



Reproductive Technologies, Inc.

# THE SPERM BANK OF CALIFORNIA

## EXPANDED CARRIER SCREENING RESULTS DONOR 5984

Expanded carrier screening for 268 autosomal recessive conditions was completed by Invitae and reported on 03/02/2022.

The results were **NEGATIVE** for all 268 conditions.

| Disease                 | Result   | Residual risk to be a carrier |
|-------------------------|--|-------------------------------|
| Cystic Fibrosis         | Negative   | 1 in 2,700                    |
| Spinal Muscular Atrophy | Negative - 2 copies exon 7<br>Negative for c.*3+80T>G<br>variant in exon 7 | 1 in 784                      |
| HBB Hemoglobinopathies  | Negative   | 1 in 1,600                    |
| Alpha Thalassemia       | Negative   | 1 in 241                      |

Genetic screening tests can significantly reduce, but never completely eliminate, the chance that a person is a carrier for a particular disorder.

Please refer to the donor's Invitae expanded carrier test report for more information on the testing completed and the donor's results.

**Please also see the Health Problems List for a summary of the information that this donor has provided to us regarding personal and family medical history.**

Sincerely,

Janine Mash  
LCGC Certified Genetic  
Counselor San Francisco  
Genetic Counseling

|                               |            |                                |            |                       |                     |
|-------------------------------|------------|--------------------------------|------------|-----------------------|---------------------|
| <b>Patient name:</b>          | 5984 DONOR | <b>Sample type:</b>            | Saliva     | <b>Report date:</b>   | 03/02/2022          |
| <b>DOB:</b>                   |            | <b>Sample collection date:</b> | 02/16/2022 | <b>Invitae #:</b>     | RQ3201247           |
| <b>Sex assigned at birth:</b> | Male       | <b>Sample accession date:</b>  | 02/17/2022 | <b>Clinical team:</b> | Janine Mash         |
| <b>Gender:</b>                |            | <b>MRN:</b>                    |            |                       | Lorraine Bonner, MD |

**Reason for testing**

Gamete donor

**Test performed**

Invitae Comprehensive Carrier Screen without X-linked Disorders

- Primary Panel (CF, SMA)
- Add-on Comprehensive Carrier Screen without X-linked Disorders genes


**RESULT: NEGATIVE**

This carrier test evaluated 268 gene(s) for genetic changes (variants) that are associated with an increased risk of having a child with a genetic condition. Knowledge of carrier status for one of these conditions may provide information that can be used to assist with family planning and/or preparation.

This test did not identify any genetic changes in the gene(s) analyzed that are currently recognized as clinically significant. This negative result reduces, but does not eliminate, the chance that this individual is a carrier for conditions caused by any of the genes tested. This individual may still be a carrier for a genetic condition that is not evaluated by this test.

## Next steps

- 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 conditions listed.
- Discussion with a physician and/or genetic counselor is recommended to further review the implications of this test result and to understand these results in the context of any family history of a genetic condition.
- 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.

## 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. For genes associated with both dominant and recessive inheritance, the numbers in this table apply to the recessive condition(s) associated with the gene, unless otherwise noted. Residual risk values are provided for disorders when carrier frequency is greater than 1 in 500. For disorders with carrier frequency equal to, or 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 ethnic background of an individual. For 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 a 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-hydroxy-3-methylglutaryl-CoA lyase deficiency (AR)<br>NM_000191.2  | HMGCL           | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
|  |                 | Portuguese                 | 1 in 160                           | 1 in 15900                                  |
| ABCB11-related conditions (AR)<br>NM_003742.2  | ABCB11          | Pan-ethnic                 | 1 in 100                           | 1 in 9900                                   |
| ABCC8-related conditions (AR)<br>NM_000352.4<br>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           | 1 in 52                            | 1 in 5100                                   |
|  |                 | Finnish                    | 1 in 100                           | 1 in 9900                                   |
|  |                 | Pan-ethnic                 | 1 in 177                           | 1 in 17600                                  |
| Abetalipoproteinemia (AR)<br>NM_000253.3   | MTTP            | Ashkenazi Jewish           | 1 in 131                           | 1 in 13000                                  |
|  |                 | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Achromatopsia (CNGB3-related) (AR)<br>NM_019098.4  | CNGB3           | Pan-ethnic                 | 1 in 93                            | 1 in 9200                                   |
| ACOX1-related conditions (AR)<br>NM_004035.6   | ACOX1           | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Acrodermatitis enteropathica (AR)<br>NM_130849.3   | SLC39A4         | Pan-ethnic                 | 1 in 354                           | 1 in 35300                                  |
| Adenosine deaminase deficiency (AR)<br>NM_000022.2   | ADA             | Pan-ethnic                 | 1 in 224                           | 1 in 2788                                   |
| Aicardi-Goutieres syndrome 5 (AR)<br>NM_015474.3   | SAMHD1          | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Aldosterone synthase deficiency (AR)<br>NM_000498.3  | CYP11B2         | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
|  |                 | Sephardic Jewish (Iranian) | 1 in 30                            | 1 in 2900                                   |
| Alpha-mannosidosis (AR)<br>NM_000528.3   | MAN2B1          | Pan-ethnic                 | 1 in 354                           | 1 in 35300                                  |
| Alpha-thalassemia (AR)<br>NM_000558.4, NM_000517.4   | HBA1/<br>HBA2 * | African-American           | 1 in 30                            | 1 in 291                                    |
|  |                 | Asian                      | 1 in 20                            | 1 in 191                                    |
|  |                 | Caucasian                  | ≤1 in 500                          | Reduced                                     |
|  |                 | Pan-ethnic                 | 1 in 25                            | 1 in 241                                    |
| Alport syndrome (COL4A3-related) (AR)<br>NM_000091.4   | COL4A3          | Ashkenazi Jewish           | 1 in 192                           | 1 in 19100                                  |
|  |                 | Caucasian                  | 1 in 284                           | 1 in 28300                                  |
|  |                 | Pan-ethnic                 | 1 in 354                           | 1 in 35300                                  |
| Alport syndrome (COL4A4-related) (AR)<br>NM_000092.4   | COL4A4          | Pan-ethnic                 | 1 in 353                           | 1 in 35200                                  |
| Alström syndrome (AR)<br>NM_015120.4   | ALMS1           | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Arginase deficiency (AR)<br>NM_000045.3  | ARG1            | Pan-ethnic                 | 1 in 274                           | 1 in 27300                                  |
| Argininosuccinate lyase deficiency (AR)<br>NM_000048.3   | ASL             | Pan-ethnic                 | 1 in 133                           | 1 in 1321                                   |
| Aromatase deficiency (AR)<br>NM_031226.2   | CYP19A1         | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Asparagine synthetase deficiency (AR)<br>NM_133436.3   | ASNS            | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |

