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Genetic Testing Summary

Enclosed are the genetic testing results for

CB 481

No amount of genetic testing can guarantee that a child will not be affected with a genetic condition. Genetic testing can inform you of the likelihood of passing on the genetic conditions that are tested for, but it cannot eliminate the risk of passing on any genetic condition.

The genetic conditions Cryobio tests for are inherited in an autosomal recessive manner. This means that the child would have to inherit a genetic mutation from both the sperm source and the egg source to be affected with the condition. When both the sperm source and the egg source have undergone genetic carrier screening and the test results are negative, the risk of a child being affected with the conditions tested for is significantly reduced, but it cannot be completely eliminated.

All recipients should discuss both or their own risk for passing on genetic conditions and whether would benefit from genetic counseling and testing with their health care provider. Before using a donor that is a carrier for a specific recessive genetic condition or conditions, we strongly recommend that the recipient (or egg source, if different) consider genetic counseling and testing to determine if they are a carrier for the same genetic condition or conditions as the donor.

Screening and testing have changed dramatically over the years, and so the screening and testing done on each donor may very depending on the testing that was in place when he was actively in Cryobio's donor program. Earlier donors may not have had as extensive testing as later donors. Screening and testing may change again in the future, so please review the results each time before ordering as both the testing done and the results may change.

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CARRIER SCREENING REPORT

Patient	Sample	Referring Doctor
Patient Name: CB481 Donor **Date of Birth:** [redacted] **Reference #:** [redacted] **Indication:** Carrier Testing **Test Type:** Expanded Carrier Screen (283)	**Specimen Type:** Blood **Lab #:** [redacted] **Date Collected:** [redacted] **Date Received:** [redacted] **Final Report:** [redacted]	**David Prescott, M.D.** **Cryobiology, Inc.** **4830-D Knightsbridge Blvd.** **Columbus, OH 43214** Fax: **614-451-5284**

RESULT SUMMARY

THIS PATIENT WAS TESTED FOR 283 DISEASES.
Please see Table 1 for list of diseases tested.

POSITIVE for holocarboxylase synthetase deficiency
A heterozygous (one copy) likely pathogenic variant, c.1533dupT, p.V512CfsX65, was detected in the *HLCS* gene

NEGATIVE for the remaining diseases

Recommendations

Testing the partner for the above positive disorder(s) and genetic counseling are recommended.

Please note that for female carriers of X-linked diseases, follow-up testing of a male partner is not indicated. In addition, CGG repeat analysis of *FMR1* for fragile X syndrome is not performed on males as repeat expansion of premutation alleles is not expected in the male germline.

Individuals of Asian, African, Hispanic and Mediterranean ancestry should also be screened for hemoglobinopathies by CBC and hemoglobin electrophoresis.

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.

Interpretation for holocarboxylase synthetase deficiency

A heterozygous (one copy) likely pathogenic frameshift variant, c.1533dupT, p.V512CfsX65, was detected in the *HLCS* gene (NM_000411.6). When this variant is present in trans with a pathogenic variant, it is considered to be causative for holocarboxylase synthetase deficiency. Therefore, this individual is expected to be at least a carrier for holocarboxylase synthetase deficiency. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is holocarboxylase synthetase deficiency?

Holocarboxylase synthetase deficiency is an autosomal recessive disorder caused by pathogenic variants in the gene *HLCS*, and although it is considered to be a pan-ethnic disorder, it is most commonly seen among those of Faroese and Asian descent. Affected individuals will usually present with symptoms before three months of age, which include feeding difficulties, breathing problems, skin rash, hair loss, and lack of energy. Untreated individuals can progress and experience developmental delay, seizures, coma, and eventually death during childhood. Treatment with biotin supplements is generally effective and potentially capable of reversing certain disease side effects, making the prognosis of the disease favorable. Certain aspects of disease severity and response to treatment may be predicted in some cases based on the inherited variants.

