

Donor 4235

Genetic Testing Summary

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

Last Updated: 05/17/21

Donor Reported Ancestry: English, Swedish, German

Jewish Ancestry: No

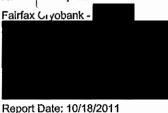
Genetic Test*	Result	Comments/Donor's Residual Risk**		
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities		
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, 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	1/310		
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 in the SMN1 gene	1/700		
Hb Beta Chain-Related Hemoglobinopathy (including Beta Thalassemia and Sickle Cell Disease) by genotyping	Negative for 28 mutations tested in the HBB gene	1/1500 for Beta-Thalassemia <1/500 for Sickle Cell		
Special Testing				
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (CYP21A2)	Negative by gene sequencing in the CYP21A2 gene	1/1300- classic variant 1/200 non-classic (milder) variant		
Non-Syndromic Hearing Loss (GJB2)	Negative by gene sequencing in the GJB2 gene	1/600		
Progressive Familial Intrahepatic Cholestasis Type 2 (ABCB11)	Negative by gene sequencing in the ABCB11 gene	1/950		
Usher Syndrome Type 2A (USH2A)	Negative by gene sequencing in the USH2A gene	1/230		

*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.

info@fairfaxcryobank.com



Result ciplent



Male Name: DONOR 4235 DOB: Ethnicity: Northern European Sample Type: OG-500 Saliva Date of Collection: 10/06/2011 Barcode: Indication: Egg or Sperm Donor

Female

Not tested

Counsyl Test Results (Egg or Sperm Donor)

The Counsyl test uses targeted DNA mutation analysis to simultaneously determine the carrier status of an individual for a number of Mendelian diseases. This report indicates which mutations, if any, were detected for each mutation panel. Because only select mutations are tested, the percentage of carriers detected varies by ethnicity. A negative test result does not eliminate the possibility that the individual is a carrier. Interpretation is given as an estimate of the risk of conceiving a child affected with a disease, which is based on reported ethnicity, the test results, and an assumption of no family history.*



DONOR 4235

DONOR 4235's DNA test shows that he is not a carrier of any disease-causing mutation tested.



Partner

The reproductive risk presented is based on a hypothetical pairing with a partner of the same ethnic group.

Reproductive Risk Summary

No increased reproductive risks to highlight. Please refer to the following pages for detailed information about the results.

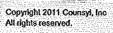
Clinical notes:

 Individuals of African, Southeast Asian, and Mediterranean ancestry are at increased risk for being carriers for hemoglobinopathles and may also benefit from carrier testing by CBC and hemoglobin electrophoresis or HPLC. ACOG Practice Bulletin No. 78. Obstet Gynecol 2007;109:229-37.

To schedule a free appointment to speak with a genetic counselor about your results, please visit www.counsyl.com/appointment.

*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, and technical errors. The reproductive risk summary is provided as an aid to genetic counseling. Inaccurate reporting of ethnicity may cause errors in risk calculation.

This test was developed and its performance characteristics determined by Counsyl, Inc. The laboratory is regulated under the Clinical Laboratory Improvement Americana and a qualified to perform high-complexity clinical testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. These results are adjunctive to the ordering physician's workup. CLIA Number: #05D1102604. Lab Directors: Jessita Jacobson, MD, William K. Seltzer, PhD, FACMG.



2200 Bridge Parkway, Suite 103, Redwood City, CA 94065 (888) COUNSYL | http://www.counsyl.com



Male

Name: DONOR 4235 DOB:

Full Results

Below are the full test results for all diseases on the panel. Noted are the specific genetic mutations for which the patient tested positive or negative. If there was insufficient data to determine the genotype for any variant, this will be noted as "no call." Also listed in this section is the patient's post-test risk of being a carrier of each disease as well as the odds that his future children could inherit each disease.

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Beta Thalassemia	Less than 1 in 1,000,000	1 in 250,000	
			!

DONOR 4235: No mutations detected. This does not rule out the possibility of being a carrier of untested mutations. The post-test risk of being a carrier, assuming a negative family history, is 1 in 1,500. 83% detection rate.

Gene: HBB. Variants (27): K17X, Q39X, Phe41fs, Ser9fs, IVS-II-654, IVS-II-745, IVS-II-850, IVS-I-6, IVS-I-110, IVS-I-5, IVS-I-1(G>A), -88C>T, -28A>G, -29A>G, Lys8fs, Phe71fs, IVS-II-849(A>C), IVS-II-849(A>G), Gly24 T>A, -87C>G, Hb C, W15X, Gly16fs, Glu6fs, Hb E, Hb D-Punjab, Hb O-Arab.

