# Donor 6973

## Genetic Testing Summary

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

Last Updated: 03/13/24

Donor Reported Ancestry: Scottish, English, French, German, Mexican  Jewish Ancestry: No

| Genetic Test* | Result | Comments/Donor's Residual Risk** |
|---|---|---|
| Chromosome analysis (karyotype) | Normal male karyotype | No evidence of clinically significant chromosome abnormalities |
| Hemoglobin evaluation | Normal hemoglobin fractionation and MCV/MCH results | Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies |
| Expanded Genetic Disease Carrier Screening Panel attached- 514 diseases by gene sequencing. | Carrier: Polycystic kidney disease (PKHD1-related)<br><br>Carrier: Sandhoff disease (HEXB)<br><br>Carrier: Xeroderma pigmentosum, variant type (POLH)<br><br>Negative for other genes sequenced. | Partner testing recommended before using this donor.<br><br>Residual risks for negative results can be seen here:<br><br>https://www.invitae.com/carrier-residual-risks/ |

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.

**Donor residual risk is the chance the donor is still a carrier after testing negative.

INVITAE

# INVITAE CARRIER SCREEN RESULTS

| | | | | | |
|---|---|---|---|---|---|
| **Patient name:** | Donor 6973 | **Sample type:** | Blood | **Report date:** | 26-MAY-2023 |
| **DOB:** | [redacted] | **Sample collection date:** | 18-MAY-2023 | **Invitae #:** | [redacted] |
| **Sex assigned at birth:** | Male | **Sample accession date:** | 19-MAY-2023 | **Clinical team:** | [redacted] |
| **Gender:** | | | | | |
| **Patient ID (MRN):** | 6973-[redacted] | | | | |

**Reason for testing**

Gamete donor

**Test performed**

Invitae Carrier Screen

## RESULT: POSITIVE

This carrier test evaluated 514 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. Carrier screening is not intended for diagnostic purposes. To identify a potential genetic basis for a condition in the individual being tested, diagnostic testing for the gene(s) of interest is recommended.

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

| RESULTS | GENE | VARIANT(S) | INHERITANCE | PARTNER TESTING RECOMMENDED |
|---|---|---|---|---|
| **Carrier:** Polycystic kidney disease (PKHD1-related) | PKHD1 | c.3766del (p.Gln1256Argfs*47) | Autosomal recessive | Yes |
| **Carrier:** Sandhoff disease | HEXB | c.1250C>T (p.Pro417Leu) | Autosomal recessive | Yes |
| **Carrier:** Xeroderma pigmentosum, variant type | POLH | c.1066C>T (p.Arg356*) | Autosomal recessive | Yes |

## Next steps

- See the table above for recommendations regarding testing of this individual's reproductive partner.
- Even for genes that have a negative test result, there is always a small risk that an individual could still be a carrier. This is called “residual risk.” See the Carrier detection rates and residual risks document.
- 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.

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# Clinical summary

## RESULT: CARRIER

## Polycystic kidney disease (PKHD1-related)

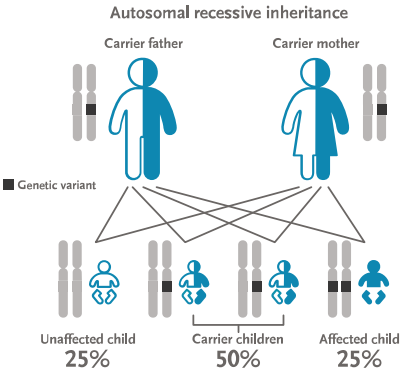
A single Pathogenic variant, c.3766del (p.Gln1256Argfs*47), was identified in PKHD1.

### What is polycystic kidney disease (PKHD1-related)?

Polycystic kidney disease (PKD) is part of the spectrum of conditions called ciliopathies, which involve defects in the microscopic, finger-like projections (cilia) that are located on the surface of cells and that are involved in cell movement and signaling. Ciliopathies affect many parts of the body. PKD can be caused by changes in different genes. Autosomal recessive polycystic kidney disease (ARPKD) is characterized by clusters of fluid-filled sacs (cysts) in the kidneys, which interfere with the kidneys' ability to filter waste products from the blood, leading to kidney dysfunction, enlargement (nephromegaly), and failure. Liver abnormalities may include cysts, an enlarged liver (hepatomegaly), and thickening and scarring of liver tissue that is present at birth (congenital hepatic fibrosis). Additional symptoms include high blood pressure (hypertension), dilated bile ducts, heart valve abnormalities, and underdeveloped fetal lungs during pregnancy. Age of onset, disease progression, and severity are variable. Approximately one third of affected individuals present prenatally or in infancy, one third in childhood, and one third present in adulthood. Some individuals with a single disease-causing PKHD1 variant (heterozygous carriers) have developed polycystic liver disease in adulthood (PMID: 28862642). Prognosis depends on the severity of symptoms. Life span is often reduced, although with treatment, many affected individuals survive into adulthood. Follow-up depends on each affected individual's specific situation, and discussion with a healthcare provider should be considered.

## Next steps

Carrier testing for the reproductive partner is recommended.




### If your partner tests positive:

In autosomal recessive inheritance, an individual must have disease-causing genetic changes in each copy of the PKHD1 gene to be affected. Carriers, who have a disease-causing genetic change in only one copy of the gene, typically do not have symptoms. When both reproductive partners are carriers of an autosomal recessive condition, there is a 25% chance for each child to have the condition.