This patient was tested for a panel of diseases using a combination of sequencing, targeted genotyping and 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 see Table 1 for a list of genes and diseases tested, and http://go.sema4.com/residualrisk for specific detection rates and residual risk by ethnicity. With individuals of mixed ethnicity, it is recommended to use the highest residual risk estimate. Only variants determined to be pathogenic or likely pathogenic are reported in this carrier screening test.

TEST SPECIFIC RESULTS

Alpha-thalassemia

NEGATIVE for alpha-thalassemia
HBA1 copy number: 2
HBA2 copy number: 2
No pathogenic copy number variants detected
HBA1 and *HBA2* sequence analysis: No pathogenic or likely pathogenic variants identified
Reduced risk of being an alpha-thalassemia carrier (aa/aa)

Genes analyzed: *HBA1* (NM_000558.4) and *HBA2* (NM_000517.4)
Inheritance: Autosomal Recessive

Recommendations
Individuals of Asian, African, Hispanic and Mediterranean ancestry should also be screened for hemoglobinopathies by CBC and hemoglobin electrophoresis.

Patient:	CB481 Donor	DOB:	[redacted]	Lab #:	[redacted]

Interpretation
No pathogenic or likely pathogenic copy number variants or sequence variants were detected in this patient, suggesting that four copies of the alpha-globin gene are present (aa/aa). Typically, individuals have four functional alpha-globin genes: 2 copies of *HBA1* and 2 copies of *HBA2*, whose expression is regulated by a cis-acting regulatory element HS-40. Alpha-thalassemia carriers have three (silent carrier) or two (carrier of the alpha-thalassemia trait) functional alpha-globin genes with or without a mild phenotype. Individuals with only one functional alpha-globin gene have HbH disease with microcytic, hypochromic hemolytic anemia and hepatosplenomegaly. Loss of all four alpha-globin genes results in Hb Barts syndrome with the accumulation of Hb Barts in red blood cells and hydrops fetalis, which is fatal in utero or shortly after birth.

This individual was negative for all *HBA* deletions, duplications and variants that were tested. These negative results reduce but do not eliminate the possibility that this individual is a carrier. See *Table of Residual Risks Based on Ethnicity*. With individuals of mixed ethnicity, it is recommended to use the highest residual risk estimate.

Table of Residual Risks Based on Ethnicity

Ethnicity	Carrier Frequency	Detection Rate	Residual Risk
Caucasian	1 in 500	95%	1 in 10,000
African American	1 in 30	95%	1 in 580
Asian	1 in 20	95%	1 in 380
Worldwide	1 in 25	95%	1 in 480

Congenital Adrenal Hyperplasia (21-Hydroxylase Deficiency)

NEGATIVE for congenital adrenal hyperplasia (due to 21-hydroxylase deficiency)
CYP21A2 copy number: 2
No pathogenic copy number variants detected
No pathogenic sequence variants detected in *CYP21A2*
Reduced risk of being a congenital adrenal hyperplasia carrier

Genes analyzed: *CYP21A2* (NM_000500.6)
Inheritance: Autosomal Recessive

Recommendations
Consideration of residual risk by ethnicity (see below) after a negative carrier screen is recommended, especially in the case of a positive family history of congenital adrenal hyperplasia.

Interpretation
This individual was negative for all pathogenic *CYP21A2* copy number variants that were tested, and no pathogenic or likely pathogenic variants were identified by sequence analysis. These negative results reduce but do not eliminate the possibility that this individual is a carrier. See *Table of Residual Risks Based on Ethnicity*. With individuals of mixed ethnicity, it is recommended to use the highest residual risk estimate.

