Fairfax Cryobank
The Trusted Choice for Donor Sperm

Donor 4849

Genetic Testing Summary

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

Last Updated: 1/16/20

Donor Reported Ancestry: French Canadian, German, Irish, Canadian, English, Polish 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 99 mutations tested in the CFTR gene. Negative by gene sequencing in the CFTR gene Negative by duplication and deletion testing in the CFTR gene.	1/2401
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 in the SMN1 gene	1/610
Hb Beta Chain Related Hemoglobinopathies including Beta Thalassemia and Sickle Cell Disease)	Negative for 28 mutations tested in the HBB gene	1/290
Tays Sachs Disease by enzyme analysis	Non-carrier by Hexosaminidase A analysis	

*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
[redacted]
Report Date: 05/13/2014

Male
Name: DONOR 4849
DOB: [redacted]
Ethnicity: Northern European
Sample Type: OG-510 Saliva
Date of Collection: 05/08/2014
Date Received: 05/09/2014
Barcode: [redacted]
Indication: Egg or Sperm Donor
Test Type: The Counsyl Test

Female
Not tested

Counsyl Test Results Summary (Egg or Sperm Donor)

The Counsyl test (**Fairfax Cryobank Fundamental Panel**) uses targeted genotyping and copy number analysis as described in the methods section on page 2 to determine carrier status associated with **3 diseases**. Please refer to page 3 for a complete list of diseases and genes included in this panel.

DONOR 4849

DONOR 4849'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

- 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/.

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Methods and Limitations

DONOR 4849: The Counsyl Test - 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

Jelena Brezo

Jelena Brezo, PhD, FACMG

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Counsyl

Male

Name: DONOR 4849
DOB [redacted]

Female

Not tested

ENTERED 6/5/14/14

Diseases Tested

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, R117C, L206W, G330*, T338I, R352Q, S364P, G480C, C524*, S549R, 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, 1949del84, 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, G25, 87C>G, E7K, W16*, c.51delC, c.20delA, E27K, E122Q, E122K. **Detection rate:** Northern European 83%.

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

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Male

Name: DONOR 4849
DOB: [redacted]

Female

Not tested

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 4849 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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RESULTS RECIPIENT
[redacted]
Report Date: 03/28/2015

MALE
SPERM DONOR 4849
DOB: [redacted]
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 03/18/2015
Date Received: 03/20/2015
Date Tested: 03/28/2015
Barcode: [redacted]
Indication: Egg or sperm donor

FEMALE
N/A

Family Prep Screen

NEGATIVE

ABOUT THIS TEST

The Counsyl Family Prep Screen (version 2.0) utilizes sequencing, maximizing coverage across all DNA regions tested, to help you learn about your chance to have a child with a genetic disease.

PANEL DETAILS

Cystic Fibrosis Panel (1 disease tested)

VERSION

SPERM DONOR 4849 (Family Prep Screen 2.0)

RESULTS SUMMARY

NEGATIVE
No known or potential disease-causing mutations were detected.

ENTERED
KO 3.30.15

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/.

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Methods and Limitations

SPERM DONOR 4849 (Family Prep Screen 2.0): sequencing and targeted genotyping.

Targeted genotyping: Targeted DNA mutation analysis is used to simultaneously determine the genotype of 99 variants associated with 1 disease. The test is not validated for detection of homozygous mutations, and although rare, asymptomatic individuals affected by the disease may not be genotyped accurately.

Sequencing: High-throughput sequencing is used to analyze 27 exons in 1 gene, as well as selected intergenic and intronic regions. These regions are sequenced to high coverage and the sequences are compared to standards and references of normal variation. Mutations may not be detected in areas of lower sequence coverage. On average, more than 99% of all bases in the exons listed for each gene are sequenced at the minimum read depth. Variants discovered in other exons of these genes will also be reported if they meet quality control criteria. Triplet repeats and large deletions and duplications may not be detected. Small insertions and deletions may not be as accurately determined as single nucleotide variants. Genes that have closely related pseudogenes are not well analyzed by this method.

High-throughput sequencing detects, on average, 94% of known clinically significant variants. Disease-specific detection rates and residual risks are reported as "greater than (>)" and "less than (<)" the values for targeted genotyping, respectively. More precise values are not currently available, but may become available in the future.