| DISORDER (INHERITANCE)  | GENE    | ETHNICITY                              | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|---|---------|--|------------------------------------|---|
|   |         | Sephardic Jewish (Iranian)             | 1 in 80                            | 1 in 7900                                   |
| Aspartylglucosaminuria (AR)<br>NM_000027.3  | AGA     | Finnish                                | 1 in 69                            | 1 in 6800                                   |
|   |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Ataxia with vitamin E deficiency (AR)<br>NM_000370.3  | TTPA    | Italian                                | 1 in 274                           | 1 in 2731                                   |
|   |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| ATM-related conditions (AR)<br>NM_000051.3  | ATM     | Pan-ethnic                             | 1 in 100                           | 1 in 9900                                   |
|   |         | Sephardic Jewish                       | 1 in 69                            | 1 in 6800                                   |
| Autoimmune polyendocrinopathy with candidiasis and ectodermal dysplasia (AR)<br>NM_000383.3 | 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 congenital ichthyosis (TGM1-related) (AR)<br>NM_000359.2                | TGM1    | Norwegian                              | 1 in 151                           | 1 in 3000                                   |
|   |         | Pan-ethnic                             | 1 in 224                           | 1 in 4460                                   |
| Autosomal recessive spastic ataxia of Charlevoix-Saguenay (AR)<br>NM_014363.5               | SACS    | French Canadian (Saguenay-Lac-St-Jean) | 1 in 21                            | 1 in 2000                                   |
|   |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Bardet-Biedl syndrome (BBS10-related) (AR)<br>NM_024685.3                                   | BBS10   | Pan-ethnic                             | 1 in 354                           | 1 in 35300                                  |
| Bardet-Biedl syndrome (BBS12-related) (AR)<br>NM_152618.2                                   | BBS12   | Pan-ethnic                             | 1 in 708                           | Reduced                                     |
| BBS1-related conditions (AR)<br>NM_024649.4   | BBS1    | Faroese                                | 1 in 30                            | 1 in 2900                                   |
|   |         | Pan-ethnic                             | 1 in 330                           | 1 in 32900                                  |
| BBS2-related conditions (AR)<br>NM_031885.3   | BBS2    | Ashkenazi Jewish                       | 1 in 140                           | 1 in 13900                                  |
|   |         | Pan-ethnic                             | 1 in 560                           | Reduced                                     |
| BCS1L-related conditions (AR)<br>NM_004328.4  | BCS1L   | Caucasian                              | 1 in 407                           | 1 in 40600                                  |
|   |         | Finnish                                | 1 in 108                           | 1 in 10700                                  |
|   |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Beta-ketothiolase deficiency (AR)<br>NM_000019.3  | ACAT1   | Caucasian                              | 1 in 354                           | 1 in 35300                                  |
|   |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Bioppterin-deficient hyperphenylalaninemia (PTS-related) (AR)<br>NM_000317.2                | PTS     | Chinese                                | 1 in 122                           | 1 in 12100                                  |
|   |         | Pan-ethnic                             | 1 in 433                           | 1 in 43200                                  |
| Bloom syndrome (AR)<br>NM_000057.3  | BLM     | Ashkenazi Jewish                       | 1 in 100                           | 1 in 9900                                   |
|   |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| BSND-related conditions (AR)<br>NM_057176.2   | BSND    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Canavan disease (AR)<br>NM_000049.2   | ASPA    | Ashkenazi Jewish                       | 1 in 57                            | 1 in 5600                                   |
|   |         | Pan-ethnic                             | 1 in 159                           | 1 in 15800                                  |
| Carbamoyl phosphate synthetase I deficiency (AR)<br>NM_001875.4                             | CPS1    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Carnitine palmitoyltransferase I deficiency (AR)<br>NM_001876.3                             | CPT1A   | Hutterite                              | 1 in 16                            | 1 in 1500                                   |
|   |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Carnitine palmitoyltransferase II deficiency (AR)<br>NM_000098.2                            | CPT2    | Ashkenazi Jewish                       | 1 in 45                            | 1 in 4400                                   |
|   |         | Pan-ethnic                             | 1 in 182                           | 1 in 18100                                  |
| Carpenter syndrome (RAB23-related) (AR)<br>NM_183227.2                                      | RAB23   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Cartilage-hair hypoplasia-anauxetic dysplasia spectrum disorders (AR)<br>NR_003051.3        | RMRP    | Amish                                  | 1 in 10                            | 1 in 900                                    |
|   |         | Finnish                                | 1 in 76                            | 1 in 7500                                   |
|   |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| CDH23-related conditions (AR)<br>NM_022124.5  | CDH23   | Pan-ethnic                             | 1 in 202                           | 1 in 4020                                   |
| CEP290-related conditions (AR)<br>NM_025114.3   | CEP290  | Pan-ethnic                             | 1 in 185                           | 1 in 18400                                  |
| Cerebrotendinous xanthomatosis (AR)<br>NM_000784.3  | CYP27A1 | Pan-ethnic                             | 1 in 112                           | 1 in 5550                                   |
|   |         | Sephardic Jewish                       | 1 in 76                            | 1 in 3750                                   |
| CERKL-related conditions (AR)<br>NM_001030311.2   | CERKL   | Pan-ethnic                             | 1 in 137                           | 1 in 13600                                  |
|   |         | Sephardic Jewish                       | 1 in 24                            | 1 in 2300                                   |

| DISORDER (INHERITANCE)   | GENE      | ETHNICITY  | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|--|-----------|--|------------------------------------|---|
| CFTR-related conditions (AR)<br>NM_000492.3  | 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 type 4D (AR)<br>NM_006096.3  | NDRG1     | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
|  |           | Roma   | 1 in 22                            | 1 in 2100                                   |
| Chorea-acanthocytosis (AR)<br>NM_033305.2  | VPS13A *  | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
| Chronic granulomatous disease (CYBA-related) (AR)<br>NM_000101.3   | CYBA      | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
|  |           | Sephardic Jewish (Moroccan)                        | 1 in 13                            | 1 in 1200                                   |
| Citrin deficiency (AR)<br>NM_014251.2  | SLC25A13  | Chinese  | 1 in 65                            | 1 in 6400                                   |
|  |           | Japanese   | 1 in 65                            | 1 in 6400                                   |
|  |           | Korean   | 1 in 112                           | 1 in 11100                                  |
|  |           | Pan-ethnic   | 1 in 313                           | 1 in 31200                                  |
|  |           | Southern Chinese and Taiwanese                     | 1 in 48                            | 1 in 4700                                   |
| Citrullinemia type 1 (AR)<br>NM_000050.4   | ASS1      | Pan-ethnic   | 1 in 120                           | 1 in 2975                                   |
| CLN3-related conditions (AR)<br>NM_001042432.1   | CLN3      | Pan-ethnic   | 1 in 230                           | 1 in 22900                                  |
| CLRN1-related conditions (AR)<br>NM_174878.2   | CLRN1     | Ashkenazi Jewish                                   | 1 in 120                           | 1 in 11900                                  |
|  |           | Pan-ethnic   | 1 in 533                           | Reduced                                     |
| Cobalamin C deficiency (AR)<br>NM_015506.2   | MMACHC    | Pan-ethnic   | 1 in 123                           | 1 in 12200                                  |
| Cobalamin D deficiency (AR)<br>NM_015702.2   | MMADHC *  | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
| Cockayne syndrome A (AR)<br>NM_000082.3  | ERCC8     | Pan-ethnic   | 1 in 514                           | Reduced                                     |
| Cockayne syndrome B (AR)<br>NM_000124.3  | ERCC6     | Pan-ethnic   | 1 in 377                           | 1 in 37600                                  |
| Cohen syndrome (AR)<br>NM_017890.4   | VPS13B    | Amish (Ohio)                                       | 1 in 12                            | 1 in 1100                                   |
|  |           | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
| Combined malonic and methylmalonic aciduria (AR)<br>NM_174917.4  | ACSF3     | Pan-ethnic   | 1 in 87                            | 1 in 8600                                   |
| Combined oxidative phosphorylation deficiency 1 (AR)<br>NM_024996.5                                      | GFM1      | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
| Combined oxidative phosphorylation deficiency 3 (AR)<br>NM_001172696.1                                   | TSFM *    | Finnish  | 1 in 80                            | 1 in 1129                                   |
|  |           | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
| Combined pituitary hormone deficiency (LHX3-related) (AR)<br>NM_014564.4                                 | LHX3      | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
| Combined pituitary hormone deficiency (PROP1-related) (AR)<br>NM_006261.4                                | PROP1     | Pan-ethnic   | 1 in 45                            | 1 in 2200                                   |
| Congenital adrenal hyperplasia due to 3-beta-hydroxysteroid dehydrogenase deficiency (AR)<br>NM_000198.3 | HSD3B2    | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
| Congenital adrenal hyperplasia due to 21-hydroxylase deficiency (AR)<br>NM_000500.7                      | CYP21A2 * | Pan-ethnic   | 1 in 61                            | 1 in 751                                    |
| Congenital disorder of glycosylation (SLC35A3-related) (AR)<br>NM_012243.2                               | SLC35A3   | Ashkenazi Jewish                                   | 1 in 469                           | 1 in 46800                                  |
|  |           | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |
| Congenital disorder of glycosylation type Ia (AR)<br>NM_000303.2   | 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 disorder of glycosylation type Ib (AR)<br>NM_002435.2   | MPI       | Pan-ethnic   | ≤1 in 500                          | Reduced                                     |