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	Reproductive risk:	Risk before testing:	Removalish
Cystic Fibrosis	1 in 34,000	1 in 3,000	

DONOR 4235: No mutations detected. This does not rule out the possibility of being a carrier of untested mutations. The post-test risk of being a carrier, assuming a negative family history, is 1 in 310. 91% detection rate.

Gene: CFTR. Varlants (99): G85E, R117H, R334W, R347P, A455E, G542X, G551D, R553X, R560T, R1162X, W1282X, N1303K, F508del, I507del, 2184delA, 3659delC, 621+1G>T, 711+1G>T, 1717-1G>A, 1898+1G>A, 2789+5G>A, 3120+1G>A, 3849+10kbC>T, E60X, R75X, E92X, V122X, G178R, R347H, Q493X, V520F, S549N, P574H, M1101K, D1152H, 2143delT, 394delT, 444delA, 1717-1G>A, 1898+1G>A, 2789+5G>A, 3120+1G>A, 3849+10kbC>T, E60X, R75X, E92X, V122X, G178R, R347H, Q493X, V520F, S549N, P574H, M1101K, D1152H, 2143delT, 444delA, 1717-1G>A, 38905insT, 1812-1G>A, 3272-26A>G, 2183AA>G, S549(A)

		And the second	
	Reproductive risk:	Risk before testing:	Reduced risk
Sickle Cell Disease	Less than 1 in 1,000,000	less than 1 in 1,000,000	
DONOR 4235: No mutations detected. This does not rule out the p assuming a negative family history, is < 1 in 500. 70% detection ra Gene: HBB. Variants (28): Hb S, K17X, Q39X, Phe41fs, Ser9fs, IVS-II-654, IVS-II II-849(A>C), IVS-II-849(A>G), Gh24 T>A, -87C>G, Hb C, W15X, Gly16fs, Glu6fs, I			
	Reproductive risk:	Risk before testing:	Reduced risk
Spinal Muscular Atrophy	1 in 97,000	1 în 4,800	
DONOR 4235: No mutations detected. This does not rule out the	possibility of being a carrier of untested m	utations. The post-test risk of be	ing a carrier,

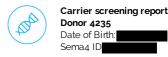
assuming a negative family history, is 1 in 700. 95% detection rate.

Gene: SMN1, Variants (1): Exon 7 deletion,

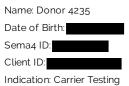
This test was developed and its performance characteristics determined by Counsyl. Inc. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. These results are adjunctive to the ordering physician's workup. CLIA Number: #05D1102604. Lab Directors: Jessica Jacobson, MD, William K. Selfzer, PhD, FACMG.

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Patient Information



Specimen Information

Specimen Type: Purified DNA Date Collected: 04/05/2021 Date Received: 04/14/2021 Final Report: 04/28/2021 **Referring Provider**

Fairfax Cryobank, Inc.

Custom Carrier Screen (ECS)

Number of genes tested: 4

SUMMARY OF RESULTS AND RECOMMENDATIONS

⊖ Negative
Negative for all genes tested: ABCB11, GJB2, USH2A, and CYP21A2
To view a full list of genes and diseases tested
please see Table 1 in this report

AR=Autosomal recessive; XL=X-linked

Recommendations

• Consideration of residual risk by ethnicity after a negative carrier screen is recommended for the other diseases on the panel, especially in the case of a positive family history for a specific disorder.

Test description

This patient was tested for the genes listed above using one or more of the following methodologies: target capture and short-read sequencing, long-range PCR followed by short-read sequencing, targeted genotyping, and/or copy number analysis. Please note that negative results reduce but do not eliminate the possibility that this individual is a carrier for one or more of the disorders tested. Please view the Table of Residual Risks Based on Ethnicity at the end of this report or at **go.sema4.com/residualrisk** for gene transcripts, sequencing exceptions, specific detection rates, and residual risk estimates after a negative screening result. With individuals of mixed ethnicity, it is recommended to use the highest residual risk estimate. Only known pathogenic or likely pathogenic variants are reported. This carrier screening test does not report likely benign variants and variants of uncertain significance (VUS). If reporting of likely benign variants and VUS are desired in this patient, please contact the laboratory at 800-298-6470, option 2 to request an amended report.