### If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for polycystic kidney disease (PKHD1-related). These values are provided only as a guide, are based on the detection rate for the condition as tested at Invitae, and assume a negative family history, the absence of symptoms, and vary based on the ethnic background of an individual. For genes associated with both dominant and recessive inheritance, the numbers provided apply to the recessive condition(s) associated with the gene.

| DISORDER (INHERITANCE) | GENE | ETHNICITY | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|---|---|---|---|---|
| Polycystic kidney disease (PKHD1-related) (AR) NM_138694.3 | PKHD1 * | Pan-ethnic | 1 in 70 | 1 in 6900 |

## RESULT: CARRIER

# Sandhoff disease

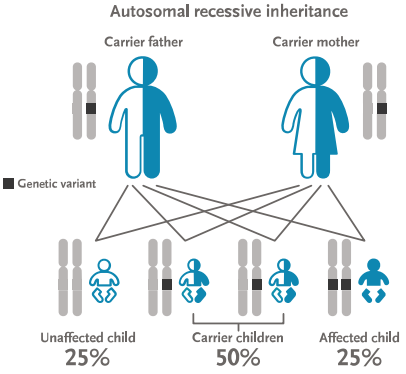
A single Pathogenic variant, c.1250C>T (p.Pro417Leu), was identified in HEXB.

### What is Sandhoff disease?

Sandhoff disease is a condition that affects lysosomes, which are structures in the cell that break down and recycle other molecules. Due to absent or reduced activity of the enzymes beta-hexosaminidase A and B (HEXA and HEXB), individuals with Sandhoff disease have difficulty breaking down a fatty substance called GM2 ganglioside and other substances. These substances accumulate in the cells, and are particularly toxic to the nerve cells in the central nervous system, leading to the destruction of neurons in the brain and spinal cord. The severity and age of onset of Sandhoff disease can vary, but the vast majority present in infancy with progressive weakness, loss of motor skills, and an increased startle reflex. Symptoms progress to include intellectual disability, hearing and vision loss, and seizures, with abnormal muscle tensing (spasticity). Affected individuals typically also have a characteristic cherry red spot at the back of the eye. Death usually occurs by age 3 or 4. Milder forms of the condition may be characterized by later onset, slower symptom progression, and more variable neurologic findings, including difficulty coordinating movements (ataxia) and psychiatric illness. Follow-up depends on each affected individual's specific situation, and discussion with a healthcare provider should be considered.

## Next steps

Carrier testing for the reproductive partner is recommended.




### If your partner tests positive:

In autosomal recessive inheritance, an individual must have disease-causing genetic changes in each copy of the HEXB gene to be affected. Carriers, who have a disease-causing genetic change in only one copy of the gene, typically do not have symptoms. When both reproductive partners are carriers of an autosomal recessive condition, there is a 25% chance for each child to have the condition.

### If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for Sandhoff disease. These values are provided only as a guide, are based on the detection rate for the condition as tested at Invitae, and assume a negative family history, the absence of symptoms, and vary based on the ethnic background of an individual. For genes associated with both dominant and recessive inheritance, the numbers provided apply to the recessive condition(s) associated with the gene.

| DISORDER (INHERITANCE) | GENE | ETHNICITY | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|---|---|---|---|---|
| Sandhoff disease (AR)<br>NM_000521.3 | HEXB | Pan-ethnic | 1 in 180 | 1 in 17900 |

## RESULT: CARRIER

# Xeroderma pigmentosum, variant type

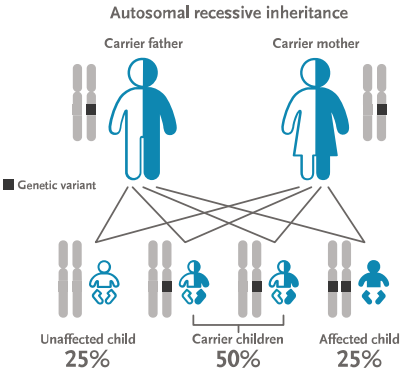
A single Pathogenic variant, c.1066C>T (p.Arg356*), was identified in POLH.

### What is xeroderma pigmentosum, variant type?

Xeroderma pigmentosum (XP) is a condition that causes extreme sensitivity to sunlight. XP can be caused by changes in several different genes. Symptoms of XP, including variant type, typically present during infancy or early childhood. The skin and eyes are extremely sensitive to sunlight, which may lead to severe sunburn with redness and blistering, freckle-like pigmentation (lentigos) on the face, lips, and arms, and eye problems such as increased sensitivity to light (photophobia) and growths on the eye that may impair vision. Damage from sun exposure poses a significant risk for skin cancers, usually on the face, lips, and eyelids, as well as various other forms of cancer. Some affected individuals develop neurologic problems such as deafness, poor coordination, difficulties with swallowing, movement and walking, seizures, and a decline in cognitive abilities. Life expectancy is generally reduced (less than 40 years) due to cancer and because the neurologic problems worsen over time. Treatment involves sun avoidance, symptom management, and regular skin cancer screenings beginning at a young age.

## Next steps

Carrier testing for the reproductive partner is recommended.




### If your partner tests positive:

In autosomal recessive inheritance, an individual must have disease-causing genetic changes in each copy of the POLH gene to be affected. Carriers, who have a disease-causing genetic change in only one copy of the gene, typically do not have symptoms. When both reproductive partners are carriers of an autosomal recessive condition, there is a 25% chance for each child to have the condition.

### If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for xeroderma pigmentosum, variant type. These values are provided only as a guide, are based on the detection rate for the condition as tested at Invitae, and assume a negative family history, the absence of symptoms, and vary based on the ethnic background of an individual. For genes associated with both dominant and recessive inheritance, the numbers provided apply to the recessive condition(s) associated with the gene.

| DISORDER (INHERITANCE) | GENE | ETHNICITY | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|---|---|---|---|---|
| Xeroderma pigmentosum, variant type (AR) NM_006502.2 | POLH | Pan-ethnic | ≤1 in 500 | Reduced |

## Results to note

### SMN1

- Negative result. SMN1: 2 copies; c.*3+80T>G not detected.

### Pseudodeficiency allele(s)

- Benign changes, c.1685T>C (p.Ile562Thr), known to be pseudodeficiency alleles, identified in the GALC gene. Pseudodeficiency alleles are not known to be associated with disease, including Krabbe disease.
- The presence of a pseudodeficiency allele does not impact this individual's risk to be a carrier. Individuals with pseudodeficiency alleles may exhibit false positive results on related biochemical tests, including newborn screening. However, pseudodeficiency alleles are not known to cause disease, even when there are two copies of the variant (homozygous) or when in combination with another disease-causing variant (compound heterozygous). Carrier testing for the reproductive partner is not indicated based on this result.