| DISORDER (INHERITANCE)   | GENE     | ETHNICITY                              | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|--|----------|--|------------------------------------|---|
| Congenital disorder of glycosylation type Ic (AR)<br>NM_013339.3                   | ALG6 *   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Congenital insensitivity to pain with anhidrosis (AR)<br>NM_001012331.1            | NTRK1    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Congenital myasthenic syndrome (CHRNE-related) (AR)<br>NM_000080.3                 | CHRNE    | European Roma                          | 1 in 25                            | 1 in 2400                                   |
|  |          | Pan-ethnic                             | 1 in 200                           | 1 in 19900                                  |
| Congenital nephrotic syndrome type 1 (AR)<br>NM_004646.3                           | NPHS1    | Finnish                                | 1 in 46                            | 1 in 4500                                   |
|  |          | Old Order Mennonite                    | 1 in 12                            | 1 in 1100                                   |
|  |          | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Congenital nephrotic syndrome type 2 (AR)<br>NM_014625.3                           | NPHS2    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Corneal dystrophy and perceptive deafness (AR)<br>NM_032034.3                      | SLC4A11  | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| CRB1-related conditions (AR)<br>NM_201253.2  | CRB1     | Pan-ethnic                             | 1 in 112                           | 1 in 11100                                  |
| CYP11B1-related conditions (AR)<br>NM_000497.3                                     | CYP11B1  | Pan-ethnic                             | 1 in 194                           | 1 in 19300                                  |
|  |          | Sephardic Jewish (Moroccan)            | 1 in 40                            | 1 in 3900                                   |
| CYP17A1-related conditions (AR)<br>NM_000102.3                                     | CYP17A1  | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Cystinosis (AR)<br>NM_004937.2   | CTNS     | French Canadian (Saguenay-Lac-St-Jean) | 1 in 39                            | 1 in 3800                                   |
|  |          | Pan-ethnic                             | 1 in 158                           | 1 in 15700                                  |
|  |          | Sephardic Jewish (Moroccan)            | 1 in 100                           | 1 in 9900                                   |
| DHDDS-related conditions (AR)<br>NM_024887.3                                       | DHDDS    | Ashkenazi Jewish                       | 1 in 117                           | 1 in 11600                                  |
|  |          | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Dihydroliipoamide dehydrogenase deficiency (AR)<br>NM_000108.4                     | DLD      | Ashkenazi Jewish                       | 1 in 107                           | 1 in 5300                                   |
|  |          | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Distal renal tubular acidosis with deafness (ATP6V1B1-related) (AR)<br>NM_001692.3 | ATP6V1B1 | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
|  |          | Sephardic Jewish                       | 1 in 140                           | 1 in 13900                                  |
| DYSF-related conditions (AR)<br>NM_003494.3  | DYSF     | Pan-ethnic                             | 1 in 311                           | 1 in 31000                                  |
|  |          | Sephardic Jewish (Libyan)              | 1 in 10                            | 1 in 900                                    |
| Dyskeratosis congenita spectrum disorders (RTEL1-related) (AR)<br>NM_001283009.1   | RTEL1    | Ashkenazi Jewish                       | 1 in 222                           | 1 in 22100                                  |
|  |          | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Dystrophic epidermolysis bullosa (AR)<br>NM_000094.3                               | COL7A1   | Pan-ethnic                             | 1 in 370                           | 1 in 12300                                  |
| Ehlers-Danlos syndrome, dermatosparaxis type (AR)<br>NM_014244.4                   | ADAMTS2  | Ashkenazi Jewish                       | 1 in 187                           | 1 in 18600                                  |
|  |          | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Ellis-van Creveld syndrome (EVC-related) (AR)<br>NM_153717.2                       | EVC      | Amish                                  | 1 in 8                             | 1 in 700                                    |
|  |          | Pan-ethnic                             | 1 in 220                           | 1 in 21900                                  |
| Ethylmalonic encephalopathy (AR)<br>NM_014297.3                                    | ETHE1    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| EVC2-related conditions (AR)<br>NM_147127.4  | EVC2     | Pan-ethnic                             | 1 in 199                           | 1 in 19800                                  |
| Familial chylomicronemia syndrome (AR)<br>NM_000237.2                              | LPL      | French Canadian (Saguenay-Lac-St-Jean) | 1 in 46                            | 1 in 4500                                   |
|  |          | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Familial dysautonomia (AR)<br>NM_003640.3  | ELP1     | Ashkenazi Jewish                       | 1 in 36                            | 1 in 3500                                   |
|  |          | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Familial hypercholesterolemia (LDLR-related) (AD)<br>NM_000527.4                   | LDLR     | Afrikaner                              | 1 in 72                            | 1 in 7100                                   |
|  |          | Ashkenazi Jewish                       | 1 in 69                            | 1 in 6800                                   |
|  |          | French Canadian                        | 1 in 270                           | 1 in 26900                                  |
|  |          | Pan-ethnic                             | 1 in 250                           | 1 in 24900                                  |
| Familial hypercholesterolemia (LDLRAP1-related) (AR)<br>NM_015627.2                | LDLRAP1  | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
|  |          | Sardinian                              | 1 in 143                           | 1 in 14200                                  |
| Fanconi anemia type A (AR)<br>NM_000135.2  | FANCA    | Afrikaner                              | 1 in 83                            | 1 in 8200                                   |
|  |          | Pan-ethnic                             | 1 in 345                           | 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)<br>NM_000136.2                               | FANCC   | Ashkenazi Jewish            | 1 in 89                            | 1 in 8800                                   |
|   |         | Pan-ethnic                  | 1 in 417                           | 1 in 41600                                  |
| Fanconi anemia type G (AR)<br>NM_004629.1                               | FANCG   | African-American            | 1 in 100                           | 1 in 9900                                   |
|   |         | Pan-ethnic                  | ≤1 in 500                          | Reduced                                     |
| FH-related conditions (AR)<br>NM_000143.3                               | FH      | Pan-ethnic                  | ≤1 in 500                          | Reduced                                     |
| Galactokinase deficiency galactosemia (AR)<br>NM_000154.1               | GALK1   | Pan-ethnic                  | 1 in 122                           | 1 in 12100                                  |
|   |         | Roma                        | 1 in 47                            | 1 in 4600                                   |
| Galactosemia (GALT-related) (AR)<br>NM_000155.3                         | 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                                   |
| GBA-related conditions including Gaucher disease (AR)<br>NM_001005741.2 | GBA *   | Ashkenazi Jewish            | 1 in 15                            | 1 in 234                                    |
|   |         | Pan-ethnic                  | 1 in 158                           | 1 in 561                                    |
| GBE1-related conditions (AR)<br>NM_000158.3                             | GBE1    | Ashkenazi Jewish            | 1 in 68                            | 1 in 6700                                   |
|   |         | Pan-ethnic                  | 1 in 387                           | 1 in 38600                                  |
| Gitelman syndrome (AR)<br>NM_000339.2                                   | SLC12A3 | Pan-ethnic                  | 1 in 100                           | 1 in 9900                                   |
| GJB2-related conditions (AR)<br>NM_004004.5                             | GJB2    | Ashkenazi Jewish            | 1 in 13                            | 1 in 1200                                   |
|   |         | Pan-ethnic                  | 1 in 50                            | 1 in 4900                                   |
|   |         | Thai                        | 1 in 9                             | 1 in 800                                    |
| GLB1-related conditions (AR)<br>NM_000404.2                             | GLB1    | Pan-ethnic                  | 1 in 158                           | 1 in 15700                                  |
|   |         | Roma                        | 1 in 50                            | 1 in 4900                                   |
|   |         | South Brazilian             | 1 in 58                            | 1 in 5700                                   |
| GLE1-related conditions (AR)<br>NM_001003722.1                          | GLE1    | Finnish                     | 1 in 100                           | 1 in 9900                                   |
|   |         | Pan-ethnic                  | ≤1 in 500                          | Reduced                                     |
| Glutaric acidemia type I (AR)<br>NM_000159.3                            | 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 IIA (AR)<br>NM_000126.3                          | ETFA    | Pan-ethnic                  | ≤1 in 500                          | Reduced                                     |
| Glutaric acidemia type IIC (AR)<br>NM_004453.3                          | ETFDH   | Asian                       | 1 in 87                            | 1 in 8600                                   |
|   |         | Pan-ethnic                  | 1 in 250                           | 1 in 24900                                  |
| Glycine encephalopathy (AMT-related) (AR)<br>NM_000481.3                | AMT     | Finnish                     | 1 in 142                           | 1 in 14100                                  |
|   |         | Pan-ethnic                  | 1 in 325                           | 1 in 32400                                  |
| Glycine encephalopathy (GLDC-related) (AR)<br>NM_000170.2               | GLDC    | Caucasian                   | 1 in 141                           | 1 in 14000                                  |
|   |         | Pan-ethnic                  | 1 in 165                           | 1 in 16400                                  |
| Glycogen storage disease type Ia (AR)<br>NM_000151.3                    | G6PC    | Ashkenazi Jewish            | 1 in 71                            | 1 in 1400                                   |
|   |         | Pan-ethnic                  | 1 in 177                           | 1 in 3520                                   |
| Glycogen storage disease type II (Pompe disease) (AR)<br>NM_000152.3    | GAA     | African-American            | 1 in 60                            | 1 in 5900                                   |
|   |         | 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)<br>NM_000642.2                   | 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 V (AR)<br>NM_005609.3                     | PYGM    | Caucasian                   | 1 in 158                           | 1 in 15700                                  |
|   |         | Pan-ethnic                  | 1 in 171                           | 1 in 17000                                  |
|   |         | Sephardic Jewish (Kurdish)  | 1 in 84                            | 1 in 8300                                   |
| Glycogen storage disease type VII (AR)<br>NM_000289.5                   | PFKM    | Ashkenazi Jewish            | 1 in 250                           | 1 in 24900                                  |
|   |         | Pan-ethnic                  | ≤1 in 500                          | Reduced                                     |
| GNE-related conditions (AR)<br>NM_001128227.2                           | GNE     | Pan-ethnic                  | 1 in 179                           | 1 in 17800                                  |
|   |         | Sephardic Jewish (Iranian)  | 1 in 10                            | 1 in 900                                    |