All variants that are a recognized cause of the disease will be reported. In addition, variants that have not previously been established as a recognized cause of disease may be identified. In these cases, only variants classified as "predicted" or "likely" pathogenic are reported. Predicted/likely pathogenic variants are described elsewhere in the report as "predicted/likely to have a negative impact on gene function". In general, predicted pathogenic variants are those which are predicted to be pathogenic based on the nature of the sequence change, while likely pathogenic variants are evaluated by reviewing reports of allele frequencies in cases and controls, functional studies, variant annotation and effect prediction, and segregation studies. Benign variants, variants of uncertain significance, and variants not directly associated with the intended disease phenotype are not reported. Literature citations validating reported variants are available upon request.

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.

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 evaluation. CLIA Number: **#05D1102604.**

LAB DIRECTORS

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Diseases Tested

Autosomal Recessive Disorders

SEQUENCING AND 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. **Exons:** NM_000492:1-27. IVS8-5T allele analysis is only reported in the presence of the R117H mutation. **Detection rate:** Northern European > 91%.

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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	SPERM DONOR 4849 Residual Risk	Reproductive Risk
Cystic Fibrosis	< 1 in 300	< 1 in 33,000

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Ambry Genetics™

FINAL REPORT - 07/31/15

Ordered By Contact ID: 31112 Org ID: 07815
Physician: Stern, Harvey, MD, PhD
Clien[redacted]
Additional Authorized Recipient
[redacted]

Patient Name: **Donor, 4849**
Accession #: [redacted]
AP2 Order ID: P125812
Specimen#: Donor 4849
Specimen: Blood EDTA (Purple top)
Birth Date: [redacted]
Age: [redacted]
Gender: M
MRN#: [redacted]
Family#:
Collected: 07/16/15
Received: 07/17/15
Authorized: 07/20/15
Indication: Carrier screening
Ethnicity: Caucasian

ENTERED 8/11/15

CYSTIC FIBROSIS: Deletion/Duplication Analysis of CFTR

RESULTS

CFTR DEL/DUP Gross Deletion(s)/Duplication(s): None Detected

INTERPRETATION

No gross deletions or duplications were detected in the *CFTR* gene. Gene sequencing analysis of the *CFTR* gene was performed by another laboratory on a previous specimen. Assuming the accuracy of those results, the combined sequencing and gross deletion/duplication results indicate a decreased likelihood that this individual's clinical condition is due to alterations in the *CFTR* gene. Clinical correlation is recommended.

Genetic counseling is a recommended option for all patients undergoing genetic testing.

Alterations of Unlikely Clinical Significance - any alterations classified as "likely benign" or "benign" are not included on results reports as available evidence strongly argues against pathogenicity. While these findings are more likely benign, the available evidence is insufficient to completely rule out a disease-causing or contributing role at this time. Should enough evidence emerge to warrant a significant classification update for any of these findings, a reclassification alert will automatically be sent to the ordering clinician(s).

ELECTRONICALLY SIGNED BY

Brigette Tippin Davis, Ph.D., DABMG, CGMBS, on 07/31/2015 at 01:09:47 PM

Patient Name: **Donor, 4849**
Accession #: [redacted]

CYSTIC FIBROSIS ASSAY INFORMATION (Supplement to Test Results)

Cystic Fibrosis General Information Cystic Fibrosis (CF) is an autosomal recessive genetic disease affecting approximately 30,000 children and adults in the United States. CF has an incidence of approximately 1/3200 live births. The carrier frequency for non-Hispanic Caucasians is about one in 25, and lower in other ethnic groups. Two defective CF alleles cause the body to produce abnormally thick, sticky mucus that clogs the lungs and leads to life-threatening lung infections. People with CF have a variety of other symptoms including high sweat chloride levels, persistent coughing, wheezing or shortness of breath, and excessive appetite but poor weight gain. These thick secretions also obstruct the pancreas and prevent digestive enzymes from reaching the intestines to help break down and absorb food, contributing to pancreatitis. CF mutations may also lead to congenital bilateral absence of the vas deferens (CBAVD) and infertility. The severity of symptoms varies greatly between individuals diagnosed with CF due, in part, to the more than 1,500 different CF mutations described to date.

Methodology Genomic deoxyribonucleic acid (gDNA) is isolated from the patient's specimen using a standardized kit and quantified. When only the deltaF508 mutation is to be analyzed, traditional Sanger dideoxy terminator DNA sequencing technique is utilized to identify the presence of dF508 allele. When *CFTR* full gene sequence analysis is requested, a TruSeq Custom Amplicon (TSCA) sequencing protocol is utilized, and the sequencing is performed on a next-generation sequencing instrument from Illumina. When full gene sequence analysis plus reflexing to gross deletion/duplication (Ambry Test: CF AMPLIFIED™) is requested, gene deletion/duplication analysis is performed using Multiplex Ligation-dependent Probe Amplification (MLPA, MRC Holland). When specific alteration(s) in the *CFTR* gene is (are) requested, traditional Sanger dideoxy terminator DNA sequencing technique and/or MLPA are used.