Table of Residual Risk Based On Ethnicity - Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency

Ethnicity	Carrier Frequency	Detection Rate	Residual Risk
Ashkenazi Jewish	1 in 40	>95%	1 in 780
Caucasian	1 in 67	>95%	1 in 1300
Worldwide	1 in 60	>95%	1 in 1200

Table of Residual Risk Based On Ethnicity - Non-Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency

Ethnicity	Carrier Frequency	Detection Rate	Residual Risk
Ashkenazi Jewish	1 in 7	>95%	1 in 120
Caucasian	1 in 11	>95%	1 in 200
Worldwide	1 in 16	>95%	1 in 300

<u>Fragile X syndrome</u>

Fragile X CGG triplet repeat expansion testing was not performed at this time, as the patient has either been previously tested or is a male. Sequencing of the *FMR1* gene by next generation sequencing did not identify any clinically significant variants.

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Spinal Muscular Atrophy

NEGATIVE for spinal muscular atrophy
SMN1 Copy Number: 2
SMN2 Copy Number: 1
c.*3+80T>G: Negative

Negative copy number result
Decreased risk of being an *SMN1* silent (2+0) carrier (see *SMA Table*)

Genes analyzed: *SMN1* (NM_000344.3) and *SMN2* (NM_017411.3)
Inheritance: Autosomal Recessive

Recommendations
Consideration of residual risk by ethnicity after a negative carrier screen is recommended, especially in the case of a positive family history for spinal muscular atrophy.

Interpretation
This patient is negative for loss of *SMN1* copy number. Complete loss of *SMN1* is causative in spinal muscular atrophy (SMA). Two copies of *SMN1* were detected in this individual, which significantly reduces the risk of being an SMA carrier. Parallel testing to assess the presence of an *SMN1* duplication allele was also performed to detect a single nucleotide polymorphism (SNP), c.*3+80T>G, in intron 7 of the *SMN1* gene. This individual was found to be negative for this change and is therefore, at a decreased risk of being a silent (2+0) carrier, see *SMA Table* for residual risk estimates based on ethnicity.

SMA Table: Carrier detection and residual risk estimates before and after testing for c.*3+80T>G

Ethnicity	Carrier Frequency	Detection rate	Residual risk after negative result*	Detection rate with *SMN1* c.*3+80T>G	Residual risk c.*3+80T>G negative	Residual risk c.*3+80T>G positive
African American	1 in 85	71%	1 in 160	91%	1 in 455	1 in 49
Ashkenazi Jewish	1 in 76	90%	1 in 672	93%	1 in 978	1 in 10
East Asian	1 in 53	94%	1 in 864	95%	1 in 901	1 in 12
Caucasian	1 in 48	95%	1 in 803	95%	1 in 894	1 in 23
Latino	1 in 63	91%	1 in 609	94%	1 in 930	1 in 47
South Asian	1 in 103	87%	1 in 637	87%	1 in 637	1 in 608
Sephardic Jewish	1 in 34	96%	1 in 696	97%	1 in 884	1 in 12

*Residual risk with two copies *SMN1* detected using dosage sensitive methods. The presence of three or more copies of *SMN1* reduces the risk of being an *SMN1* carrier between 5 - 10 fold, depending on ethnicity.
FOR INDIVIDUALS WITH MIXED ETHNICITY, USE HIGHEST RESIDUAL RISK ESTIMATE
^ Parental follow-up will be requested for confirmation

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Tay-Sachs Disease Enzyme Analysis

Results: **Non-carrier**

Specimen	Hexosaminidase Activity	Hex A%	Non-Carrier Range	Comment
Tay-Sachs WBC	1707 nmol/hr/mg	70.4	55.0 - 72.0	Non-Carrier
Tay-Sachs Plasma	546 nmol/hr/ml	66.5	58.0 - 72.0	Non-Carrier

Expected Carrier Ranges:
Hex A% <54% (Serum/Plasma), Hex A%<50% (WBC)

Interpretation:

The test was performed in the patient's plasma and white blood cells (WBC). The Hex A% activities are both within the non-carrier range. These findings are consistent with the patient being a **non-carrier** for Tay-Sachs disease.

