screening	Carrier residual risk after negative result
X-linked severe combined immunodeficiency (XL)	IL2RG	Pan-ethnic	≤1 in 500	Reduced
Xeroderma pigmentosum complementation group A (AR)	XPA	Japanese Pan-ethnic	1 in 100 1 in 1667	1 in 9900 Reduced
Xeroderma pigmentosum complemetation group C (AR)	XPC	Pan-ethnic Tunisian	1 in 763 1 in 50	Reduced 1 in 4900
Zellweger spectrum disorder (PEX1-related) (AR)	PEX1	Pan-ethnic	1 in 144	1 in 14300
Zellweger spectrum disorder (PEX2-related) (AR)	PEX2	Ashkenazi Jewish Pan-ethnic	1 in 227 ≤1 in 500	1 in 22600 Reduced
Zellweger spectrum disorder (PEX6-related) (AR)	PEX6	French Canadian Pan-ethnic Sephardic Jewish	1 in 55 1 in 294 1 in 18	1 in 5400 1 in 29300 1 in 1700
Zellweger spectrum disorder (PEX10-related) (AR)	PEX10	Pan-ethnic	1 in 606	Reduced
Zellweger spectrum disorder (PEX12-related) (AR)	PEX12	Pan-ethnic	1 in 409	1 in 40800

Technical methods

- Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol, and sequenced using Illumina technology. Unless otherwise indicated, all targeted regions are sequenced with ≥50x depth or are supplemented with additional analysis. Reads are aligned to a reference sequence (GRCh37), and sequence changes are identified and interpreted in the context of a single clinically relevant transcript, indicated below. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 10bp of flanking intronic sequence, and other specific genomic regions demonstrated to be causative of disease at the time of assay design. Promoters, untranslated regions, and other non-coding regions are not otherwise interrogated. Exonic deletions and duplications are called using an in-house algorithm that determines copy number at each target by comparing the read depth for each target in the proband sequence with both mean read-depth and read-depth distribution, obtained from a set of clinical samples. All clinically significant observations are confirmed by orthogonal technologies, except individually validated variants. Confirmation technologies include any of the following: Sanger sequencing, Pacific Biosciences SMRT sequencing, MLPA, MLPA-seq, Array CGH. Array CGH confirmation of NGS CNV calling performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778). The following analyses are performed if relevant to the requisition. For GBA, the reference genome has been modified to mask the sites of polymorphic paralog sequence variants (PSVs) in both GBA and GBAP1. If one or more reportable variants is identified (see Limitations), GBA is amplified by long-range PCR; PacBio sequencing of the long-range amplicons is used to confirm the variant. Gene conversion events are flagged by our NGS pipeline and reportable pseudogene-derived variants are identified by long-range PCR of GBA followed by PacBio sequencing of the long-range amplicons. For HBA1/2, the reference genome has been modified to force some sequencing reads derived from HBA1 to align to HBA2, and variant calling algorithms are modified to support an expectation of 4 alleles in these regions. HBA1/2 copy number calling is performed by a custom hypothesis testing algorithm which generates diplotype calls. If sequence data for a sample does not support a unique high confidence match from among hypotheses tested, that sample is flagged for manual review. Copy number variation is only reported for coding sequence of HBA1 and HBA2 and the HS-40 region. This assay does not distinguish among the -α3.7 subtypes, and all -α3.7 variants are called as HBA1 deletions. This assay may not detect overlapping copy gain and copy loss events when the breakpoints of those events are similar. For FMR1, triplet repeats are detected by PCR with fluorescently labeled primers followed by capillary electrophoresis. Sizing accuracy is expected to be ±1 for CGG repeat alleles less than or equal to 90 repeat units and ±3 for CGG repeat alleles greater than 90 repeat units. If the two CGG repeats listed are the same, this may indicate that both alleles are the same size or that one allele is the reported size and the other allele is too small to be detected by this analysis. Reference ranges: Normal: <45 CGG repeats, intermediate: 45-54 CGG repeats, premutation: 55-200 CGG repeats, full mutation: >200 repeats. Technical component of confirmatory sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778).