## Variant details

HEXB, Exon 11, c.1250C>T (p.Pro417Leu), heterozygous, PATHOGENIC

- This sequence change replaces proline, which is neutral and non-polar, with leucine, which is neutral and non-polar, at codon 417 of the HEXB protein (p.Pro417Leu). RNA analysis indicates that this missense change induces altered splicing and may result in an absent or disrupted protein product.
- This variant is present in population databases (rs28942073, gnomAD 0.1%), and has an allele count higher than expected for a pathogenic variant.
- This missense change has been observed in individuals with Sandhoff disease (PMID: 1531140, 7557963, 21150067, 22789865, 24263030). It has also been observed to segregate with disease in related individuals.
- This variant is also known as Pro405Leu.
- ClinVar contains an entry for this variant (Variation ID: 3878).
- Advanced modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) has been performed at Invitae for this missense variant, however the output from this modeling did not meet the statistical confidence thresholds required to predict the impact of this variant on HEXB protein function.
- Studies have shown that this missense change results in exon 11 skipping and the activation of a cryptic splice site and introduces a premature termination codon (PMID: 1386607, 1531140). The resulting mRNA is expected to undergo nonsense-mediated decay.
- For these reasons, this variant has been classified as Pathogenic.

PKHD1, Exon 32, c.3766del (p.Gln1256Argfs*47), heterozygous, PATHOGENIC

- This sequence change creates a premature translational stop signal (p.Gln1256Argfs*47) in the PKHD1 gene. It is expected to result in an absent or disrupted protein product. Loss-of-function variants in PKHD1 are known to be pathogenic (PMID: 19940839).
- This variant is present in population databases (rs746972457, gnomAD 0.7%), and has an allele count higher than expected for a pathogenic variant.
- This premature translational stop signal has been observed in individual(s) with autosomal recessive polycystic kidney disease and is commonly reported in cis with a benign variant, c.3761C>G (PMID: 11898128, 12846734, 12874454, 15805161, 26721323, 31980526).
- This variant is also known as c.3761_3762delinsG (p.Ala1254Glyfs*49).
- ClinVar contains an entry for this variant (Variation ID: 188746).
- For these reasons, this variant has been classified as Pathogenic.

POLH, Exon 9, c.1066C>T (p.Arg356*), heterozygous, PATHOGENIC

- This sequence change creates a premature translational stop signal (p.Arg356*) in the POLH gene. It is expected to result in an absent or disrupted protein product. Loss-of-function variants in POLH are known to be pathogenic (PMID: 11773631, 24130121, 25256075).
- This variant is present in population databases (rs559497462, gnomAD 0.01%).
- This premature translational stop signal has been observed in individual(s) with xeroderma pigmentosum (PMID: 11773631).
- ClinVar contains an entry for this variant (Variation ID: 1459259).
- For these reasons, this variant has been classified as Pathogenic.

## Residual risk

No carrier test can detect 100% of carriers. There still remains a small risk of being a carrier after a negative test (residual risk). Residual risk values assume a negative family history and are inferred from published carrier frequencies and estimated detection rates based on testing technologies used at Invitae. You can view Invitae's complete Carrier detection rates and residual risks document (containing all carrier genes) online at **https://www.invitae.com/carrier-residual-risks/**. Additionally, the order-specific information for this report is available to download in the portal (under this order's documents) or can be requested by contacting Invitae Client Services. The complete Carrier detection rates and residual risks document will not be applicable for any genes with specimen-specific limitations in sequencing and/or deletion/duplication coverage. Please see the final bullet point in the Limitations section of this report to view if this specimen had any gene-specific coverage gaps.

## Genes analyzed

This table represents a complete list of genes analyzed for this individual, including the relevant gene transcript(s). 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. An asterisk (*) indicates that this gene has a limitation. Please see the Limitations section for details. Results are negative, unless otherwise indicated in the report.