This case has been reviewed and electronically signed by Anastasia Larmore, PhD, Assistant Director

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

Patient:	CB481 Donor	DOB:	[redacted]	Lab #:	[redacted]

Test Methods and Comments

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

Fragile X CGG Repeat Analysis (Analytical Detection Rate >99%)
PCR amplification using Asuragen, Inc. AmplideX® *FMR1* PCR reagents followed by capillary electrophoresis for allele sizing was performed. Samples positive for *FMR1* CGG repeats in the premutation and full mutation size range were further analyzed by Southern blot analysis to assess the size and methylation status of the *FMR1* CGG repeat.

Genotyping (Analytical Detection Rate >99%)
Multiplex PCR amplification and allele specific primer extension analyses using the MassARRAY® System were used to identify variants that are complex in nature or are present in low copy repeats. Rare sequence variants may interfere with assay performance.

Multiplex Ligation-Dependent Probe Amplification (MLPA) (Analytical Detection Rate >99%)
MLPA® probe sets and reagents from MRC-Holland were used for copy number analysis of specific targets versus known control samples. False positive or negative results may occur due to rare sequence variants in target regions detected by MLPA probes. Analytical sensitivity and specificity of the MLPA method are both 99%.

For alpha thalassemia, the copy numbers of the *HBA1* and *HBA2* genes were analyzed. Alpha-globin gene deletions, triplications, and the Constant Spring (CS) mutation are assessed. This test is expected to detect approximately 90% of all alpha-thalassemia mutations, varying by ethnicity. Carriers of alpha-thalassemia with three or more *HBA* copies on one chromosome, and one or no copies on the other chromosome, may not be detected. With the exception of triplications, other benign alpha-globin gene polymorphisms will not be reported. Analyses of *HBA1* and *HBA2* are performed in association with long-range PCR of the coding regions followed by short-read sequencing.

For Duchenne muscular dystrophy, the copy numbers of all *DMD* exons were analyzed. Potentially pathogenic single exon deletions and duplications are confirmed by a second method. Analysis of *DMD* is performed in association with sequencing of the coding regions.

For congenital adrenal hyperplasia, the copy number of the *CYP21A2* gene was analyzed. This analysis can detect large deletions due to unequal meiotic crossing-over between *CYP21A2* and the pseudogene *CYP21A1P*. These 30-kb deletions make up approximately 20% of *CYP21A2* pathogenic alleles. This test may also identify certain point mutations in *CYP21A2* caused by gene conversion events between *CYP21A2* and *CYP21A1P*. Some carriers may not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *CYP21A2* gene on one chromosome and loss of *CYP21A2* (deletion) on the other chromosome. Analysis of *CYP21A2* is performed in association with long-range PCR of the coding regions followed by short-read sequencing.

For spinal muscular atrophy (SMA), the copy numbers of the *SMN1* and *SMN2* genes were analyzed. The individual dosage of exons 7 and 8 as well as the combined dosage of exons 1, 4, 6 and 8 of *SMN1* and *SMN2* were assessed. Copy number gains and losses can be detected with this assay. Depending on ethnicity, 6 - 29 % of carriers will not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *SMN1* gene on one chromosome and loss of *SMN1* (deletion) on the other chromosome (silent 2+0 carrier) or individuals that carry an intragenic mutation in *SMN1*. Please also note that 2% of individuals with SMA have an *SMN1* mutation that occurred *de novo*. Typically in these cases, only one parent is an SMA carrier.

The presence of the c.*3+80T>G (chr5:70,247,901T>G) variant allele in an individual with Ashkenazi Jewish or Asian ancestry is typically indicative of a duplication of *SMN1*. When present in an Ashkenazi Jewish or Asian individual with two copies of *SMN1*, c.*3+80T>G is likely indicative of a silent (2+0) carrier. In individuals with two copies of *SMN1* with African American, Hispanic or Caucasian ancestry, the presence or absence of c.*3+80T>G significantly increases or decreases, respectively, the likelihood of being a silent 2+0 silent carrier.

