Fairfax Cryobank
The Trusted Choice for Donor Sperm

Donor 5002

Genetic Testing Summary

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

Last Updated: 03/19/19

Donor Reported Ancestry: German, Scotch, Dutch Jewish Ancestry: No

Genetic Test*	Result	Comments/Donor's Residual Risk**
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Cystic Fibrosis (CF) carrier screening	Negative by genotyping of 99 mutations in the CFTR gene	1/300
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 of the SMN1 gene	1/610
Hb Beta Chain-Related Hemoglobinopathy (including Beta Thalassemia and Sickle Cell Disease) by genotyping	Negative for 28 mutations tested in the HBB gene	1/290
Special Testing		
Non-Syndromic Hearing Loss and Deafness (GJB2)	Carrier: Non-Syndromic Hearing Loss and Deafness (GJB2)	Partner testing is recommended before using this donor.
Maple Syrup Urine Disease, Type 1b (BCKDHB)	Negative by gene sequencing in the BCKDHB gene	1/983
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1)	Negative by gene sequencing in the MCCC1 gene	1/592
3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2)	Negative by gene sequencing in the MCCCC2 gene	1/272

*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.

Counsyl

RESULTS RECIPIENT
FAIRFAX JBANK - FAIRFAX
Attn: Dr. Harvey Stern
[redacted]
NPI: 1417048786
Report Date: 12/07/2014

MALE
DONOR # 5002
DOB: [redacted]
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 12/01/2014
Date Received: 12/03/2014
Date Tested: 12/07/2014
Barcode: [redacted]
Indication: Egg or Sperm Donor

FEMALE
N/A

Family Prep Screen

NEGATIVE

ABOUT THIS TEST

The Counsyl Family Prep Screen (version 1.0) tests known mutations to help you learn about your chance to have a child with a genetic disease.

PANEL DETAILS

Fairfax Cryobank Fundamental Panel (3 diseases tested)

VERSION

DONOR # 5002 (Family Prep Screen 1.0)

RESULTS SUMMARY

NEGATIVE

No known or potential disease-causing mutations were detected.

[redacted]

CLINICAL NOTES

- None

NEXT STEPS

- If necessary, patients can discuss residual risks with their physician or a genetic counselor.
- To schedule a complimentary appointment to speak with a clinical expert about these results, please visit counsyl.com/my/consults/.

Methods and Limitations

DONOR # 5002 (Family Prep Screen 1.0): targeted genotyping and copy number analysis.

Targeted genotyping: Targeted DNA mutation analysis is used to simultaneously determine the genotype of 127 variants associated with 2 diseases. The test is not validated for detection of homozygous mutations, and although rare, asymptomatic individuals affected by the disease may not be genotyped accurately.

Copy number analysis: Targeted copy number analysis is used to determine the copy number of exon 7 of the SMN1 gene relative to other genes. Other mutations may interfere with this analysis. Some individuals with two copies of SMN1 are carriers with two SMN1 genes on one chromosome and a SMN1 deletion on the other chromosome. In addition, a small percentage of SMA cases are caused by nondeletion mutations in the SMN1 gene. Thus, a test result of two SMN1 copies significantly reduces the risk of being a carrier; however, there is still a residual risk of being a carrier and subsequently a small risk of future affected offspring for individuals with two or more SMN1 gene copies. Some SMA cases arise as the result of de novo mutation events which will not be detected by carrier testing.

Limitations: In an unknown number of cases, nearby genetic variants may interfere with mutation detection. Other possible sources of diagnostic error include sample mix-up, trace contamination, bone marrow transplantation, blood transfusions and technical errors. If more than one variant is detected in a gene, additional studies may be necessary to determine if those variants lie on the same chromosome or different chromosomes. The Counsyl test does not fully address all inherited forms of intellectual disability, birth defects and genetic disease. A family history of any of these conditions may warrant additional evaluation. Furthermore, not all mutations will be identified in the genes analyzed and additional testing may be beneficial for some patients. For example, individuals of African, Southeast Asian, and Mediterranean ancestry are at increased risk for being carriers for hemoglobinopathies, which can be identified by CBC and hemoglobin electrophoresis or HPLC (*ACOG Practice Bulletin No. 78. Obstet. Gynecol. 2007;109:229-37*).

This test was developed and its performance characteristics determined by Counsyl, Inc. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA does not require this test to go through premarket review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. These results are adjunctive to the ordering physician's workup. CLIA Number: **#05D1102604**.