Note: For blood spot samples, if *CFTR* full gene sequence analysis is requested, double stranded sequencing in sense and anti-sense directions is used to detect sequence variations.

Analytical Range 508 FIRST detects only the deltaF508 mutation. For full gene sequence analysis, the analytical range includes: exons 1 to 27 coding domains, as well as at least 20 bases into the 5'- and 3'-ends of all introns, 5'- and 3'-untranslated regions (5'UTR and 3'UTR). This assay is also capable in assessing the poly-T tract within intron 8 and in identifying the c.1679+1634A>G (c.1811+1634A>G or c.1811+1.6kb) mutation in intron 12 and the c.3717+12191C>T (c.3849+10kbC>T) mutation in intron 22. Gross deletion/duplication analysis determines gene copy number for any of the 27 exons. All 23 ACOG and ACMG recommended mutations are analyzed using the Ambry Test: CF and Ambry Test: CF AMPLIFIED. Novel variants are always reported. Polymorphisms and the poly T status will be reported upon request. The following sites are used to search for previously described CF mutations and polymorphisms: Toronto Sick Children's CF database, HGMD, and online search engines (i.e., PubMed). Sequence analysis is based on the following NCBI reference sequence: NM_000492.3.

Result Reports In result reports, alterations in the following classifications are always reported, and are based on the following definitions and clinical recommendations:

- **Pathogenic Mutation**: alterations with sufficient evidence to classify as pathogenic (capable of causing disease). Targeted testing of at-risk relatives and appropriate changes in medical management for pathogenic mutation carriers recommended.
- **Variant, Likely Pathogenic (VLP)**: alterations with strong evidence in favor of pathogenicity. Targeted testing of at-risk relatives and appropriate changes in medical management for VLP carriers typically recommended.
- **Variant, Unknown Significance (VUS)**: alterations with limited and/or conflicting evidence regarding pathogenicity. Familial testing via the Family Studies Program recommended. Medical management to be based personal/family clinical histories, not VUS carrier status.

Alterations of unlikely clinical significance (those with strong/very strong evidence to argue against pathogenicity) are not routinely included on results reports. These include findings classified as "likely benign" and "benign" alterations as well as ACMG interpretive category 6 variants (see ACMG Recommendations. Revision 2007. *Genet Med.* 2008;10:294 for more information).

Carrier Risk and Detection Rates

						Individuals with CF and	
Ethnic Group	Estimated Detection Rate***		Before Test	Carrier Risk** After Negative Test		No CF Mutations	One CF Mutation
	CF gene sequence	CF gene sequence and del/dup		CF gene sequence	CF gene sequence and del/dup	CF gene sequence and del/dup	
Ashkenazi Jewish	97-98%	~99%	1/24	~1 in 959	~1 in 2301	~0.01%	~2%
Non-Hispanic Caucasian	97-98%	~99%	1/25	~1 in 1001	~1 in 2401	~0.01%	~2%
African American	97-98%	~99%	1/61	~1 in 2501	~1 in 6001	~0.01%	~2%
Hispanic American *	97-98%	~99%	1/58	~1 in 2378	~1 in 5701	~0.01%	~2%
Asian American	97-98%	~99%	1/94	~1 in 3876	~1 in 9301	~0.01%	~2%

*This is a pooled set of data and requires additional information to predict risk accurately for specific Hispanic populations. **Based on a negative family history. *** Based on Ambry's empirical data.