Pathogenic or likely pathogenic sequence variants in exon 7 may be detected during testing for the c.*3+80T>G variant allele; these will be reported if confirmed to be located in SMN1 using locus-specific Sanger primers

MLPA for Gaucher disease (*GBA*), cystic fibrosis (*CFTR*), and non-syndromic hearing loss (*GJB2/GJB6*) will only be performed if indicated for confirmation of detected CNVs. If *GBA* analysis was performed, the copy numbers of exons 1, 3, 4, and 6 - 10 of the *GBA* gene (of 11 exons total) were analyzed. If *CFTR* analysis was performed, the copy numbers of all 27 *CFTR* exons were analyzed. If *GJB2/GJB6* analysis was performed, the copy number of the two *GJB2* exons were analyzed, as well as the presence or absence of the two upstream deletions of the *GJB2* regulatory region, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854).

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Next Generation Sequencing (NGS) (Analytical Detection Rate >95%)
NGS was performed on a panel of genes for the purpose of identifying pathogenic or likely pathogenic variants.

Agilent SureSelect™QXT 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 the Illumina 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 a specific genotyping assay or Sanger sequencing, if indicated. Any benign variants, likely benign 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 an exon-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 a custom 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 pathogenic single-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-targeted exon-focused array capable of detecting medically relevant microdeletions and microduplications at a much higher resolution than traditional aCGH methods. Each array matrix 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 CGH probes 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/probe sets that specific to the target region and a control region with known genomic copy number. 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 the tandem allele and this patient is therefore less likely to be a carrier. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to

determine the phase (cis/trans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing is required 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 the ABI 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. False negative results may occur if rare variants interfere with amplification or annealing.

Tay-Sachs Disease (TSD) Enzyme Analysis (Analytical Detection Rate ≥98%)

Hexosaminidase activity and Hex A% activity were measured by a standard heat-inactivation, fluorometric method using artificial 4-MU-β-N-acetyl glucosaminide (4-MUG) substrate. This assay is highly sensitive and accurate in detecting Tay-Sachs carriers and individuals affected with TSD. Normal ranges of Hex A% activity are 55.0-72.0 for white blood cells and 58.0-72.0 for plasma. It is estimated that less than 0.5% of Tay-Sachs carriers have non-carrier levels of percent Hex A activity, and therefore may not be identified by this assay. In addition, this assay may detect individuals that are carriers of or are affected with Sandhoff disease. False positive results may occur if benign variants, such as pseudodeficiency alleles, interfere with the enzymatic assay. False negative results may occur if both *HEXA* and *HEXB* pathogenic or pseudodeficiency variants are present in the same individual.

Please note these tests were developed and their performance characteristics were determined by Mount Sinai Genomics, Inc. They have not been cleared or approved by the FDA. These analyses generally provide highly accurate information regarding the patient's carrier or affected status. Despite this high level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, or other rare genetic variants that interfere with analysis. Families should understand that rare diagnostic errors may occur for these reasons.

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Additional disease-specific references available upon request.

Patient:	CB481 Donor	DOB:	[redacted]	Lab #:	[redacted]

Table 1. List of genes and diseases tested.
Please see http://go.sema4.com/residualrisk for specific detection rates and residual risk by ethnicity.