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Fatimah Nahhas-Alwan, Ph.D., DABMGG, Laboratory Director Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D



Genes and diseases tested

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

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

Gene	Inheritance Pattern	Status	Detailed Summary
CYP21A2	AR	Reduced Risk (see table below)	<i>CYP21A2</i> copy number: 2 <i>CYP21A2</i> sequencing: Negative
GJB2	AR	Reduced Risk (see table below)	
ABCB11	AR	Reduced Risk (see table below)	
USH2A	AR	Reduced Risk (see table below)	
	GJB2 ABCB11	GenePatternCYP21A2ARGJB2ARABCB11AR	Gene Pattern Status Pattern Status CYP21A2 AR Reduced Risk (see table below) GJB2 AR Reduced Risk (see table below) ABCB11 AR Reduced Risk (see table below) USH2A AR Reduced Risk (see table below)

AR=Autosomal recessive; XL=X-linked

Table 2: Residual Risk by ethnicity for negative results

Disease (Inheritance)	Gene	Ethnicity	Carrier Frequency	Detection Rate	Residual Risk	Analytical Detection Rate
Congenital Adrenal Hyperplasia due to 21-	CYP21A2	Ashkenazi Jewish	1 in 40	95%	1 in 780	95%
Hydroxylase Deficiency - Classic (AR)		European (Non-Finnish)	1 in 67	95%	1 in 1,300	
NM_000500.6		Worldwide	1 in 60	95%	1 in 1,200	
Congenital Adrenal Hyperplasia due to 21-	CYP21A2	Ashkenazi Jewish	1 in 7	95%	1 in 120	95%
Hydroxylase Deficiency - Non-Classic (AR)		European (Non-Finnish)	1 in 11	95%	1 in 200	
NM_000500.6		Worldwide	1 in 16	95%	1 in 300	
Non-Syndromic Hearing Loss (GJB2 -Related) (AR)	GJB2 [‡]	African	1 in 56	85%	1 in 360	99%
NM_004004.5		Ashkenazi Jewish	1 in 13	94%	1 in 210	
		East Asian	1 in 5	98%	1 in 280	
		Finnish	1 in 16	99%	1 in 1,400	
		European (Non-Finnish)	1 in 18	97%	1 in 600	
		Native American	1 in 28	96%	1 in 610	
		South Asian	1 in 55	94%	1 in 970	
		Worldwide	1 in 18	97%	1 in 530	
Progressive Familial Intrahepatic Cholestasis, Type 2	ABCB11	African	1 in 295	52%	1 in 610	99%
(AR)		East Asian	1 in 153	61%	1 in 390	
NM_003742.2		Finnish	1 in 835	52%	1 in 1,700	
		European (Non-Finnish)	1 in 276	71%	1 in 950	
		Native American	1 in 390	57%	1 in 910	
		South Asian	1 in 654	74%	1 in 2,500	
		Worldwide	1 in 306	65%	1 in 880	

sema4



Usher Syndrome, Type IIA (AR)	USH2A	African	1 in 69	75%	1 in 280	98%
NM_206933.2		Ashkenazi Jewish	1 in 40	95%	1 in 750	
		East Asian	1 in 27	50%	1 in 52	
		Finnish	1 in 142	97%	1 in 4,300	
		European (Non-Finnish)	1 in 46	80%	1 in 230	
		Native American	1 in 51	84%	1 in 320	
		South Asian	1 in 68	64%	1 in 190	
		Worldwide	1 in 49	77%	1 in 210	
		Sephardic Jewish – Iragi and Iranian	1 in 36	71%	1 in 120	

* Carrier detection by HEXA enzyme analysis has a detection rate of approximately 98% (Applies to HEXA gene testing only).

+ Carrier frequencies include milder and reduced penetrance forms of the disease. Therefore, carrier frequencies may appear higher than reported in the literature (Applies to BTD, F.g., GJB2, GJB1, GLA, and MEFV gene testing only).

+ Please note that *GJB*2 testing includes testing for the two upstream deletions, del(GJB6-D13S1830) and del(GJB6-D13S1854) (PMID:11807148 and 15994881) (Applies to *GJB*2 gene testing only). AR Autosomal recessive; N/A: Not available; XL: X-linked

Test methods and comments

Genomic DNA isolated from this patient was analyzed by one or more of the following methodologies, as applicable:

Next Generation Sequencing (NGS) (Analytical Detection Rate >95%)

NGS was performed on a panel of genes for the purpose of identifying pathogenic or likelypathogenic variants.

Agilent SureSelectTMQXT technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Samples were pooled and sequenced on the Illumina HiSeq 2500 platform in the Rapid Run mode or theIllumina NovaSeq platform in the Xp workflow, using 100 bp paired-end reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house.

The coding exons and splice junctions of the known protein-coding RefSeq genes were assessed for the average depth of coverage (minimum of 20X) and data quality threshold values. Most exons not meeting a minimum of >20X read depth across the exon are further analyzed by Sanger sequencing. Please note that several genomic regions present difficulties in mapping or obtaining read depth >20X. The exons contained within these regions are noted within Table 1 (as "Exceptions") and will not be reflexed to Sanger sequencing if the mapping quality or coverage is poor. Any variants identified during testing in these regions are confirmed by a second method and reported if determined to be pathogenic or likely pathogenic. However, as there is a possibility of false negative results within these regions, detection rates and residual risks for these genes have been calculated with the presumption that variants in these exons will not be detected, unless included in the MassARRAY® genotyping platform.