| GENE | TRANSCRIPT |
|---|---|
| AAAS | NM_015665.5 |
| ABCA12 | NM_173076.2 |
| ABCA3 | NM_001089.2 |
| ABCA4 | NM_000350.2 |
| ABCB11 | NM_003742.2 |
| ABCB4 | NM_000443.3 |
| ABCC2* | NM_000392.4 |
| 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 |
| ADAMTSL4 | NM_019032.5 |
| ADGRG1 | NM_005682.6 |
| ADGRV1 | NM_032119.3 |
| AGA | NM_000027.3 |
| AGL | NM_000642.2 |
| AGPS | NM_003659.3 |
| AGXT | NM_000030.2 |
| AHI1 | NM_017651.4 |
| AIPL1* | NM_014336.4 |
| AIRE | NM_000383.3 |
| ALDH3A2 | NM_000382.2 |
| ALDH7A1 | NM_001182.4 |
| ALDOB | NM_000035.3 |
| ALG1 | NM_019109.4 |
| ALG6 | NM_013339.3 |
| ALMS1 | NM_015120.4 |
| ALPL | NM_000478.5 |
| AMN* | NM_030943.3 |
| AMT | NM_000481.3 |
| ANO10* | NM_018075.3 |
| AP1S1 | NM_001283.3 |
| AQP2 | NM_000486.5 |
| ARG1 | NM_000045.3 |
| ARL6 | NM_177976.2 |
| 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 |
| ATP8B1* | NM_005603.4 |
| BBS1 | NM_024649.4 |
| BBS10 | NM_024685.3 |
| BBS12 | NM_152618.2 |
| BBS2 | NM_031885.3 |
| BBS4 | NM_033028.4 |
| BBS5 | NM_152384.2 |
| BBS7 | NM_176824.2 |
| BBS9* | NM_198428.2 |
| BCKDHA | NM_000709.3 |
| BCKDHB | NM_183050.2 |
| BCS1L | NM_004328.4 |
| BLM | NM_000057.3 |
| BLOC1S3 | NM_212550.4 |
| BLOC1S6 | NM_012388.3 |
| BMP1 | NM_006129.4;NM_001199.3 |
| BRIP1 | NM_032043.2 |
| BSND | NM_057176.2 |
| BTD | NM_000060.3 |
| CAD | NM_004341.4 |
| CANT1 | NM_138793.3 |
| CAPN3 | NM_000070.2 |
| CASQ2 | NM_001232.3 |
| CBS | NM_000071.2 |
| CC2D1A | NM_017721.5 |
| CC2D2A | NM_001080522.2 |
| CCDC103 | NM_213607.2 |
| CCDC39 | NM_181426.1 |
| CCDC88C | NM_001080414.3 |
| CD3D | NM_000732.4 |
| CD3E | NM_000733.3 |
| CD40 | NM_001250.5 |
| CD59 | NM_203330.2 |
| CDH23 | NM_022124.5 |
| CEP152 | NM_014985.3 |
| CEP290 | NM_025114.3 |
| CERKL | NM_001030311.2 |
| CFTR* | NM_000492.3 |
| CHAT | NM_020549.4 |
| CHRNE | NM_000080.3 |
| CHRNG | NM_005199.4 |
| CIITA | NM_000246.3 |
| CLCN1 | NM_000083.2 |
| CLN3 | NM_001042432.1 |
| CLN5 | NM_006493.2 |
| CLN6 | NM_017882.2 |
| CLN8 | NM_018941.3 |
| CLRN1 | NM_174878.2 |
| CNGB3 | NM_019098.4 |
| COL11A2* | NM_080680.2 |
| COL17A1 | NM_000494.3 |
| COL27A1 | NM_032888.3 |
| COL4A3 | NM_000091.4 |
| COL4A4 | NM_000092.4 |
| COL7A1 | NM_000094.3 |
| COX15 | NM_004376.6 |
| CPS1 | NM_001875.4 |
| CPT1A | NM_001876.3 |
| CPT2 | NM_000098.2 |

| GENE | TRANSCRIPT |
|---|---|
| CRB1 | NM_201253.2 |
| CRTAP | NM_006371.4 |
| CTNS | NM_004937.2 |
| CTSA | NM_000308.3 |
| CTSC | NM_001814.5 |
| CTSD | NM_001909.4 |
| CTSK | NM_000396.3 |
| CYBA | NM_000101.3 |
| CYP11A1 | NM_000781.2 |
| CYP11B1 | NM_000497.3 |
| CYP11B2 | NM_000498.3 |
| CYP17A1 | NM_000102.3 |
| CYP19A1 | NM_031226.2 |
| CYP1B1 | NM_000104.3 |
| CYP21A2* | NM_000500.7 |
| CYP27A1 | NM_000784.3 |
| CYP27B1 | NM_000785.3 |
| CYP7B1 | NM_004820.3 |
| DBT | NM_001918.3 |
| DCAF17 | NM_025000.3 |
| DCLRE1C | NM_001033855.2 |
| DDX11* | NM_030653.3 |
| DFNB59 | NM_001042702.3 |
| DGAT1 | NM_012079.5 |
| DGUOK | NM_080916.2 |
| DHCR7 | NM_001360.2 |
| DHDDS | NM_024887.3 |
| DLD | NM_000108.4 |
| DLL3 | NM_016941.3 |
| DNAH11 | NM_001277115.1 |
| DNAH5 | NM_001369.2 |
| DNAI1 | NM_012144.3 |
| DNAI2 | NM_023036.4 |
| DNMT3B | NM_006892.3 |
| DOK7 | NM_173660.4 |
| DUOX2* | NM_014080.4 |
| DYNC2H1 | NM_001080463.1 |
| DYSF | NM_003494.3 |
| EIF2AK3 | NM_004836.6 |

| GENE | TRANSCRIPT |
|---|---|
| EIF2B1 | NM_001414.3 |
| EIF2B2 | NM_014239.3 |
| EIF2B3 | NM_020365.4 |
| EIF2B4 | NM_015636.3 |
| EIF2B5 | NM_003907.2 |
| ELP1 | NM_003640.3 |
| EPG5 | NM_020964.2 |
| ERCC2 | NM_000400.3 |
| ERCC6 | NM_000124.3 |
| ERCC8 | NM_000082.3 |
| ESCO2 | NM_001017420.2 |
| ETFA | NM_000126.3 |
| ETFB | NM_001985.2 |
| ETFDH | NM_004453.3 |
| ETHE1 | NM_014297.3 |
| EVC | NM_153717.2 |
| EVC2 | NM_147127.4 |
| EXOSC3 | NM_016042.3 |
| EYS* | NM_001142800.1 |
| FAH* | NM_000137.2 |
| FAM161A | NM_001201543.1 |
| FANCA | NM_000135.2 |
| FANCC | NM_000136.2 |
| FANCD2* | NM_033084.3 |
| FANCE | NM_021922.2 |
| FANCG | NM_004629.1 |
| FANCI | NM_001113378.1 |
| FANCL* | NM_018062.3 |
| FBP1 | NM_000507.3 |
| FBXO7 | NM_012179.3 |
| FH* | NM_000143.3 |
| FKBP10 | NM_021939.3 |
| FKRP | NM_024301.4 |
| FKTN | NM_001079802.1 |
| FMO3 | NM_006894.6 |
| FOXN1 | NM_003593.2 |
| FOXRED1 | NM_017547.3 |
| FRAS1 | NM_025074.6 |
| FREM2 | NM_207361.5 |