Gene	Disease
ACADM	Medium Chain Acyl-CoA Dehydrogenase Deficiency
ABCB11	Progressive Familial Intrahepatic Cholestasis, Type 2
ABCC8	Familial Hyperinsulinism (ABCC8-Related)
ABCD1	Adrenoleukodystrophy, X-Linked
ACAD9	Mitochondrial Complex I Deficiency (ACAD9-Related)
ACADVL	Very Long Chain Acyl-CoA Dehydrogenase Deficiency
ACAT1	Beta-Ketothiolase Deficiency
ACOX1	Acyl-CoA Oxidase I Deficiency
ACSF3	Combined Malonic and Methylmalonic Aciduria
ADA	Adenosine Deaminase Deficiency
ADAMTS2	Ehlers-Danlos Syndrome, Type VIIC
AGA	Aspartylglycosaminuria
AGL	Glycogen Storage Disease, Type III
AGPS	Rhizomelic Chondrodysplasia Punctata, Type 3
AGXT	Primary Hyperoxaluria, Type 1
AIRE	Polyglandular Autoimmune Syndrome, Type 1
ALDH3A2	Sjogren-Larsson Syndrome
ALDOB	Hereditary Fructose Intolerance
ALG6	Congenital Disorder of Glycosylation, Type Ic
ALMS1	Alstrom Syndrome
ALPL	Hypophosphatasia
AMT	Glycine Encephalopathy (AMT-Related)
AQP2	Nephrogenic Diabetes Insipidus, Type II
ARSA	Metachromatic Leukodystrophy
ARSB	Mucopolysaccharidosis type VI
ASL	Argininosuccinic Aciduria
ASNS	Asparagine Synthetase Deficiency
ASPA	Canavan Disease
ASS1	Citrullinemia, Type 1
ATM	Ataxia-Telangiectasia
ATP6V1B1	Renal Tubular Acidosis and Deafness
ATP7A	Menkes Disease
ATP7B	Wilson Disease
ATRX	Alpha-Thalassemia Mental Retardation Syndrome
BBS1	Bardet-Biedl Syndrome (BBS1-Related)
BBS10	Bardet-Biedl Syndrome (BBS10-Related)
BBS12	Bardet-Biedl Syndrome (BBS12-Related)
BBS2	Bardet-Biedl Syndrome (BBS2-Related)
BCKDHA	Maple Syrup Urine Disease, Type 1a
BCKDHB	Maple Syrup Urine Disease, Type 1b
BCS1L	GRACILE Syndrome and Other BCS1L-Related Disorders
BLM	Bloom Syndrome
BSND	Bartter Syndrome, Type 4A
BTD	Biotinidase Deficiency
CAPN3	Limb-Girdle Muscular Dystrophy, Type 2A
CBS	Homocystinuria (CBS-Related)
CDH23	Usher Syndrome, Type ID
CEP290	Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies
CERKL	Re initis Pigmentosa 26

Gene	Disease
CFTR	Cystic Fibrosis
CHM	Choroideremia
CHRNE	Congenital Myasthenic Syndrome (CHRNE-Related)
CIITA	Bare Lymphocyte Syndrome, Type II
CLN3	Neuronal Ceroid-Lipofuscinosis (CLN3-Related)
CLN5	Neuronal Ceroid-Lipofuscinosis (CLN5-Related)
CLN6	Neuronal Ceroid-Lipofuscinosis (CLN6-Related)
CLN8	Neuronal Ceroid-Lipofuscinosis (CLN8-Related)
CLRN1	Usher Syndrome, Type III
CNGB3	Achromatopsia
COL27A1	Steel Syndrome
COL4A3	Alport Syndrome (COL4A3-Related)
COL4A4	Alport Syndrome (COL4A4-Related)
COL4A5	Alport Syndrome (COL4A5-Related)
COL7A1	Dystrophic Epidermolysis Bullosa
CPS1	Carbamoylphosphate Synthetase I Deficiency
CPT1A	Carnitine Palmitoyltransferase IA Deficiency
CPT2	Carnitine Palmitoyltransferase II Deficiency
CRB1	Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy
CTNS	Cystinosis
CTSK	Pycnodysostosis
CYBA	Chronic Granulomatous Disease (CYBA-related)
CYBB	Chronic Granulomatous Disease (CYBB-related)
CYP11B2	Corticosterone Methyloxidase Deficiency
CYP17A1	Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency
CYP21A2	Classic Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency
CYP19A1	Aromatase Deficiency
CYP27A1	Cerebrotendinous Xanthomatosis
DCLRE1C	Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type
DHCR7	Smith-Lemli-Opitz Syndrome
DHDDS	Retinitis Pigmentosa 59
DLD	Lipoamide Dehydrogenase Deficiency
DMD	Duchenne Muscular Dystrophy / Becker Muscular Dystrophy
DNAH5	Primary Ciliary Dyskinesia (DNAH5-Related)
DNAI1	Primary Ciliary Dyskinesia (DNAI1-Related)
DNAI2	Primary Ciliary Dyskinesia (DNAI2-related)
DYSF	Limb-Girdle Muscular Dystrophy, Type 2B
EDA	Hypohidrotic Ectodermal Dysplasia 1
EIF2B5	Leukoencephalopathy with Vanishing White Matter
EMD	Emery-Dreifuss Myopathy 1
ESCO2	Roberts Syndrome
ETFA	Glutaric Acidemia, Type IIa
ETFDH	Glutaric Acidemia, Type IIc
ETHE1	Ethylmalonic Encephalopathy
EVC	Ellis-van Creveld Syndrome (EVC-Related)
EYS	Retinitis Pigmentosa 25
F11	Factor XI Deficiency
F9	Factor IX Deficiency
FAH	Tyrosinemia, Type I