LAB DIRECTORS

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Rebecca Mar-Heyming, PhD, DABMG

Counsyl

RESULTS - RECIPIENT
FAIRFAX OBANK - FAIRFAX
Attn: Dr. Harvey Stern
NPI: 1417048786
Report Date: 12/07/2014

MALE
DONOR # 5002
DOB: [redacted]
Ethnicity: Northern European
Barcode: [redacted]

FEMALE
N/A

Diseases Tested

Autosomal Recessive Disorders

TARGETED GENOTYPING

Cystic Fibrosis - Gene: CFTR. Variants (99): G85E, R117H, R334W, R347P, A455E, G542*, G551D, R553*, R560T, R1162*, W1282*, N1303K, c.1521_1523delCTT, c.1519_1521delATC, c.2052delA, c.3528delC, c.489+1G>T, c.579+1G>T, c.1585-1G>A, c.1766+1G>A, 2789+5G>A, c.2988+1G>A, 3849+10kbC>T, E60*, R75*, E92*, Y122*, G178R, R347H, Q493*, V520F, S549N, P574H, M1101K, D1152H, c.2012delT, c.262_263delTT, c.313delA, c.948delT, c.3744delA, c.3773dupT, c.1680-1G>A, 3272-26A>G, c.2051_2052delAAinsG, S549R(c.1645A>C), R117C, L206W, G330*, T338I, R352Q, S364P, G480C, C524*, S549R(c.1647T>G), Q552*, A559T, G622D, R709*, K710*, R764*, Q890*, R1066C, W1089*, Y1092X, R1158*, S1196*, W1204*, Q1238*, S1251N, S1255*, c.3067_3072del6, c.442delA, c.531delT, c.803delA, c.805_806delAT, c.1545_1546delTA, M607_Q643del, c.1911delG, c.1923_1931del9ins1, c.1976delA, c.3039delC, c.3536_3539delCCAA, c.3659delC, c.1155_1156dupTA, c.2052dupA, c.2175dupA, c.2738insG, 296+12T>C, c.273+1G>A, 405+3A>C, c.274-1G>A, 711+5G>A, c.580-1G>T, c.1766+1G>T, 1898+5G>T, Q996, c.325_327delTATinsG, 3849+4A>G, c.1075_1079del5ins5. IVS8-5T allele analysis is only reported in the presence of the R117H mutation. **Detection rate:** Northern European 91%.

Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - Gene: HBB. **Variants (28):** E7V, K18*, Q40*, c.126_129delCTTT, c.27dupG, IVS-II-654, IVS-II-745, c.315+1G>A, IVS-I-6, IVS-I-110, IVS-I-5, c.92+1G>A, -88C>T, -28A>G, -29A>G, c.25_26delAA, c.217dupA, c.316-2A>C, c.316-2A>G, G2S, -87C>G, E7K, W16*, c.51delC, c.20delA, E27K, E122Q, E122K. **Detection rate:** Northern European 83%.

COPY NUMBER ANALYSIS

Spinal Muscular Atrophy - Gene: SMN1. **Variant (1):** SMN1 copy number. **Detection rate:** Northern European 95%.

Counsyl

RESULTS RECIPIENT
FAIRFAX JBANK - FAIRFAX
Attn: Dr. Harvey Stern
NPI: 1417048786
Report Date: 12/07/2014

MALE
DONOR # 5002
DOB: [redacted]
Ethnicity: Northern European
Barcode: [redacted]

FEMALE
N/A

Risk Calculations

Below are the risk calculations for all diseases tested. Since negative results do not completely rule out the possibility of being a carrier, the **residual risk** represents the patient's post-test likelihood of being a carrier and the **reproductive risk** represents the likelihood the patient's future children could inherit each disease. These risks are inherent to all carrier screening tests, may vary by ethnicity, are predicated on a negative family history and are present even after a negative test result. Inaccurate reporting of ethnicity may cause errors in risk calculation.

Disease	DONOR # 5002 Residual Risk	Reproductive Risk
Cystic Fibrosis	1 in 300	1 in 33,000
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	1 in 290	1 in 58,000
Spinal Muscular Atrophy	SMN1: 2 copies 1 in 610	1 in 84,000

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CARRIER SCREENING REPORT

Patient	Sample	Referring Doctor
Patient Name: Donor 5002 **Date of Birth:** [redacted] **Reference #:** P0637973 **Indication:** Carrier Testing **Test Type:** NGS single gene full sequencing test	**Specimen Type:** Purified DNA [redacted] **Date Collected:** 4/25/2018 [redacted]	**Harvey Stern, M.D.** **Fairfax Cryobank, Inc.** **2015 Williams Drive** **Suite 110** **Fairfax, VA 22031** Fax: **703-698-3933**

RESULT SUMMARY

NGS single gene full sequencing test

Results: A heterozygous (one copy) pathogenic variant, chr13:hg38.g.20223037_20531807del308770, del(GJB6-D13S1830), was detected in the *GJB2* gene

No clinically significant variants detected in the *BCKDHB*, *MCCC1*, and *MCCC2* genes

Gene(s) analyzed: *GJB2*, *BCKDHB*, *MCCC1*, and *MCCC2*

Recommendations: Genetic counseling is recommended.