| DISORDER (INHERITANCE)   | GENE      | ETHNICITY                    | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|--|-----------|------------------------------|------------------------------------|---|
| GNPTAB-related conditions (AR)<br>NM_024312.4                                    | GNPTAB    | Irish Traveller              | 1 in 15                            | 1 in 1400                                   |
|  |           | Pan-ethnic                   | 1 in 200                           | 1 in 19900                                  |
| Guanidinoacetate methyltransferase deficiency (AR)<br>NM_000156.5                | GAMT      | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
|  |           | Portuguese                   | 1 in 125                           | 1 in 12400                                  |
| Gyrate atrophy of the choroid and retina (AR)<br>NM_000274.3                     | OAT *     | Finnish                      | 1 in 126                           | 1 in 12500                                  |
|  |           | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
|  |           | Sephardic Jewish             | 1 in 177                           | 1 in 17600                                  |
| HADHA-related conditions (AR)<br>NM_000182.4                                     | HADHA     | Caucasian                    | 1 in 250                           | 1 in 24900                                  |
|  |           | Finnish                      | 1 in 125                           | 1 in 12400                                  |
|  |           | Pan-ethnic                   | 1 in 350                           | 1 in 34900                                  |
| HBB-related hemoglobinopathies (AR)<br>NM_000518.4                               | 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)<br>NM_000035.3                              | 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 type 2 (HJV-related) (AR)<br>NM_213653.3              | HJV       | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
| Hereditary hemochromatosis type 3 (AR)<br>NM_003227.3                            | TFR2      | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
| Hermansky-Pudlak syndrome type 1 (AR)<br>NM_000195.4                             | HPS1      | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
|  |           | Puerto Rican (Northwestern)  | 1 in 21                            | 1 in 2000                                   |
| Hermansky-Pudlak syndrome type 3 (AR)<br>NM_032383.4                             | HPS3      | Ashkenazi Jewish             | 1 in 235                           | 1 in 23400                                  |
|  |           | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
|  |           | Puerto Rican (Central)       | 1 in 63                            | 1 in 6200                                   |
| HGSNAT-related conditions (AR)<br>NM_152419.2                                    | HGSNAT    | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
| Holocarboxylase synthetase deficiency (AR)<br>NM_000411.6                        | HLCS      | Faroese                      | 1 in 20                            | 1 in 1900                                   |
|  |           | Japanese                     | 1 in 158                           | 1 in 15700                                  |
|  |           | Pan-ethnic                   | 1 in 224                           | 1 in 22300                                  |
| Homocystinuria due to cobalamin E deficiency (AR)<br>NM_002454.2                 | MTRR      | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
| Homocystinuria due to cystathionine beta-synthase deficiency (AR)<br>NM_000071.2 | 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)<br>NM_005957.4                       | MTHFR *   | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
|  |           | Sephardic Jewish (Bukharian) | 1 in 39                            | 1 in 3800                                   |
| HSD17B4-related conditions (AR)<br>NM_000414.3                                   | HSD17B4   | Pan-ethnic                   | 1 in 158                           | 1 in 15700                                  |
| Hydrolethalus syndrome type 1 (AR)<br>NM_145014.2                                | HYLS1     | Finnish                      | 1 in 40                            | 1 in 3900                                   |
|  |           | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
| Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome (AR)<br>NM_014252.3  | SLC25A15  | Metis (Saskatchewan)         | 1 in 19                            | 1 in 1800                                   |
|  |           | Pan-ethnic                   | ≤1 in 500                          | Reduced                                     |
| Hypophosphatasia (AR)<br>NM_000478.5   | ALPL      | Mennonite                    | 1 in 25                            | 1 in 480                                    |
|  |           | Pan-ethnic                   | 1 in 150                           | 1 in 2980                                   |
| Isovaleric acidemia (AR)<br>NM_002225.3  | IVD       | Pan-ethnic                   | 1 in 250                           | 1 in 24900                                  |
| Joubert syndrome and related disorders (MKS1-related) (AR)<br>NM_017777.3        | MKS1      | Finnish                      | 1 in 47                            | 1 in 920                                    |
|  |           | Pan-ethnic                   | 1 in 260                           | 1 in 5180                                   |
| Joubert syndrome and related disorders (RPGRIPL-related) (AR)<br>NM_015272.2     | RPGRIPL * | Pan-ethnic                   | 1 in 259                           | 1 in 5160                                   |