| GENE | TRANSCRIPT |
|---|---|
| FUCA1 | NM_000147.4 |
| G6PC | NM_000151.3 |
| G6PC3 | NM_138387.3 |
| GAA | NM_000152.3 |
| GALC* | NM_000153.3 |
| GALE* | NM_000403.3 |
| GALK1 | NM_000154.1 |
| GALNS | NM_000512.4 |
| GALNT3 | NM_004482.3 |
| GALT | NM_000155.3 |
| GAMT | NM_000156.5 |
| GATM | NM_001482.2 |
| GBA* | NM_001005741.2 |
| GBE1 | NM_000158.3 |
| GCDH | NM_000159.3 |
| GCH1 | NM_000161.2 |
| GDF5 | NM_000557.4 |
| GFM1 | NM_024996.5 |
| GHR* | NM_000163.4 |
| GJB2 | NM_004004.5 |
| GLB1 | NM_000404.2 |
| GLDC | NM_000170.2 |
| GLE1 | NM_001003722.1 |
| GNE* | NM_001128227.2 |
| GNPAT | NM_014236.3 |
| GNPTAB | NM_024312.4 |
| GNPTG | NM_032520.4 |
| GNS | NM_002076.3 |
| GORAB | NM_152281.2 |
| GRHPR | NM_012203.1 |
| GRIP1 | NM_021150.3 |
| GSS | NM_000178.2 |
| GUCY2D | NM_000180.3 |
| GUSB | NM_000181.3 |
| HADH | NM_005327.4 |
| HADHA | NM_000182.4 |
| HADHB | NM_000183.2 |
| HAMP | NM_021175.2 |
| HAX1 | NM_006118.3 |

| GENE | TRANSCRIPT |
|---|---|
| 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 |
| HMOX1 | NM_002133.2 |
| HOGA1 | NM_138413.3 |
| HPD | NM_002150.2 |
| HPS1 | NM_000195.4 |
| HPS3 | NM_032383.4 |
| HPS4 | NM_022081.5 |
| HPS5 | NM_181507.1 |
| HPS6 | NM_024747.5 |
| HSD17B3 | NM_000197.1 |
| HSD17B4 | NM_000414.3 |
| HSD3B2 | NM_000198.3 |
| HYAL1 | NM_153281.1 |
| HYLS1 | NM_145014.2 |
| IDUA | NM_000203.4 |
| IGHMBP2 | NM_002180.2 |
| IKBKB | NM_001556.2 |
| IL7R | NM_002185.3 |
| INVS | NM_014425.3 |
| ITGA6 | NM_000210.3 |
| ITGB3 | NM_000212.2 |
| ITGB4 | NM_001005731.2 |
| IVD | NM_002225.3 |
| JAK3 | NM_000215.3 |
| KCNJ1 | NM_000220.4 |
| KCNJ11 | NM_000525.3 |
| LAMA2 | NM_000426.3 |
| LAMA3 | NM_000227.4 |
| LAMB3 | NM_000228.2 |
| LAMC2 | NM_005562.2 |
| LARGE1 | NM_004737.4 |
| LCA5 | NM_181714.3 |
| LDLR | NM_000527.4 |
| LDLRAP1 | NM_015627.2 |
| LHX3 | NM_014564.4 |
| LIFR* | NM_002310.5 |
| LIG4 | NM_002312.3 |
| LIPA | NM_000235.3 |
| LMBRD1 | NM_018368.3 |
| LOXHD1 | NM_144612.6 |
| LPL | NM_000237.2 |
| LRAT | NM_004744.4 |
| LRP2 | NM_004525.2 |
| LRPPRC | NM_133259.3 |
| LYST | NM_000081.3 |
| MAK | NM_001242957.2 |
| MAN2B1 | NM_000528.3 |
| MANBA | NM_005908.3 |
| MCEE | NM_032601.3 |
| MCOLN1 | NM_020533.2 |
| MCPH1 | NM_024596.4 |
| MECR | NM_016011.3 |
| MED17 | NM_004268.4 |
| MESP2 | NM_001039958.1 |
| MFSD8 | NM_152778.2 |
| MKKS | NM_018848.3 |
| MKS1 | NM_017777.3 |
| MLC1* | NM_015166.3 |
| MLYCD | NM_012213.2 |
| MMAA | NM_172250.2 |
| MMAB | NM_052845.3 |
| MMACHC | NM_015506.2 |
| MMADHC | NM_015702.2 |
| MOCS1 | NM_001358530.2 |
| MOCS2A | NM_176806.3 |
| MOCS2B | NM_004531.4 |
| MPI | NM_002435.2 |
| MPL | NM_005373.2 |
| MPV17 | NM_002437.4 |
| MRE11 | NM_005591.3 |
| MTHFR* | NM_005957.4 |
| MTR | NM_000254.2 |
| MTRR | NM_002454.2 |
| MTTP | NM_000253.3 |
| MUSK | NM_005592.3 |
| MUT | NM_000255.3 |
| MVK | NM_000431.3 |
| MYO15A | NM_016239.3 |
| MYO7A | NM_000260.3 |
| NAGA | NM_000262.2 |
| NAGLU | NM_000263.3 |
| NAGS | NM_153006.2 |
| NBN | NM_002485.4 |
| NCF2 | NM_000433.3 |
| NDRG1 | NM_006096.3 |
| NDUFAF2 | NM_174889.4 |
| NDUFAF5 | NM_024120.4 |
| NDUFS4 | NM_002495.3 |
| NDUFS6 | NM_004553.4 |
| NDUFS7 | NM_024407.4 |
| NDUFV1 | NM_007103.3 |
| NEB* | NM_001271208.1 |
| NEU1 | NM_000434.3 |
| NGLY1 | NM_018297.3 |
| NPC1 | NM_000271.4 |
| NPC2 | NM_006432.3 |
| NPHP1 | NM_000272.3 |
| NPHS1 | NM_004646.3 |
| NPHS2 | NM_014625.3 |
| NR2E3 | NM_014249.3 |
| NSMCE3 | NM_138704.3 |
| NTRK1 | NM_001012331.1 |
| OAT* | NM_000274.3 |
| OCA2 | NM_000275.2 |
| OPA3 | NM_025136.3 |
| OSTM1 | NM_014028.3 |
| OTOA* | NM_144672.3 |
| OTOF | NM_194248.2;NM_194323.2 |
| P3H1 | NM_022356.3 |