CARRIER SCREENING REPORT

Patient:	CB481 Donor	DOB:	[redacted]	Lab #:	[redacted]

Gene	Disease
FAM161A	Retinitis Pigmentosa 28
FANCA	Fanconi Anemia, Group A
FANCC	Fanconi Anemia, Group C
FANCG	Fanconi Anemia, Group G
FH	Fumarase Deficiency
FKRP	Limb-Girdle Muscular Dystrophy, Type 2I
FKTN	Walker-Warburg Syndrome and Other FKTN-Related Dystrophies
FMR1	Fragile X Syndrome
G6PC	Glycogen Storage Disease, Type Ia
GAA	Glycogen Storage Disease, Type II
GALC	Krabbe Disease
GALK1	Galactokinase Deficiency
GALT	Galactosemia
GAMT	Cerebral Creatine Deficiency Syndrome 2
GBA	Gaucher Disease
GBE1	Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease
GCDH	Glutaric Acidemia, Type I
GFM1	Combined Oxidative Phosphorylation Deficiency 1
GJB1	Charcot-Marie-Tooth Disease, X-Linked
GJB2†	Non-Syndromic Hearing Loss (GJB2-Related)
GLA	Fabry Disease
GLB1	Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis
GLDC	Glycine Encephalopa hy (GLDC-Related)
GLE1	Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease
GNE	Inclusion Body Myopathy 2
GNPTAB	Mucolipidosis II / IIIA
GNPTG	Mucolipidosis III Gamma
GNS	Mucopolysaccharidosis Type IIID
GP1BA	Bernard-Soulier Syndrome, Type A1
GP9	Bernard-Soulier Syndrome, Type C
GPR56	Bilateral Frontoparietal Polymicrogyria
GRHPR	Primary Hyperoxaluria, Type 2
HADHA	Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency
HAX1	Congenital Neutropenia (HAX1-Related)
HBA1/HBA2	Alpha-Thalassemia
HBB	Beta-Globin-Related Hemoglobinopathies
HEXA	Tay-Sachs Disease
HEXB	Sandhoff Disease
HFE2	Hemochromatosis, Type 2A
HGSNAT	Mucopolysaccharidosis Type IIIC
HLCS	Holocarboxylase Synthetase Deficiency
HMGCL	HMG-CoA Lyase Deficiency
HOGA1	Primary Hyperoxaluria, Type 3
HPS1	Hermansky-Pudlak Syndrome, Type 1
HPS3	Hermansky-Pudlak Syndrome, Type 3
HSD17B4	D-Bifunctional Protein Deficiency
HSD3B2	3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency
HYAL1	Mucopolysaccharidosis type IX
HYLS1	Hydrolethalus Syndrome
IDS	Mucopolysaccharidosis Type II