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- The following transcripts were used in this analysis: ABCB11 (NM_003742.2), ABCC8 (NM_000352.4), ABCD1 (NM_000033.3), ACAD9 (NM_014049.4), ACADM (NM_000016.5), ACADVL (NM_000018.3), ACAT1 (NM_000019.3), ACOX1 (NM_004035.6), ACSF3 (NM_174917.4), ADA (NM_000022.2), ADAMTS2 (NM_014244.4), ADGRG1 (NM_005682.6), AGA (NM_000027.3), AGL (NM_000642.2), AGPS (NM_003659.3), AGXT (NM_000030.2), AIRE (NM_000383.3), ALDH3A2 (NM_000382.2), ALDOB (NM_000035.3), ALG6 (NM_013339.3), ALMS1 (NM_015120.4), ALPL (NM_000478.5), AMT (NM_000481.3), AQP2 (NM_000486.5), ARG1 (NM_000045.3), ARSA (NM_000487.5), ARSB (NM_000046.3), ASL (NM_000048.3), ASNS (NM_133436.3), ASPA (NM_000049.2), ASS1 (NM_000050.4), ATM (NM_000051.3), ATP6V1B1 (NM_001692.3), ATP7A (NM_000052.6), ATP7B (NM_000053.3), ATRX (NM_000489.4), BBS1 (NM_024649.4), BBS10 (NM_024685.3), BBS12 (NM_152618.2), BBS2 (NM_031885.3), BCKDHA (NM_000709.3), BCKDHB (NM_183050.2), BCS1L (NM_004328.4), BLM (NM_000057.3), BSND (NM_057176.2), CAPN3 (NM_000070.2), CBS (NM_000071.2), CDH23 (NM_022124.5), CEP290 (NM_025114.3), CERKL (NM_001030311.2), CFTR (NM_000492.3), CHM (NM_000390.2), CHRNE (NM_000080.3), CIITA (NM_000246.3), CLN3 (NM_001042432.1), CLN5 (NM_006493.2), CLN6 (NM_017882.2), CLN8 (NM_018941.3), CLRN1 (NM_174878.2), CNGB3 (NM_019098.4), COL27A1 (NM_032888.3), COL4A3 (NM_000091.4), COL4A4 (NM_000092.4), COL4A5 (NM_000495.4), COL7A1 (NM_000094.3), CPS1 (NM_001875.4), CPT1A (NM_001876.3), CPT2 (NM_000098.2), CRB1 (NM_201253.2), CTNS (NM_004937.2), CTSK (NM_000396.3), CYBA (NM_000101.3), CYBB (NM_000397.3), CYP11B1 (NM_000497.3), CYP11B2 (NM_000498.3), CYP17A1 (NM_000102.3), CYP19A1 (NM_031226.2), CYP27A1 (NM_000784.3), DBT (NM_001918.3), DCLRE1C (NM_001033855.2), DHCR7 (NM_001360.2), DHDDS (NM_024887.3), DLD (NM_000108.4), DMD (NM_004006.2), DNAH5 (NM_001369.2), DNAI1 (NM_012144.3), DNAI2 (NM_023036.4), DYSF (NM_003494.3), EDA (NM_001399.4), EIF2B5 (NM_003907.2), ELP1 (NM_003640.3), EMD (NM_000117.2), ERCC6 (NM_000124.3), ERCC8 (NM_000082.3), ESCO2 (NM_001017420.2), ETFA (NM_000126.3), ETFDH (NM_004453.3), ETHE1 (NM_014297.3), EVC (NM_153717.2), EVC2 (NM_147127.4), EYS (NM_001142800.1), F9 (NM_000133.3), FAH (NM_000137.2), FAM161A (NM_001201543.1), FANCA (NM_000135.2), FANCC (NM_000136.2), FANCG (NM_004629.1), FH (NM_000143.3), FKRP (NM_024301.4), FKTN (NM_001079802.1), FMR1 (NM_002024.5), G6PC (NM_000151.3), GAA (NM_000152.3), GALC (NM_000153.3), GALK1 (NM_000154.1), GALT (NM_000155.3), GAMT (NM_000156.5), GBA (NM_001005741.2), GBE1 (NM_000158.3), GCDH (NM_000159.3), GFM1 (NM_024996.5), GJB1 (NM_000166.5), GJB2 (NM_004004.5), GLA (NM_000169.2), GLB1 (NM_000404.2), GLDC (NM_000170.2), GLE1 (NM_001003722.1), GNE (NM_001128227.2), GNPTAB (NM_024312.4), GNPTG (NM_032520.4), GNS (NM_002076.3), GRHPR (NM_012203.1), HADHA (NM_000182.4), HAX1 (NM_006118.3), HBA1 (NM_000558.4), HBA2 (NM_000517.4), HBB (NM_000518.4), HEXA (NM_000520.4), HEXB (NM_000521.3), HGSNAT (NM_152419.2), HJV (NM_213653.3), HLCS (NM_000411.6), HMGCL (NM_000191.2), HOGA1 (NM_138413.3), HPS1 (NM_000195.4), HPS3 (NM_032383.4), HSD17B4 (NM_000414.3), HSD3B2 (NM_000198.3), HYAL1 (NM_153281.1), HYLS1 (NM_145014.2), IDS (NM_000202.6), IDUA (NM_000203.4), IL2RG (NM_000206.2), IVD (NM_002225.3), KCNJ11 (NM_000525.3), LAMA2 (NM_000426.3), LAMA3 (NM_000227.4), LAMB3 (NM_000228.2), LAMC2 (NM_005562.2), LCA5 (NM_181714.3), LDLR (NM_000527.4), LDLRAP1 (NM_015627.2), LHX3 (NM_014564.4), LIFR (NM_002310.5), LIPA (NM_000235.3), LOXHD1 (NM_144612.6), LPL (NM_000237.2), LRPPRC (NM_133259.3), MAN2B1 (NM_000528.3), MCOLN1 (NM_020533.2), MED17 (NM_004268.4), MESP2 (NM_001039958.1), MFSD8 (NM_152778.2), MKS1 (NM_017777.3), MLC1 (NM_015166.3), MMAA (NM_172250.2), MMAB (NM_052845.3), MMACHC (NM_015506.2), MMADHC (NM_015702.2), MPI (NM_002435.2), MPL (NM_005373.2), MPV17 (NM_002437.4), MTHFR (NM_005957.4), MTM1 (NM_000252.2), MTRR (NM_002454.2), MTTP (NM_000253.3), MUT (NM_000255.3), MYO7A (NM_000260.3), NAGLU (NM_000263.3), NAGS (NM_153006.2), NBN (NM_002485.4), NDRG1 (NM_006096.3), NDUFAF5 (NM_024120.4), NDUFS6 (NM_004553.4), NEB (NM_001271208.1), NPC1 (NM_000271.4), NPC2 (NM_006432.3), NPHS1 (NM_004646.3), NPHS2 (NM_014625.3), NR2E3 (NM_014249.3), NTRK1 (NM_001012331.1), OAT (NM_000274.3), OPA3 (NM_025136.3), OTC (NM_000531.5), PAH (NM_000277.1), PC (NM_000920.3), PCCA (NM_000282.3), PCCB (NM_000532.4), PCDH15 (NM_033056.3), PDHA1 (NM_000284.3), PDHB (NM_000925.3), PEX1 (NM_000466.2), PEX10 (NM_153818.1), PEX12 (NM_000286.2), PEX2 (NM_000318.2), PEX6 (NM_000287.3), PEX7 (NM_000288.3), PFKM (NM_000289.5), PHGDH (NM_006623.3), PKHD1 (NM_138694.3), PMM2 (NM_000303.2), POMGNT1 (NM_017739.3), PPT1 (NM_000310.3), PROP1 (NM_006261.4), PRPS1 (NM_002764.3), PSAP (NM_002778.3), PTS (NM_000317.2), PUS1 (NM_025215.5), PYGM (NM_005609.3), RAB23 (NM_183227.2), RAG2 (NM_000536.3), RAPSN (NM_005055.4), RARS2 (NM_020320.3), RDH12 (NM_152443.2), RMRP (NR_003051.3), RPE65 (NM_000329.2), RPGRIP1L (NM_015272.2), RS1 (NM_000330.3), RTEL1 (NM_001283009.1), SACS (NM_014363.5), SAMHD1 (NM_015474.3), SEPSECS (NM_016955.3), SGCA (NM_000023.2), SGCB (NM_000232.4), SGCG (NM_000231.2), SGSH (NM_000199.3), SLC12A3 (NM_000339.2), SLC12A6 (NM_133647.1), SLC17A5 (NM_012434.4), SLC22A5 (NM_003060.3), SLC25A13 (NM_014251.2), SLC25A15 (NM_014252.3), SLC26A2 (NM_000112.3), SLC26A4 (NM_000441.1), SLC35A3 (NM_012243.2), SLC37A4 (NM_001164277.1), SLC39A4 (NM_130849.3), SLC4A11 (NM_032034.3), SLC6A8 (NM_005629.3), SLC7A7 (NM_001126106.2), SMARCAL1 (NM_014140.3), SMN1 (NM_000344.3), SMPD1 (NM_000543.4), STAR (NM_000349.2), SUMF1 (NM_182760.3), TAT (NM_000353.2), TCIRG1 (NM_006019.3), TECPR2 (NM_014844.3), TFR2 (NM_003227.3), TGM1 (NM_000359.2), TH (NM_199292.2), TMEM216 (NM_001173990.2), TPP1 (NM_000391.3), TRMU (NM_018006.4), TSFM (NM_001172696.1), TTPA (NM_000370.3), TYMP (NM_001953.4), USH1C (NM_005709.3),