| GENE | TRANSCRIPT |
|---|---|
| PAH | NM_000277.1 |
| PANK2 | NM_153638.2 |
| PC | NM_000920.3 |
| PCBD1 | NM_000281.3 |
| PCCA | NM_000282.3 |
| PCCB | NM_000532.4 |
| PCDH15 | NM_033056.3 |
| PCNT | NM_006031.5 |
| PDHB | NM_000925.3 |
| PEPD | NM_000285.3 |
| PET100 | NM_001171155.1 |
| PEX1* | NM_000466.2 |
| PEX10 | NM_153818.1 |
| PEX12 | NM_000286.2 |
| PEX13 | NM_002618.3 |
| PEX16 | NM_004813.2 |
| PEX2 | NM_000318.2 |
| PEX26 | NM_017929.5 |
| PEX5 | NM_001131025.1 |
| PEX6 | NM_000287.3 |
| PEX7 | NM_000288.3 |
| PFKM | NM_000289.5 |
| PGM3 | NM_001199917.1 |
| PHGDH | NM_006623.3 |
| PHKB | NM_000293.2;NM_001031835.2 |
| PHKG2 | NM_000294.2 |
| PHYH | NM_006214.3 |
| PIGN | NM_176787.4 |
| PKHD1* | NM_138694.3 |
| PLA2G6 | NM_003560.2 |
| PLEKHG5 | NM_020631.4 |
| PLOD1 | NM_000302.3 |
| PMM2 | NM_000303.2 |
| PNPO | NM_018129.3 |
| POLG | NM_002693.2 |
| POLH | NM_006502.2 |
| POMGNT1 | NM_017739.3 |
| POMT1 | NM_007171.3 |
| POMT2 | NM_013382.5 |

| GENE | TRANSCRIPT |
|---|---|
| POR | NM_000941.2 |
| POU1F1 | NM_000306.3 |
| PPT1 | NM_000310.3 |
| PRCD | NM_001077620.2 |
| PRDM5 | NM_018699.3 |
| PRF1 | NM_001083116.1 |
| PROP1 | NM_006261.4 |
| PSAP | NM_002778.3 |
| PTPRC* | NM_002838.4 |
| PTS | NM_000317.2 |
| PUS1 | NM_025215.5 |
| PYGM | NM_005609.3 |
| QDPR | NM_000320.2 |
| RAB23 | NM_183227.2 |
| RAG1 | NM_000448.2 |
| RAG2 | NM_000536.3 |
| RAPSN | NM_005055.4 |
| RARS2 | NM_020320.3 |
| RDH12 | NM_152443.2 |
| RLBP1 | NM_000326.4 |
| RMRP | NR_003051.3 |
| RNASEH2A | NM_006397.2 |
| RNASEH2B | NM_024570.3 |
| RNASEH2C | NM_032193.3 |
| RPE65 | NM_000329.2 |
| RPGRIP1L | NM_015272.2 |
| RTEL1 | NM_001283009.1 |
| RXYLT1 | NM_014254.2 |
| RYR1 | NM_000540.2 |
| SACS | NM_014363.5 |
| SAMD9 | NM_017654.3 |
| SAMHD1 | NM_015474.3 |
| SCO2 | NM_005138.2 |
| SEC23B | NM_006363.4 |
| SEPSECS | NM_016955.3 |
| SGCA | NM_000023.2 |
| SGCB | NM_000232.4 |
| SGCD | NM_000337.5 |
| SGCG | NM_000231.2 |

| GENE | TRANSCRIPT |
|---|---|
| SGSH | NM_000199.3 |
| SKIV2L | NM_006929.4 |
| SLC12A1 | NM_000338.2 |
| SLC12A3 | NM_000339.2 |
| SLC12A6 | NM_133647.1 |
| SLC17A5 | NM_012434.4 |
| SLC19A2 | NM_006996.2 |
| SLC19A3 | NM_025243.3 |
| SLC1A4 | NM_003038.4 |
| SLC22A5 | NM_003060.3 |
| SLC25A13 | NM_014251.2 |
| SLC25A15 | NM_014252.3 |
| SLC25A20 | NM_000387.5 |
| SLC26A2 | NM_000112.3 |
| SLC26A3 | NM_000111.2 |
| SLC26A4 | NM_000441.1 |
| SLC27A4 | NM_005094.3 |
| SLC35A3 | NM_012243.2 |
| SLC37A4 | NM_001164277.1 |
| SLC38A8 | NM_001080442.2 |
| SLC39A4 | NM_130849.3 |
| SLC45A2 | NM_016180.4 |
| SLC4A11 | NM_032034.3 |
| SLC5A5 | NM_000453.2 |
| SLC7A7 | NM_001126106.2 |
| SMARCAL1 | NM_014140.3 |
| SMN1* | NM_000344.3 |
| SMPD1 | NM_000543.4 |
| SNAP29 | NM_004782.3 |
| SPG11 | NM_025137.3 |
| SPR | NM_003124.4 |
| SRD5A2 | NM_000348.3 |
| ST3GAL5 | NM_003896.3 |
| STAR | NM_000349.2 |
| STX11 | NM_003764.3 |
| STXBP2 | NM_006949.3 |
| SUMF1 | NM_182760.3 |
| SUOX | NM_000456.2 |
| SURF1 | NM_003172.3 |