| DISORDER (INHERITANCE)   | GENE    | ETHNICITY                  | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|--|---------|----------------------------|------------------------------------|---|
| Joubert syndrome and related disorders (TMEM216-related) (AR)<br>NM_001173990.2          | TMEM216 | Ashkenazi Jewish           | 1 in 92                            | 1 in 9100                                   |
|  |         | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Junctional epidermolysis bullosa (LAMC2-related) (AR)<br>NM_005562.2                     | LAMC2   | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| KCNJ11-related conditions (AR)<br>NM_000525.3  | KCNJ11  | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Krabbe disease (AR)<br>NM_000153.3   | GALC *  | Druze                      | 1 in 6                             | 1 in 500                                    |
|  |         | Pan-ethnic                 | 1 in 158                           | 1 in 15700                                  |
| LAMA2-related muscular dystrophy (AR)<br>NM_000426.3                                     | LAMA2   | Pan-ethnic                 | 1 in 87                            | 1 in 8600                                   |
| LAMA3-related conditions (AR)<br>NM_000227.4   | LAMA3   | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| LAMB3-related conditions (AR)<br>NM_000228.2   | LAMB3   | Pan-ethnic                 | 1 in 317                           | 1 in 31600                                  |
| Leber congenital amaurosis 5 (AR)<br>NM_181714.3   | LCA5    | Pan-ethnic                 | 1 in 645                           | Reduced                                     |
| Leukoencephalopathy with vanishing white matter (EIF2B5-related) (AR)<br>NM_003907.2     | EIF2B5  | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Limb-girdle muscular dystrophy (CAPN3-related) (AR)<br>NM_000070.2                       | CAPN3   | Pan-ethnic                 | 1 in 134                           | 1 in 13300                                  |
| Limb-girdle muscular dystrophy type 2C (AR)<br>NM_000231.2                               | 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)<br>NM_000023.2                               | SGCA    | Caucasian                  | 1 in 286                           | 1 in 28500                                  |
|  |         | Finnish                    | 1 in 150                           | 1 in 14900                                  |
|  |         | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Limb-girdle muscular dystrophy type 2E (AR)<br>NM_000232.4                               | SGCB    | Caucasian                  | 1 in 404                           | 1 in 5038                                   |
|  |         | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Lipoid congenital adrenal hyperplasia (AR)<br>NM_000349.2                                | STAR    | Korean                     | 1 in 170                           | 1 in 16900                                  |
|  |         | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Lysinuric protein intolerance (AR)<br>NM_001126106.2                                     | 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)<br>NM_000235.3                                     | LIPA    | Caucasian                  | 1 in 112                           | 1 in 1850                                   |
|  |         | Pan-ethnic                 | 1 in 359                           | 1 in 5967                                   |
|  |         | Sephardic Jewish (Iranian) | 1 in 33                            | 1 in 534                                    |
| Major histocompatibility complex class II deficiency (CIITA-related) (AR)<br>NM_000246.3 | CIITA   | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Maple syrup urine disease type 1A (AR)<br>NM_000709.3                                    | BCKDHA  | Mennonite                  | 1 in 10                            | 1 in 900                                    |
|  |         | Pan-ethnic                 | 1 in 373                           | 1 in 37200                                  |
| Maple syrup urine disease type 1B (AR)<br>NM_183050.2                                    | BCKDHB  | Ashkenazi Jewish           | 1 in 97                            | 1 in 9600                                   |
|  |         | Pan-ethnic                 | 1 in 346                           | 1 in 34500                                  |
| Maple syrup urine disease type 2 (AR)<br>NM_001918.3                                     | DBT     | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
| Medium-chain acyl-CoA dehydrogenase deficiency (AR)<br>NM_000016.5                       | ACADM   | Northern European          | 1 in 40                            | 1 in 3900                                   |
|  |         | Pan-ethnic                 | 1 in 66                            | 1 in 6500                                   |
| Megalencephalic leukoencephalopathy with subcortical cysts 1 (AR)<br>NM_015166.3         | MLC1    | Pan-ethnic                 | ≤1 in 500                          | Reduced                                     |
|  |         | Sephardic Jewish (Libyan)  | 1 in 40                            | 1 in 3900                                   |
| Metachromatic leukodystrophy (ARSA-related) (AR)<br>NM_000487.5                          | 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)<br>NM_172250.2                                | MMAA    | Pan-ethnic                 | 1 in 316                           | 1 in 10500                                  |

| DISORDER (INHERITANCE)   | GENE    | ETHNICITY                              | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|--|---------|--|------------------------------------|---|
| Methylmalonic acidemia (MMAB-related) (AR)<br>NM_052845.3                                      | MMAB    | Pan-ethnic                             | 1 in 456                           | 1 in 22750                                  |
| Methylmalonic acidemia (MUT-related) (AR)<br>NM_000255.3                                       | MUT     | Pan-ethnic                             | 1 in 204                           | 1 in 5075                                   |
| MFSD8-related conditions (AR)<br>NM_152778.2   | MFSD8   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Microcephaly, postnatal progressive, with seizures and brain atrophy (AR)<br>NM_004268.4       | MED17   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
|  |         | Sephardic Jewish                       | 1 in 20                            | 1 in 1900                                   |
| Mitochondrial complex I deficiency 9 (AR)<br>NM_004553.4                                       | NDUFS6  | Ashkenazi Jewish                       | 1 in 290                           | 1 in 28900                                  |
|  |         | Caucasus Jewish                        | 1 in 24                            | 1 in 2300                                   |
|  |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mitochondrial complex I deficiency 16 (AR)<br>NM_024120.4                                      | NDUFAF5 | Ashkenazi Jewish                       | 1 in 290                           | 1 in 28900                                  |
|  |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mitochondrial complex I deficiency 20/ACAD9 deficiency (AR)<br>NM_014049.4                     | ACAD9   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mitochondrial complex IV deficiency / Leigh syndrome, French Canadian type (AR)<br>NM_133259.3 | LRPPRC  | French Canadian (Saguenay-Lac-St-Jean) | 1 in 23                            | 1 in 2200                                   |
|  |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mitochondrial neurogastrointestinal encephalomyopathy (AR)<br>NM_001953.4                      | TYMP    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
|  |         | Sephardic Jewish                       | 1 in 158                           | 1 in 15700                                  |
| MPL-related conditions (AR)<br>NM_005373.2   | MPL     | Ashkenazi Jewish                       | 1 in 57                            | 1 in 5600                                   |
|  |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| MPV17-related conditions (AR)<br>NM_002437.4   | MPV17   | Navajo                                 | 1 in 20                            | 1 in 475                                    |
|  |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mucopolidosis type III gamma (AR)<br>NM_032520.4   | GNPTG   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mucopolidosis type IV (AR)<br>NM_020533.2  | MCOLN1  | Ashkenazi Jewish                       | 1 in 100                           | 1 in 9900                                   |
|  |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mucopolysaccharidosis type I (AR)<br>NM_000203.4   | IDUA    | Pan-ethnic                             | 1 in 148                           | 1 in 4900                                   |
| Mucopolysaccharidosis type IIIA (AR)<br>NM_000199.3  | SGSH    | Northern European                      | 1 in 173                           | 1 in 17200                                  |
|  |         | Pan-ethnic                             | 1 in 215                           | 1 in 21400                                  |
|  |         | Taiwanese                              | ≤1 in 500                          | Reduced                                     |
| Mucopolysaccharidosis type IIIB (AR)<br>NM_000263.3  | NAGLU   | Pan-ethnic                             | 1 in 224                           | 1 in 22300                                  |
| Mucopolysaccharidosis type IIID (AR)<br>NM_002076.3  | GNS     | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mucopolysaccharidosis type IX (AR)<br>NM_153281.1  | HYAL1   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Mucopolysaccharidosis type VI (AR)<br>NM_000046.3  | ARSB    | Pan-ethnic                             | 1 in 250                           | 1 in 24900                                  |
| Multiple sulfatase deficiency (AR)<br>NM_182760.3  | SUMF1   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Muscular dystrophy-dystroglycanopathy (FKRP-related) (AR)<br>NM_024301.4                       | FKRP    | Norwegian                              | 1 in 116                           | 1 in 11500                                  |
|  |         | Pan-ethnic                             | 1 in 158                           | 1 in 15700                                  |
| Muscular dystrophy-dystroglycanopathy (FKTN-related) (AR)<br>NM_001079802.1                    | FKTN    | Ashkenazi Jewish                       | 1 in 80                            | 1 in 7900                                   |
|  |         | Japanese                               | 1 in 188                           | 1 in 18700                                  |
|  |         | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| MYO7A-related conditions (AR)<br>NM_000260.3   | MYO7A   | Pan-ethnic                             | 1 in 200                           | 1 in 3980                                   |
| Myopathy, lactic acidosis, and sideroblastic anemia 1 (AR)<br>NM_025215.5                      | PUS1    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| N-acetylglutamate synthase deficiency (AR)<br>NM_153006.2                                      | NAGS    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Nemaline myopathy 2 (AR)<br>NM_001271208.1   | NEB *   | Ashkenazi Jewish                       | 1 in 108                           | 1 in 10700                                  |
|  |         | Pan-ethnic                             | 1 in 158                           | 1 in 3140                                   |