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USH2A (NM_206933.2), VPS13A (NM_033305.2), VPS13B (NM_017890.4), VPS45 (NM_007259.4), VRK1 (NM_003384.2), VSX2 (NM_182894.2), WNT10A (NM_025216.2), XPA (NM_000380.3), XPC (NM_004628.4), ZFYVE26 (NM_015346.3).

- Variants of uncertain significance are not included in this report; however, if additional evidence becomes available to indicate that a previously uncertain variant is clinically significant, Invitae will update this report and provide notification.
- A PMID is a unique identifier referring to a published, scientific paper. Search by PMID at http://www.ncbi.nlm.nih.gov/pubmed.
- An rsID is a unique identifier referring to a single genomic position, and is used to associate population frequency information with sequence changes at that position. Reported population frequencies are derived from a number of public sites that aggregate data from large-scale population sequencing projects, including ExAC (http://exac.broadinstitute.org), gnomAD (http://gnomad.broadinstitute.org), and dbSNP (http://ncbi.nlm.nih.gov/SNP).

Limitations

- Based on validation study results, this assay achieves >99% analytical sensitivity and specificity for single nucleotide variants, insertions and deletions <15bp in length, and exon-level deletions and duplications. Invitae's methods also detect insertions and deletions larger than 15bp but smaller than a full exon but sensitivity for these may be marginally reduced. Invitae's deletion/duplication analysis determines copy number at a single exon resolution at virtually all targeted exons. However, in rare situations, single-exon copy number events may not be analyzed due to inherent sequence properties or isolated reduction in data quality. Certain types of variants, such as structural rearrangements (e.g. inversions, gene conversion events, translocations, etc.) or variants embedded in sequence with complex architecture (e.g. short tandem repeats or segmental duplications), may not be detected. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity. Unless explicitly guaranteed, sequence changes in the promoter, non-coding exons, and other non-coding regions are not covered by this assay. Please consult the test definition on our website for details regarding regions or types of variants that are covered or excluded for this test. This report reflects the analysis of an extracted genomic DNA sample. In very rare cases, (circulating hematolymphoid neoplasm, bone marrow transplant, recent blood transfusion) the analyzed DNA may not represent the patient's constitutional genome.
- COL4A5: Deletion/duplication analysis is not offered for exons 11-12. COL27A1: Deletion/duplication analysis is not offered for exons 46-47. NEB: Deletion/duplication analysis is not offered for exons 82-105. NEB variants in this region with no evidence towards pathogenicity are not included in this report, but are available upon request. VPS13A: Deletion/duplication analysis is not offered for exons 2-3, 27-28. RPGRIP1L: Sequence analysis not offered for exon 23. MMADHC: Deletion/duplication analysis is not offered for exons 5-6. MTHFR: The NM_005957.4:c.665C>T (p.Ala222Val) (aka 677C>T) and c.1286A>C (p.Glu429Ala) (aka 1298A>C) variants are not reported in our primary report. NBN: Deletion/duplication analysis is not offered for exons 15-16. HBA1/2: This assay is designed to detect deletions and duplications of HBA1 and/or HBA2, resulting from the -alpha20.5, --MED, --SEA, --FIL/--THAI, -alpha3.7, -alpha4.2, anti3.7 and anti4.2. Sensitivity to detect other copy number variants may be reduced. Detection of overlapping deletion and duplication events will be limited to combinations of events with significantly differing boundaries. In addition, deletion of the enhancer element HS-40 and the sequence variant, Constant Spring (NM_000517.4:c.427T>C), can be identified by this assay. SMN1: Systematic exon numbering is used for all genes, including SMN1, and for this reason the exon typically referred to as exon 7 in the literature (PMID: 8838816) is referred to as exon 8 in this report. This assay unambiguously detects SMN1 exon 8 copy number. The presence of the g.27134T>G variant (also known as c.*3+80T>G) is reported if SMN1 copy number = 2. GBA: c.84dupG (p.Leu29Alafs*18), c.115+1G>A (Splice donor), c.222_224delTAC (p.Thr75del), c.475C>T (p.Arg159Trp), c.595_596delCT (p.Leu199Aspfs*62), c.680A>G (p.Asn227Ser), c.721G>A (p.Gly241Arg), c.754T>A (p.Phe252Ile), c.1226A>G (p.Asn409Ser), c.1246G>A (p.Gly416Ser), c.1263_1317del (p.Leu422Profs*4), c.1297G>T (p.Val433Leu), c.1342G>C (p.Asp448His), c.1343A>T (p.Asp448Val), c.1448T>C (p.Leu483Pro), c.1504C>T (p.Arg502Cys), c.1505G>A (p.Arg502His), c.1603C>T (p.Arg535Cys), c.1604G>A (p.Arg535His) variants only. Sensitivity to detect these variants if they result from complex gene conversion events may be reduced. IDS: Detection of complex rearrangements not offered (PMID: 7633410, 20301451). TSFM: Sequence analysis not offered for exon 5. ALG6: Deletion/duplication analysis is not offered for exons 11-12. FMR1: This assay is designed to detect and categorize CGG repeats found at the promoter region of the FMR1 locus for all alleles reported. If two equal alleles are reported, this may indicate that both alleles are the same size, or that one allele is the reported size and the other allele is too small to be detected by this analysis.

This report has been reviewed and approved by:

Placeholder for signature

Disclaimer

DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of many aspects used by the healthcare provider to help with a diagnosis and treatment plan, but it is not a diagnosis itself. This test was developed and its performance characteristics determined by Invitae. It has not been cleared or approved by the FDA. The laboratory is regulated under the Clinical Laboratory Improvement Act (CLIA) as qualified to perform high-complexity clinical tests (CLIA ID: 05D2040778). This test is used for clinical purposes. It should not be regarded as investigational or for research.

Laboratory Director Tina Hambuch, Ph.D., FACMG
NY Laboratory Director Swaroop Aradhya, Ph.D., FACMG
Invitae 1400 16th Street, San Francisco, CA 94103
E: clientservices@invitae.com **P:** 415.374.7782 or 800.436.3037