| GENE | TRANSCRIPT |
|---|---|
| SYNE4 | NM_001039876.2 |
| TANGO2 | NM_152906.6 |
| TAT | NM_000353.2 |
| TBCD | NM_005993.4 |
| TBCE* | NM_003193.4 |
| TCIRG1 | NM_006019.3 |
| TCN2 | NM_000355.3 |
| TECPR2 | NM_014844.3 |
| TERT | NM_198253.2 |
| TF | NM_001063.3 |
| TFR2 | NM_003227.3 |
| TG* | NM_003235.4 |
| TGM1 | NM_000359.2 |
| TH | NM_199292.2 |
| TK2 | NM_004614.4 |
| TMC1 | NM_138691.2 |
| TMEM216 | NM_001173990.2 |
| TMEM67 | NM_153704.5 |
| TMPRSS3 | NM_024022.2 |
| TPO | NM_000547.5 |
| TPP1 | NM_000391.3 |
| TREX1 | NM_033629.4 |
| TRIM32 | NM_012210.3 |
| TRIM37 | NM_015294.4 |
| TRMU | NM_018006.4 |
| TSEN54 | NM_207346.2 |
| TSFM* | NM_001172696.1 |
| TSHB | NM_000549.4 |
| TSHR | NM_000369.2 |
| TTC37 | NM_014639.3 |
| TTPA | NM_000370.3 |
| TULP1 | NM_003322.4 |
| TYMP | NM_001953.4 |
| TYR* | NM_000372.4 |
| TYRP1 | NM_000550.2 |
| UBR1 | NM_174916.2 |
| UNC13D | NM_199242.2 |
| USH1C* | NM_005709.3 |
| USH2A | NM_206933.2 |

| GENE | TRANSCRIPT |
|---|---|
| VDR | NM_001017535.1 |
| VLDLR | NM_003383.4 |
| VPS11 | NM_021729.5 |
| VPS13A* | NM_033305.2 |
| VPS13B | NM_017890.4 |
| VPS45 | NM_007259.4 |
| VPS53* | NM_001128159.2 |
| VRK1 | NM_003384.2 |
| VSX2 | NM_182894.2 |
| WISP3 | NM_003880.3 |
| WNT10A | NM_025216.2 |
| WRN* | NM_000553.4 |
| XPA | NM_000380.3 |
| XPC | NM_004628.4 |
| ZBTB24 | NM_014797.2 |
| ZFYVE26 | NM_015346.3 |
| ZNF469 | NM_001127464.2 |

## 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 in the Genes Analyzed table. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 20bp 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). Confirmation of the presence and location of reportable variants is performed as needed based on stringent criteria using one of several validated orthogonal approaches (PubMed ID 30610921). Sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778). Confirmatory sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778).

  The following additional 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 GJB2, the reportable range includes large upstream deletions overlapping GJB6. For HBA1/2, the reference genome has been modified to force some sequencing reads derived from HBA1 to align to HBA2, and variant calling algorithms are modified to support an expectation of 4 alleles in these regions. HBA1/2 copy number calling is performed by a custom hypothesis testing algorithm which generates diplotype calls. If sequence data for a sample does not support a unique high confidence match from among hypotheses tested, that sample is flagged for manual review. Copy number variation is only reported for coding sequence of HBA1 and HBA2 and the HS-40 region. This assay does not distinguish among the -α3.7 subtypes, and all -α3.7 variants are called as HBA1 deletions. This assay may not detect overlapping copy gain and copy loss events when the breakpoints of those events are similar. For FMR1, cytosine-guanine-guanine (CGG) triplet repeats in the 5' untranslated region (5' UTR) of the FMR1 gene are detected by triplet repeat-primed PCR (RP-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.

- 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**), gnomAD (**http://gnomad.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.
- VPS13A: Deletion/duplication analysis is not offered for exons 2-3, 27-28. GNE: Sequencing analysis for exons 8 includes only cds +/- 10 bp. GALE: Sequencing analysis for exons 10 includes only cds +/- 5 bp. DDX11: NM_030653.3:c.1763-1G>C variant only. 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. PKHD1: Deletion/duplication analysis is not offered for exon 13. OTOA: Deletion/duplication and sequencing analysis is not offered for exons 20-28. DUOX2: Deletion/duplication and sequencing analysis is not offered for exons 6-7. TBCE: Sequencing analysis for exons 2 includes only cds +/- 10 bp. PTPRC: Sequencing analysis is not offered for exons 3, 15. ABCC2: Deletion/duplication analysis is not offered for exons 24-25. BBS9: Deletion/duplication analysis is not offered for exon 4. WRN: Deletion/duplication analysis is not offered for exons 10-11. Sequencing analysis for exons 8, 10-11 includes only cds +/- 10 bp. OAT: Deletion/duplication analysis is not offered for exon 2. GHR: Deletion/duplication and sequencing analysis is not offered for exon 3. CFTR: Sequencing analysis for exons 7 includes only cds +/- 10 bp. EYS: Sequencing analysis for exons 30 includes only cds +/- 0 bp. FH: Sequencing analysis for exons 9 includes only cds +/- 10 bp. ANO10: Sequencing analysis for exons 8 includes only cds +/- 0 bp. ATP8B1: Sequencing analysis for exons 19 includes only cds +/- 10 bp. TSFM: Sequencing analysis is not offered for exon 5. VPS53: Sequencing analysis for exons 14 includes only cds +/- 5 bp. FANCD2: Deletion/duplication analysis is not offered for exons 14-17, 22 and sequencing analysis is not offered for exons 15-17. Sequencing analysis for exons 6, 14, 18, 20, 23, 25, 34 includes only cds +/- 10 bp. 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". 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. 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. COL11A2: Deletion/duplication analysis is not offered for exon 36. 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. AIPL1: Sequencing analysis for exons 2 includes only cds +/- 10 bp. 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. SMN1 or SMN2: NM_000344.3:c.*3+80T>G variant only. LIFR: Sequencing analysis for exons 3 includes only

cds +/- 5 bp. TYR: Deletion/duplication and sequencing analysis is not offered for exon 5. TG: Deletion/duplication analysis is not offered for exon 18. Sequencing analysis for exons 44 includes only cds +/- 0 bp. USH1C: Deletion/duplication analysis is not offered for exons 5-6. AMN: Deletion/duplication analysis is not offered for exon 1. FANCL: Sequencing analysis for exons 4, 10 includes only cds +/- 10 bp. ATM: Sequencing analysis for exons 6, 24, 43 includes only cds +/- 10 bp. FAH: Deletion/duplication analysis is not offered for exon 14. GALC: Deletion/duplication analysis is not offered for exon 6. MLC1: Sequencing analysis for exons 11 includes only cds +/- 10 bp. PEX1: Sequencing analysis for exons 16 includes only cds +/- 0 bp.