| DISORDER (INHERITANCE)  | GENE    | ETHNICITY                             | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|---|---------|---------------------------------------|------------------------------------|---|
| Nephrogenic diabetes insipidus (AQP2-related) (AR)<br>NM_000486.5 | AQP2    | Pan-ethnic                            | 1 in 1118                          | Reduced                                     |
| Neuronal ceroid lipofuscinosis type 1 (AR)<br>NM_000310.3         | PPT1    | Finnish                               | 1 in 70                            | 1 in 3450                                   |
|   |         | Pan-ethnic                            | 1 in 199                           | 1 in 9900                                   |
| Neuronal ceroid lipofuscinosis type 2 (AR)<br>NM_000391.3         | TPP1    | Newfoundland                          | 1 in 53                            | 1 in 1734                                   |
|   |         | Pan-ethnic                            | 1 in 250                           | 1 in 8300                                   |
| Neuronal ceroid lipofuscinosis type 5 (AR)<br>NM_006493.2         | CLN5    | Finnish                               | 1 in 115                           | 1 in 11400                                  |
|   |         | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| Neuronal ceroid lipofuscinosis type 6 (AR)<br>NM_017882.2         | CLN6    | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| Neuronal ceroid lipofuscinosis type 8 (AR)<br>NM_018941.3         | CLN8    | Finnish                               | 1 in 135                           | 1 in 13400                                  |
|   |         | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| Niemann-Pick disease type C (NPC1-related) (AR)<br>NM_000271.4    | NPC1    | Pan-ethnic                            | 1 in 183                           | 1 in 18200                                  |
| Niemann-Pick disease type C (NPC2-related) (AR)<br>NM_006432.3    | NPC2    | Pan-ethnic                            | 1 in 871                           | Reduced                                     |
| Niemann-Pick disease types A and B (AR)<br>NM_000543.4            | SMPD1   | Ashkenazi Jewish                      | 1 in 90                            | 1 in 1780                                   |
|   |         | Pan-ethnic                            | 1 in 250                           | 1 in 4980                                   |
| Nijmegen breakage syndrome (AR)<br>NM_002485.4                    | NBN *   | Eastern European                      | 1 in 155                           | 1 in 15400                                  |
|   |         | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| Nonsyndromic deafness (LOXHD1-related) (AR)<br>NM_144612.6        | LOXHD1  | Ashkenazi Jewish                      | 1 in 180                           | 1 in 17900                                  |
|   |         | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| NR2E3-related conditions (AR)<br>NM_014249.3                      | NR2E3   | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| OPA3-related conditions (AR)<br>NM_025136.3                       | OPA3    | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
|   |         | Sephardic Jewish (Iraqi)              | 1 in 10                            | 1 in 900                                    |
| Osteopetrosis (TCIRG1-related) (AR)<br>NM_006019.3                | TCIRG1  | Ashkenazi Jewish                      | 1 in 350                           | 1 in 34900                                  |
|   |         | Chuvash                               | 1 in 30                            | 1 in 2900                                   |
|   |         | Pan-ethnic                            | 1 in 317                           | 1 in 31600                                  |
| PCDH15-related conditions (AR)<br>NM_033056.3                     | PCDH15  | Ashkenazi Jewish                      | 1 in 78                            | 1 in 7700                                   |
|   |         | Pan-ethnic                            | 1 in 400                           | 1 in 39900                                  |
| PEX7-related conditions (AR)<br>NM_000288.3                       | PEX7    | Pan-ethnic                            | 1 in 157                           | 1 in 15600                                  |
| Phenylalanine hydroxylase deficiency (AR)<br>NM_000277.1          | 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 (AR)<br>NM_006623.3     | PHGDH   | Ashkenazi Jewish                      | 1 in 400                           | 1 in 39900                                  |
|   |         | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| Polycystic kidney disease (PKHD1-related) (AR)<br>NM_138694.3     | PKHD1   | Pan-ethnic                            | 1 in 70                            | 1 in 6900                                   |
| Polymicrogyria (ADGRG1-related) (AR)<br>NM_005682.6               | ADGRG1  | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| POMGNT1-related conditions (AR)<br>NM_017739.3                    | POMGNT1 | Finnish                               | 1 in 111                           | 1 in 11000                                  |
|   |         | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
|   |         | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| Pontocerebellar hypoplasia type 2D (AR)<br>NM_016955.3            | SEPSECS | Sephardic Jewish (Moroccan and Iraqi) | 1 in 43                            | 1 in 4200                                   |
| Pontocerebellar hypoplasia type 6 (AR)<br>NM_020320.3             | RARS2   | Pan-ethnic                            | ≤1 in 500                          | Reduced                                     |
| Primary carnitine deficiency (AR)<br>NM_003060.3                  | SLC22A5 | Faroese                               | 1 in 9                             | 1 in 800                                    |
|   |         | Japanese                              | 1 in 100                           | 1 in 9900                                   |
|   |         | Pan-ethnic                            | 1 in 71                            | 1 in 7000                                   |