Interpretation: Screening for the presence of mutations in the *GJB2* gene, which is associated with non-syndromic hearing loss (*GJB2*-related), was performed by next generation sequencing on DNA extracted from this patient's sample. A heterozygous (one copy) deletion, chr13:hg38.g.20223037_20531807del308770, del(GJB6-D13S1830), was detected in the *GJB2* gene. This variant is considered to be pathogenic and when present *in trans* with a pathogenic variant causative for non-syndromic hearing loss (*GJB2*-related). This deletion is located upstream of *GJB2* and eliminates regulatory regions essential for the expression of this gene. Please see PMID: 11807148 and PMID 19723508 for additional information. Therefore, this individual is expected to be at least a carrier for non-syndromic hearing loss (*GJB2*-related). Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is non-syndromic hearing loss (GJB2-related)?

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

Patient:	Donor 5002	DOB:	[redacted]	Lab #:	[redacted]

genotype. Life expectancy is not reduced.

Screening for the presence of pathogenic variants in the *BCKDHB*, *MCCC1*, and *MCCC2* genes which are associated with maple syrup urine disease, type 1b, 3-methylcrotonyl-CoA carboxylase deficiency (*MCCC1*-related), and 3-methylcrotonyl-CoA carboxylase deficiency (*MCCC2*-related), respectively, was performed by next generation sequencing and possibly genotyping for select variants on DNA extracted from this patient's sample. No clinically significant variants were detected during this analysis. This negative result does not rule out the possibility that a pathogenic variant in the genes examined is present.

This technology may not detect all small insertion/deletions and is not diagnostic for large duplications/deletions and structural genomic variation. The coding DNA sequence of the gene plus at least five base pairs flanking splice sites were sequenced and analyzed relative to the hg19 assembly. A mutation(s) deep in intronic sequences or in untranslated regions of the gene except a portion described above or a pathogenic variant(s) in other genes not included in this test could be present in this patient. The analytical sensitivity of this test is estimated at 99% for single base substitutions and 97% overall. All potentially pathogenic variants were subjected to Sanger sequencing or genotyping by allele specific primer extension analysis for confirmation of the result. Any benign variants identified during this analysis were not reported.

Please note that this carrier screening test masks likely benign variants and variants of uncertain significance (VUS) if there are any. Only known pathogenic variants or likely pathogenic variants which are expected to result in deleterious effects on protein function are reported. If reporting of likely benign variants and VUS is desired in this patient, please contact the laboratory (tel. 212-241-2537) to request an amended report.

Comments: This test was developed and its performance characteristics were determined by Mount Sinai Genomics, Inc. It is considered acceptable for patient testing. It has not been cleared or approved by the FDA. The FDA has determined that such clearance or approval is not necessary.

This type of mutation analysis generally provides highly accurate genotype information for point mutations and single nucleotide polymorphisms. Despite this level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, mosaicism or other rare genetic variants that interfere with analysis. In addition, families should understand the limitations of the testing and that rare diagnostic errors may occur for the reasons described.

For Disease Specific Standards and Guidelines:
https://www.acmg.net/
Additional disease-specific references available upon request.

This case has been reviewed and electronically signed by Ruth Kornreich, Ph.D., FACMG, Co-Laboratory Director

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

Patient:	Donor 5002	DOB:	[redacted]	Lab #:	[redacted]

Table of Residual Risks by Ethnicity

Please note: This table displays residual risks after a negative result for each of the genes and corresponding disorders. **If a patient is reported to be a carrier of a disease, their residual risk is 1 and this table does not apply for that disease.**

Disease (Inheritance)	Gene	Ethnicity	Carrier Frequency	Detection Rate	Residual Risk	Analytical Detection Rate
Maple Syrup Urine Disease, Type 1b (AR) NM_000056.3	*BCKDHB*	Caucasian	1 in 433	56%	1 in 983	>95%
		Asian	1 in 163	57%	1 in 378	>95%
		Ashkenazi Jewish	1 in 97	>95%	1 in 1921	>95%
		Worldwide	1 in 327	72%	1 in 1165	>95%
3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC1*-Related) (AR) NM_020166.4	*MCCC1*	Caucasian	1 in 137	77%	1 in 592	88%
		Worldwide	1 in 147	75%	1 in 585	>95%
3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC2*-Related) (AR) NM_022132.4	*MCCC2*	Caucasian	1 in 112	59%	1 in 272	91%
		Worldwide	1 in 120	69%	1 in 385	>95%
Non-Syndromic Hearing Loss (*GJB2*-Related) (AR) NM_004004.5	*GJB2*	Caucasian	1 in 42	88%	1 in 343	>95%
		Asian	1 in 50	83%	1 in 289	>95%
		Ashkenazi Jewish	1 in 21	>95%	1 in 401	>95%
		Worldwide	1 in 43	82%	1 in 234	>95%

AR: Autosomal Recessive