## This report has been reviewed and approved by:

Fatimah Nahhas-Alwan, PhD, FACMG
Clinical Molecular Geneticist

Nichols Institute, Chantilly

PATIENT INFORMATION
6973,DONOR

DOB: [redacted] Age: [redacted]
SEX: M

REPORT STATUS **Final**

ORDERING PHYSICIAN
[redacted]

CLIENT INFORMATION
[redacted]

SPECIMEN INFORMATION
SPECIMEN: [redacted]
REQUISITION: [redacted]
LAB REF NO: [redacted]

ID: [redacted]
PHONE: [redacted]

COLLECTED: 05/18/2023 00:00
RECEIVED: 05/19/2023 19:09
REPORTED: 05/26/2023 19:56

| Test Name | In Range | Out of Range | Reference Range | Lab |
|---|---|---|---|---|
| Hemoglobinopathy Evaluation | | | | AMD |
| Red Blood Cell Count | 5.00 | | 4.20-5.80 Mill/uL | |
| HEMOGLOBIN | 15.4 | | 13.2-17.1 g/dL | |
| Hematocrit | | | | |
| Hematocrit | 47.1 | | 38.5-50.0 % | |
| MCV | 94.2 | | 80.0-100.0 fL | |
| MCH | 30.8 | | 27.0-33.0 pg | |
| RDW | 12.7 | | 11.0-15.0 % | |
| Hemoglobin A | 97.4 | | >96.0 % | |
| Hemoglobin F | 0.0 | | <2.0 % | |
| Hemoglobin A2 (Quant) | 2.6 | | 2.2-3.2 % | |
| Interpretation | | | | |

NORMAL PATTERN

There is a normal pattern of hemoglobins and normal levels of Hb A2 and Hb F are present. No variant hemoglobins are observed. This is consistent with A/A phenotype.
If iron deficiency coexists with a mild/silent beta thalassemia trait Hb A2 may be in the normal range. Rare variant hemoglobins have no separation from hemoglobin A by capillary zone electrophoresis (CZE) or high-performance liquid chromatography (HPLC).
If clinically indicated, Thalassemia and Hemoglobinopathy Comprehensive (TC 17365) should be considered.

| | | | | |
|---|---|---|---|---|
| CBC (includes Differential and Platelets) | | | | AMD |
| CBC (includes Differential and Platelets) | | | | |
| White Blood Cell Count | 5.3 | | 3.8-10.8 Thous/uL | |
| Red Blood Cell Count | 5.00 | | 4.20-5.80 Mill/uL | |
| HEMOGLOBIN | 15.4 | | 13.2-17.1 g/dL | |
| Hematocrit | 47.1 | | 38.5-50.0 % | |
| MCV | 94.2 | | 80.0-100.0 fL | |
| MCH | 30.8 | | 27.0-33.0 pg | |
| MCHC | 32.7 | | 32.0-36.0 g/dL | |
| RDW | 12.7 | | 11.0-15.0 % | |
| PLATELET COUNT | 373 | | 140-400 Thous/uL | |
| MPV | 10.0 | | 7.5-12.5 fl | |

PATIENT INFORMATION
6973,DONOR

REPORT STATUS **Final**

Nichols Institute, Chantilly

ORDERING PHYSICIAN [redacted]

DOB: [redacted] Age: 3[redacted]
SEX: M
ID: [redacted]

COLLECTED: 05/18/2023 00:00
REPORTED: 05/26/2023 19:56

| Test Name | In Range | Out of Range | Reference Range | Lab |
|---|---|---|---|---|
| CBC (includes Differential and Platelets) (Continued) | | | | |
| Absolute Neutrophils | 2602 | | 1500-7800 cells/uL | |
| Absolute Lymphocytes | 1935 | | 850-3900 cells/uL | |
| Absolute Monocytes | 647 | | 200-950 cells/uL | |
| Absolute Eosinophils | 58 | | 15-500 cells/uL | |
| Absolute Basophils | 58 | | 0-200 cells/uL | |
| Neutrophils | 49.1 | | % | |
| Lymphocytes | 36.5 | | % | |
| Monocytes | 12.20 | | % | |
| Eosinophils | 1.10 | | % | |
| Basophils | 1.10 | | % | |
| Nucleated RBC | 0.00 | | 0 /100 WBC | |

Chromosome Analysis, Blood AMD

Chromosome Analysis, Blood

Chromosome Analysis, Blood

Order ID: [redacted]

Specimen Type: Blood

Clinical Indication: Donor screening

RESULT:
NORMAL MALE KARYOTYPE

INTERPRETATION:
Chromosome analysis revealed normal G-band patterns within the limits of standard cytogenetic analysis.

Please expect the results of any other concurrent study in a separate report.

NOMENCLATURE:
46,XY

ASSAY INFORMATION:
Method: G-Band (Digital Analysis: MetaSystems/Ikaros)
Cells Counted: 20
Band Level: 550
Cells Analyzed: 5
Cells Karyotyped: 4

This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

Debra Boles, Ph.D., FACMG, Technical Director, Cytogenetics and Genomics, 703-802-7156

Electronic Signature: 5/26/2023 7:11 PM

For additional information, please refer to

PATIENT INFORMATION
6973,DONOR

REPORT STATUS **Final**

Nichols Institute, Chantilly

ORDERING PHYSICIAN [redacted]

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COLLECTED: 05/18/2023 00:00
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| Test Name | In Range | Out of Range | Reference Range | Lab |
|---|---|---|---|---|

Chromosome Analysis, Blood (Continued)
Chromosome Analysis, Blood (Continued)
http://education.questdiagnostics.com/faq/chromsblood
(This link is being provided for informational/
educational purposes only).

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**Performing Laboratory Information:**

AMD Quest Diagnostics Nichols Institute 14225 Newbrook Drive Chantilly VA 20151 Laboratory Director: Patrick W Mason, MD PhD