| DISORDER (INHERITANCE)  | GENE    | ETHNICITY            | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|---|---------|----------------------|------------------------------------|---|
| Primary ciliary dyskinesia (DNAH5-related) (AR)<br>NM_001369.2                              | DNAH5   | Pan-ethnic           | 1 in 109                           | 1 in 10800                                  |
| Primary ciliary dyskinesia (DNAI1-related) (AR)<br>NM_012144.3                              | DNAI1   | Pan-ethnic           | 1 in 250                           | 1 in 24900                                  |
| Primary ciliary dyskinesia (DNAI2-related) (AR)<br>NM_023036.4                              | DNAI2   | Ashkenazi Jewish     | 1 in 200                           | 1 in 19900                                  |
|   |         | Pan-ethnic           | 1 in 354                           | 1 in 35300                                  |
| Primary hyperoxaluria type 1 (AR)<br>NM_000030.2  | AGXT    | Pan-ethnic           | 1 in 135                           | 1 in 13400                                  |
| Primary hyperoxaluria type 2 (AR)<br>NM_012203.1  | GRHPR   | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Primary hyperoxaluria type 3 (AR)<br>NM_138413.3  | HOGA1   | Pan-ethnic           | 1 in 354                           | 1 in 35300                                  |
| Propionic acidemia (PCCA-related) (AR)<br>NM_000282.3                                       | PCCA    | Arab                 | 1 in 100                           | 1 in 2475                                   |
|   |         | Pan-ethnic           | 1 in 224                           | 1 in 5575                                   |
| Propionic acidemia (PCCB-related) (AR)<br>NM_000532.4                                       | PCCB    | Arab                 | 1 in 100                           | 1 in 9900                                   |
|   |         | Greenlandic Inuit    | 1 in 20                            | 1 in 1900                                   |
|   |         | Pan-ethnic           | 1 in 224                           | 1 in 22300                                  |
| PSAP-related conditions (AR)<br>NM_002778.3   | PSAP    | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Pycnodysostosis (AR)<br>NM_000396.3   | CTSK    | Pan-ethnic           | 1 in 438                           | 1 in 43700                                  |
| Pyruvate carboxylase deficiency (AR)<br>NM_000920.3   | PC      | Algonquian Indian    | 1 in 10                            | 1 in 180                                    |
|   |         | Pan-ethnic           | 1 in 250                           | 1 in 4980                                   |
| Pyruvate dehydrogenase complex deficiency (PDHB-related) (AR)<br>NM_000925.3                | PDHB    | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| RAPSN-related conditions (AR)<br>NM_005055.4  | RAPSN   | Pan-ethnic           | 1 in 283                           | 1 in 28200                                  |
| RDH12-related conditions (AR)<br>NM_152443.2  | RDH12   | Pan-ethnic           | 1 in 460                           | 1 in 45900                                  |
| Retinitis pigmentosa 25 (AR)<br>NM_001142800.1  | EYS     | Pan-ethnic           | 1 in 129                           | 1 in 12800                                  |
|   |         | Sephardic Jewish     | 1 in 42                            | 1 in 4100                                   |
| Retinitis pigmentosa 28 (AR)<br>NM_001201543.1  | 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 3 (AR)<br>NM_003659.3                             | AGPS    | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Roberts syndrome (AR)<br>NM_001017420.2   | ESCO2   | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| RPE65-related conditions (AR)<br>NM_000329.2  | RPE65   | Pan-ethnic           | 1 in 228                           | 1 in 22700                                  |
|   |         | Sephardic Jewish     | 1 in 90                            | 1 in 8900                                   |
| Sandhoff disease (AR)<br>NM_000521.3  | HEXB    | Metis (Saskatchewan) | 1 in 15                            | 1 in 1400                                   |
|   |         | Pan-ethnic           | 1 in 180                           | 1 in 17900                                  |
| Schimke immuno-osseous dysplasia (AR)<br>NM_014140.3  | SMARCA1 | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Severe combined immunodeficiency due to DCLRE1C (Artemis) deficiency (AR)<br>NM_001033855.2 | DCLRE1C | Navajo and Apache    | 1 in 10                            | 1 in 900                                    |
|   |         | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Severe combined immunodeficiency due to RAG2 deficiency (AR)<br>NM_000536.3                 | RAG2    | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Severe congenital neutropenia due to HAX1 deficiency (AR)<br>NM_006118.3                    | HAX1    | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Severe congenital neutropenia due to VPS45 deficiency (AR)<br>NM_007259.4                   | VPS45   | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Sialic acid storage diseases (AR)<br>NM_012434.4  | SLC17A5 | Finnish              | 1 in 100                           | 1 in 9900                                   |
|   |         | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
| Sjögren-Larsson syndrome (AR)<br>NM_000382.2  | ALDH3A2 | Pan-ethnic           | ≤1 in 500                          | Reduced                                     |
|   |         | Swedish              | 1 in 250                           | 1 in 24900                                  |

| DISORDER (INHERITANCE)   | GENE      | ETHNICITY                              | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|--|-----------|--|------------------------------------|---|
| SLC12A6-related conditions (AR)<br>NM_133647.1   | SLC12A6   | French Canadian (Saguenay-Lac-St-Jean) | 1 in 23                            | 1 in 2200                                   |
|  |           | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| SLC26A2-related conditions (AR)<br>NM_000112.3   | SLC26A2   | Finnish                                | 1 in 75                            | 1 in 1480                                   |
|  |           | Pan-ethnic                             | 1 in 158                           | 1 in 3140                                   |
| SLC26A4-related conditions (AR)<br>NM_000441.1   | SLC26A4   | Asian                                  | 1 in 74                            | 1 in 7300                                   |
|  |           | Pan-ethnic                             | 1 in 80                            | 1 in 7900                                   |
| SLC37A4-related conditions (AR)<br>NM_001164277.1  | SLC37A4   | Pan-ethnic                             | 1 in 354                           | 1 in 7060                                   |
| Smith-Lemli-Opitz syndrome (AR)<br>NM_001360.2   | DHCR7     | African-American                       | 1 in 339                           | 1 in 33800                                  |
|  |           | Ashkenazi Jewish                       | 1 in 41                            | 1 in 4000                                   |
|  |           | Hispanic                               | 1 in 135                           | 1 in 13400                                  |
|  |           | Northern European                      | 1 in 50                            | 1 in 4900                                   |
|  |           | Pan-ethnic                             | 1 in 71                            | 1 in 7000                                   |
|  |           | Sephardic Jewish                       | 1 in 68                            | 1 in 6700                                   |
|  |           | Southern European                      | 1 in 83                            | 1 in 8200                                   |
| Spastic paraplegia type 15 (AR)<br>NM_015346.3   | ZFYVE26   | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Spastic paraplegia type 49 (AR)<br>NM_014844.3   | TECPR2    | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
|  |           | Sephardic Jewish - Bukharian           | 1 in 38                            | 1 in 3700                                   |
| Spinal muscular atrophy (AR)<br>NM_000344.3<br>SMN1: 2 copies<br>c.*3+80T>G not detected<br>Carrier residual risks listed are for 2 copy SMN1 results.<br>Carrier residual risk for >2 copies are 5- to 10-fold lower. | SMN1 *    | African-American                       | 1 in 59                            | 1 in 342                                    |
|  |           | Ashkenazi Jewish                       | 1 in 62                            | 1 in 1017                                   |
|  |           | Asian                                  | 1 in 50                            | 1 in 701                                    |
|  |           | Caucasian                              | 1 in 45                            | 1 in 880                                    |
|  |           | Hispanic                               | 1 in 48                            | 1 in 784                                    |
|  |           | Pan-ethnic                             | 1 in 49                            | 1 in 800                                    |
| Spondylocostal dysostosis (MESP2-related) (AR)<br>NM_001039958.1   | MESP2     | Pan-ethnic                             | 1 in 224                           | 1 in 22300                                  |
|  |           | Puerto Rican                           | 1 in 55                            | 1 in 5400                                   |
| Steel syndrome (AR)<br>NM_032888.3   | COL27A1 * | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
|  |           | Puerto Rican                           | 1 in 51                            | 1 in 5000                                   |
| Stüve-Wiedemann syndrome (AR)<br>NM_002310.5   | LIFR      | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Tay-Sachs disease (AR)<br>NM_000520.4  | HEXA      | Ashkenazi Jewish                       | 1 in 27                            | 1 in 2600                                   |
|  |           | 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                                  |
| Transient infantile liver failure (AR)<br>NM_018006.4  | TRMU      | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
|  |           | Sephardic Jewish (Yemenite)            | 1 in 34                            | 1 in 3300                                   |
| Tyrosine hydroxylase deficiency (AR)<br>NM_199292.2  | TH        | Caucasian                              | 1 in 224                           | 1 in 22300                                  |
|  |           | Pan-ethnic                             | ≤1 in 500                          | Reduced                                     |
| Tyrosinemia type I (AR)<br>NM_000137.2   | 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)<br>NM_000353.2  | TAT       | Pan-ethnic                             | 1 in 250                           | 1 in 24900                                  |
| USH1C-related conditions (AR)<br>NM_005709.3   | 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                                   |
| USH2A-related conditions (AR)<br>NM_206933.2   | USH2A     | Caucasian                              | 1 in 70                            | 1 in 6900                                   |
|  |           | Pan-ethnic                             | 1 in 112                           | 1 in 11100                                  |
|  |           | Sephardic Jewish                       | 1 in 36                            | 1 in 3500                                   |