Assay Information Continued on Next Page

Patient Name: **Donor, 4849**
Accession #: [redacted]

ASSAY INFORMATION *(Supplement to Test Results - Continued)*

Resources: The following references are used in variant analysis and classification when applicable for observed genetic alterations.
1.The 1000 Genomes Project Consortium.An integrated map of genetic variation from 1092 human genomes.*Nature*.2012;491:56-65.
2. Berkeley Drosophila Genome Project [Internet]. Reese MG etal. *J Comp Biol* . 1997;4:311-23. http://www.fruitfly.org/seq_tools/splice.html.
3. Database of Single Nucleotide Polymorphisms (dbSNP) [Internet]. Bethesda (MD): National Center for Biotechnology Information, National Library of Medicine (dbSNP Build ID:135) Available from:www.ncbi.nlm.nih.gov/SNP.Accessed Jan 2012).
4. ESEfinder [Internet]. Smith PJ, *et al.* (2006) *Hum Mol Genet* 15(16):2490-2508 and Cartegni L, etal *Nucleic Acid Research* 2003;31(13):3568-3571. http://rulai.cshl.edu/cgi-bin/tools/ESE3/esefinder.cgi?process=home.
5. Exome Variant Server, NHLBI Exome Sequencing Project (ESP) [Internet], Seattle WA. Available from: evs.gs.washington.edu/EVS.
6. Grantham R. Amino acid difference formula to help explain protein evolution. *Science* 1974;185(4151):862-864.
7. HGMD® [Internet]: Stenson PD etal. *Genome Med.* 2009;1(1):13 www.hgmd.cf.ac.uk.
8. Online Mendelian Inheritance In Man, OMIM®. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD), Copyright® 1966-2012. World Wide Web URL: http://omim.org
9. PolyPhen [Internet]: Adzhubei IA, etal. *Nat Methods* . 2010;7(4):248-249. genetics.bwh.harvard.edu/pph2.
10 Richards et al. ACMG recommendations for standards for interpretation and reporting of sequence variations: Revisions 2007. *Genet Med* 2008;10:294.
11.SIFT [Internet]: Ng PC & Henikoff S. *Hum Genet.* 2006;7:61-80. http://sift.jcvi.org

Disclaimer This test was developed and its performance characteristic were determined by Ambry Genetics Corporation. It has not been cleared or approved by the US Food and Drug Administration. The FDA does not require this test to go through premarket FDA review. It should not be regarded as investigational or for research. This test should be interpreted in context with other clinical findings. This report does not represent medical advice. Any questions, suggestions, or concerns regarding interpretation of results should be relegated to a genetic counselor, medical geneticist, or physician skilled in evaluating the relevant medical literature. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. 508 FIRST analyzes only the deltaF508 mutation. The Ambry Test: CF analyzes the following types of mutations: nucleotide substitutions, small deletions, small insertions, and small indels, and the Ambry Test: CF AMPLIFIED analyzes, in addition, the gene's gross deletion and duplication mutations. Neither method is intended to analyze the following types of mutations: gross insertions, gross rearrangements, deep intronic variations, and other unknown abnormalities. The pattern of mutation types varies with the gene tested and the Ambry Test detects a high but variable percentage of known and unknown mutants of the classes stated. A negative result from the analysis cannot rule out the possibility that the tested individual carries a rare unexamined mutation or mutation in the undetectable group. The Ambry Test: CF and CF AMPLIFIED are designed and validated to be capable of detecting about ~97-98% and ~99% of CF mutations, respectively (considering less than 1% being the other types of mutations). CF is a complex clinical disorder, which in the majority of cases is due to alterations in the CF gene generally detected by the Ambry Test: CF except as noted above. Mutations in other genes or the regions not tested by the Ambry Test: CF can also give rise to clinical conditions similar or identical to CF. Although molecular tests are highly accurate, rare diagnostic errors may occur. Possible diagnostic errors include sample mix-up, erroneous paternity identification, technical errors, clerical errors, and genotyping errors. Genotyping errors can result from trace contamination of PCR reactions, from maternal cell contamination in fetal samples, from rare genetic variants that interfere with analysis, low-level mosaicism or from other sources. This report does not represent medical advice. Any questions, suggestions, or concerns regarding interpretation of results should be relegated to a genetic counselor, medical geneticist, or physician skilled in evaluating the relevant medical literature. References are available upon request.

Maternal Cell Contamination (MCC) Assay Information: applies only to prenatal samples tested for MCC. Six different STRs at FGA, TPOX, D8S1179, VWA, D18S51, and CSF1PO loci and up to 10 additional STR loci can be used for MCC study of maternal and fetal DNA using polymerase chain reaction and fragment analysis by capillary electrophoresis. Unresolved cases needing even further study may be forwarded to an outside reference laboratory. Validation studies in our laboratory have shown that MCC at levels of approximately 5% and higher can be detected by our MCC assay. Separate studies with our diagnostic sequencing tests have shown that the test and interpretation are not affected until MCC reaches greater than 10%. Therefore, a negative MCC result is expected to rule out all cases of MCC that may have interfered with our molecular diagnostic result.