This test will detect variants within the exons and the intron-exon boundaries of the target regions. Variants outside these regions may not be detected, including, but not limited to, UTRs, promoters, and deep intronic areas, or regions that fall into the Exceptions mentioned above. This technology may not detect all small insertion/deletions and is not diagnostic for repeat expansions and structural genomic variation. In addition, a mutation(s) in a gene not included on the panel could be present in this patient.

Variant interpretation and classification was performed based on the American College of Medical Genetics Standards and Guidelines for the Interpretation of Sequence Variants(Richards et al, 2015). All potentially pathogenic variants may be confirmed by either aspecific genotyping assay or Sanger sequencing, if indicated. Any benign variants, likelybenign variants or variants of uncertain significance identified during this analysis will not be reported.

Copy Number Variant Analysis (Analytical Detection Rate >95%)

Large duplications and deletions were called from the relative read depths on anexon-by-exon basis using a custom exome hidden Markov model (XHMM) algorithm. Deletions or duplications determined to be pathogenic or likely pathogenic were confirmed by either acustom arrayCGH platform, quantitative PCR, or MLPA (depending on CNV size and gene content). While this algorithm is designed to pick up deletions and duplications of 2 or more exons in length, potentially pathogenicsingle-exon CNVs will be confirmed and reported, if detected.

Exon Array (Confirmation method) (Accuracy >99%)

The customized oligonucleotide microarray (Oxford Gene Technology) is a highly-targetedexon-focused array capable of detecting medically relevant microdeletions and microduplications at a much higher resolution than traditional aCGH methods. Each arraymatrix has approximately 180,000 60-mer oligonucleotide probes that cover the entire genome. This platform is designed based on human genome NCBI Build 37 (hg19) and the CGHprobes are enriched to target the exonic regions of the genes in this panel.

Quantitative PCR (Confirmation method) (Accuracy >99%)

The relative quantification PCR is utilized on a Roche Universal Library Probe (UPL)system, which relates the PCR signal of the target region in one group to another. To test for genomic imbalances, both sample DNA and reference DNA is amplified with primer/probesets that specific to the target region and a control region with known genomic copynumber. Relative genomic copy numbers are calculated based on the standard $\Delta\Delta$ Ct formula.



Long-Range PCR (Analytical Detection Rate >99%)

Long-range PCR was performed to generate locus-specific amplicons for *CYP21A2*, *HBA1* and *HBA2* and *GBA*. The PCR products were then prepared for short-read NGS sequencing and sequenced. Sequenced reads were mapped back to the original genomic locus and run through the bioinformatics pipeline. If indicated, copy number from MLPA was correlated with The sequencing output to analyze the results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where two copies of a gene are located on the same chromosome in tandem, only the second copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in thetandem allele and this patient is therefore less likely to be a carrier. When anindividual carries both a duplication allele and a pathogenic variant, or multiplepathogenic variants, the current analysis may not be able to determine the phase(cisrans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing isrequired to determine the carrier status.

Residual Risk Calculations

Carrier frequencies and detection rates for each ethnicity were calculated through the combination of internal curations of >28,000 variants and genomic frequency data from>138,000 individuals across seven ethnic groups in the gnomAD database. Additional variants in HGMD and novel deleterious variants were also incorporated into the calculation. Residual risk values are calculated using a Bayesian analysis combining the *a priori* risk of being a pathogenic mutation carrier (carrier frequency) and the detection rate. They are provided only as a guide for assessing approximate risk given a negative result, and values will vary based on the exact ethnic background of an individual. This report does not represent medical advice but should be interpreted by a genetic counselor, medical geneticist or physician skilled in genetic result interpretation and the relevant medical literature.

Sanger Sequencing (Confirmation method) (Accuracy >99%)

Sanger sequencing, as indicated, was performed using BigDye Terminator chemistry with theABI 3730 DNA analyzer with target specific amplicons. It also may be used to supplement specific guaranteed target regions that fail NGS sequencing due to poor quality or low depth of coverage (<20 reads) or as a confirmatory method for NGS positive results. Falsenegative results may occur if rare variants interfere with amplification or annealing.

SELECTED REFERENCES

Carrier Screening

Grody W et al. ACMG position statement on prenatal/preconception expanded carrier screening. Genet Med.2013 15:482-3.

Variant Classification:

Richards S et al. Standards and guidelines for the interpretation of sequence variants: ajoint consensus recommendation of the American College of Medical Genetics and Genomicsand the Association for Molecular Pathology. *Genet Med*:2015 May;17(5):405-24

Additional disease-specific references available upon request.