| DISORDER (INHERITANCE)  | GENE   | ETHNICITY        | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|---|--------|------------------|------------------------------------|---|
| Very long-chain acyl-CoA dehydrogenase deficiency (AR)<br>NM_000018.3 | ACADVL | Pan-ethnic       | 1 in 100                           | 1 in 9900                                   |
| VRK1-related conditions (AR)<br>NM_003384.2                           | VRK1   | Ashkenazi Jewish | 1 in 225                           | 1 in 22400                                  |
|   |        | Pan-ethnic       | ≤1 in 500                          | Reduced                                     |
| VSX2-related conditions (AR)<br>NM_182894.2                           | VSX2   | Pan-ethnic       | ≤1 in 500                          | Reduced                                     |
|   |        | Sephardic Jewish | 1 in 145                           | 1 in 14400                                  |
| Wilson disease (AR)<br>NM_000053.3                                    | 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 conditions (AR)<br>NM_025216.2                         | WNT10A | Pan-ethnic       | 1 in 305                           | 1 in 30400                                  |
| Xeroderma pigmentosum complementation group A (AR)<br>NM_000380.3     | XPA    | Japanese         | 1 in 100                           | 1 in 9900                                   |
|   |        | Pan-ethnic       | 1 in 1667                          | Reduced                                     |
| Xeroderma pigmentosum complementation group C (AR)<br>NM_004628.4     | XPC    | Pan-ethnic       | 1 in 763                           | Reduced                                     |
|   |        | Tunisian         | 1 in 50                            | 1 in 4900                                   |
| Zellweger spectrum disorder (PEX1-related) (AR)<br>NM_000466.2        | PEX1   | Pan-ethnic       | 1 in 144                           | 1 in 14300                                  |
| Zellweger spectrum disorder (PEX2-related) (AR)<br>NM_000318.2        | PEX2   | Ashkenazi Jewish | 1 in 227                           | 1 in 22600                                  |
|   |        | Pan-ethnic       | ≤1 in 500                          | Reduced                                     |
| Zellweger spectrum disorder (PEX6-related) (AR)<br>NM_000287.3        | PEX6   | French Canadian  | 1 in 55                            | 1 in 5400                                   |
|   |        | Pan-ethnic       | 1 in 294                           | 1 in 29300                                  |
|   |        | Sephardic Jewish | 1 in 18                            | 1 in 1700                                   |
| Zellweger spectrum disorder (PEX10-related) (AR)<br>NM_153818.1       | PEX10  | Pan-ethnic       | 1 in 606                           | Reduced                                     |
| Zellweger spectrum disorder (PEX12-related) (AR)<br>NM_000286.2       | PEX12  | Pan-ethnic       | 1 in 409                           | 1 in 40800                                  |

## 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. Markers across the X and Y chromosomes are analyzed for quality control purposes and may detect deviations from the expected sex chromosome complement. Such deviations may be included in the report in accordance with internal guidelines. Invitae utilizes a classification methodology to identify next-generation sequencing (NGS)-detected variants that require orthogonal confirmation (Lincoln, et al. J Mol Diagn. 2019 Mar;21(2):318-329.). Pathogenic and Likely Pathogenic variants that do not meet the validated quality thresholds are confirmed. Confirmation technologies may 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 the gene and pseudogene. For CYP21A2 and GBA, if one or more reportable variants, gene conversion, or fusion event is identified via our NGS pipeline (see Limitations), these variants are confirmed by PacBio sequencing of an amplicon generated by long-range PCR and subsequent short-range PCR. In some cases, it may not be possible to disambiguate between the gene and pseudogene. 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 - $\alpha$ 3.7 subtypes, and all - $\alpha$ 3.7 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. Reference ranges: Normal: <45 CGG repeats, intermediate: 45-54 CGG repeats, premutation: 55-200 CGG repeats, full mutation: >200 CGG repeats. For alleles with 55-90 triplet repeats, the region surrounding the FMR1 repeat is amplified by PCR. The PCR amplicons are then processed through PacBio SMRTBell library prep and sequenced using PacBio long read technology. The number of AGG interruptions within the 55-90 triplet repeat is read directly from the resulting DNA sequences. Technical component of confirmatory sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778).

- The following transcripts were used in this analysis. If more than one transcript is listed for a single gene, variants were reported using the first transcript listed unless otherwise indicated in the report: ABCB11 (NM\_003742.2), ABCC8 (NM\_000352.4), 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), ATP7B (NM\_000053.3), 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), 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), 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), CYP11B1 (NM\_000497.3), CYP11B2 (NM\_000498.3), CYP17A1 (NM\_000102.3), CYP19A1 (NM\_031226.2), CYP21A2 (NM\_000500.7), CYP27A1 (NM\_000784.3), DBT (NM\_001918.3), DCLRE1C (NM\_001033855.2), DHCR7 (NM\_001360.2), DHDDS (NM\_024887.3), DLD (NM\_000108.4), DNAH5 (NM\_001369.2), DNAI1 (NM\_012144.3), DNAI2 (NM\_023036.4), DYSF (NM\_003494.3), EIF2B5 (NM\_003907.2), ELP1 (NM\_003640.3), 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), FAH (NM\_000137.2), FAM161A (NM\_001201543.1), FANCA (NM\_000135.2), FANCC (NM\_000136.2), FANCG (NM\_004629.1), FH (NM\_000143.3), FKBP (NM\_024301.4), FKTN (NM\_001079802.1), G6PC (NM\_000151.3), GAA (NM\_000152.3), GALT (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), GJB2 (NM\_004004.5), 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), IDUA (NM\_000203.4), 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), MESPD (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), MTRR (NM\_002454.2), MTPP (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), PAH (NM\_000277.1), PC (NM\_000920.3), PCCA (NM\_000282.3), PCCB (NM\_000532.4), PCDH15 (NM\_033056.3), 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), PROPI (NM\_006261.4), 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 (NM\_003051.3), RPE65 (NM\_000329.2), RPGRIP1L (NM\_015272.2), RTTL1 (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), SLC7A7 (NM\_001126106.2), SMARCA1 (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), 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).

- This report only includes variants that have a clinically significant association with the conditions tested as of the report date. Variants of uncertain significance, benign variants, and likely benign variants are not included in this report. However, if additional evidence becomes available to indicate that the clinical significance of a variant has changed, Invitae may 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>) and dbSNP (<http://ncbi.nlm.nih.gov/SNP>).

## 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.

## 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. While this test is intended to reflect the analysis of extracted genomic DNA from a referred patient, in very rare cases the analyzed DNA may not represent that individual's constitutional genome, such as in the case of a circulating hematolymphoid neoplasm, bone marrow transplant, blood transfusion, chimerism, culture artifact or maternal cell contamination.
- RPGRIP1L: Sequencing analysis is not offered for exon 23. 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. Rarely, sensitivity to detect these variants may be reduced. When sensitivity is reduced, zygosity may be reported as "unknown". CYP21A2: Analysis includes the most common variants (c.92C>T (p.Pro31Leu), c.293-13C>G (intronic), c.332\_339delGAGACTAC (p.Gly111Valfs\*21), c.518T>A (p.Ile173Asn), c.710T>A (p.Ile237Asn), c.713T>A (p.Val238Glu), c.719T>A (p.Met240Lys), c.844G>T (p.Val282Leu), c.923dupT (p.Leu308Phefs\*6), c.955C>T (p.Gln319\*), c.1069C>T (p.Arg357Trp), c.1360C>T (p.Pro454Ser) and the 30Kb deletion) as well as select rare HGMD variants only (list available upon request). Full gene duplications are reported only in the presence of a pathogenic variant(s). When a duplication and a pathogenic variant(s) is identified, phase (cis/trans) cannot be determined. Full gene deletion



analysis is not offered. Sensitivity to detect these variants, if they result from complex gene conversion/fusion events, may be reduced. NBN: Deletion/duplication analysis is not offered for exons 15-16. USH1C: Deletion/duplication analysis is not offered for exons 5-6. FAH: Deletion/duplication analysis is not offered for exon 14. GALC: Deletion/duplication analysis is not offered for exon 6. 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. HBA2: Sequencing analysis is not offered for exons 1-2. 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. TSFM: Sequencing analysis is not offered for exon 5. OAT: Deletion/duplication analysis is not offered for exon 2. VPS13A: Deletion/duplication analysis is not offered for exons 2-3, 27-28. MMADHC: Deletion/duplication analysis is not offered for exons 5-6. ALG6: Deletion/duplication analysis is not offered for exons 11-12. COL27A1: Deletion/duplication analysis is not offered for exons 46-47. 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. SMN1 or SMN2: NM\_000344.3:c.\*3+80T>G variant only. 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.

### This report has been reviewed and approved by:



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