Gene	Disease
IDUA	Mucopolysaccharidosis Type I
IKBKAP	Familial Dysautonomia
IL2RG	X-Linked Severe Combined Immunodeficiency
IVD	Isovaleric Acidemia
KCNJ11	Familial Hyperinsulinism (KCNJ11-Related)
LAMA3	Junc ional Epidermolysis Bullosa (LAMA3-Related)
LAMB3	Junc ional Epidermolysis Bullosa (LAMB3-Related)
LAMC2	Junc ional Epidermolysis Bullosa (LAMC2-Related)
LCA5	Leber Congenital Amaurosis 5
LDLR	Familial Hypercholesterolemia
LDLRAP1	Familial Autosomal Recessive Hypercholesterolemia
LHX3	Combined Pituitary Hormone Deficiency 3
LIFR	Stuve-Wiedemann Syndrome
LIPA	Wolman Disease / Cholesteryl Ester Storage Disease
LOXHD1	Deafness, Autosomal Recessive 77
LPL	Lipoprotein Lipase Deficiency
LRPPRC	Leigh Syndrome, French-Canadian Type
MAN2B1	Alpha-Mannosidosis
MCCC1	3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related)
MCCC2	3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related)
MCOLN1	Mucolipidosis IV
MED17	Infantile Cerebral and Cerebellar Atrophy
MEFV	Familial Mediterranean Fever
MESP2	Spondylothoracic Dysostosis
MFSD8	Neuronal Ceroid-Lipofuscinosis (MFSD8-Related)
MKS1	Meckel syndrome 1 / Bardet-Biedl Syndrome 13
MLC1	Megalencephalic Leukoencephalopathy with Subcortical Cysts
MMAA	Methylmalonic Acidemia (MMAA-Related)
MMAB	Methylmalonic Acidemia (MMAB-Related)
MMACHC	Methylmalonic Aciduria and Homocys inuria, Cobalamin C Type
MMADHC	Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type
MPI	Congenital Disorder of Glycosylation, Type Ib
MPL	Congenital Amegakaryocytic Thrombocytopenia
MPV17	Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy
MTHFR	Homocystinuria due to MTHFR Deficiency
MTM1	Myotubular Myopathy 1
MTRR	Homocystinuria, cblE Type
MTTP	Abetalipoproteinemia
MUT	Methylmalonic Acidemia (MUT-Related)
MYO7A	Usher Syndrome, Type IB
NAGLU	Mucopolysaccharidosis Type IIIB
NAGS	N-Acetylglutamate Synthase Deficiency
NBN	Nijmegen Breakage Syndrome
NDRG1	Charcot-Marie-Tooth Disease, Type 4D
NDUFAF5	Mitochondrial Complex I Deficiency (NDUFAF5-Related)
NDUFS6	Mitochondrial Complex I Deficiency (NDUFS6-Related)
NEB	Nemaline Myopathy 2
NPC1	Niemann-Pick Disease, Type C (NPC1-Related)
NPC2	Niemann-Pick Disease, Type C (NPC2-Related)
NPHS1	Nephrotic Syndrome (NPHS1-Related) / Congenital Finnish Nephrosis

Patient:	CB481 Donor	DOB:	[redacted]	Lab #:	[redacted]

Gene	Disease
NPHS2	Nephrotic Syndrome (NPHS2-Related) / Steroid-Resistant Nephrotic Syndrome
NR2E3	Enhanced S-Cone Syndrome
NTRK1	Congenital Insensitivity to Pain with Anhidrosis
OAT	Ornithine Aminotransferase Deficiency
OPA3	3-Methylglutaconic Aciduria, Type III
OTC	Ornithine Transcarbomylase Deficiency
PAH	Phenylalanine Hydroxylase Deficiency
PCCA	Propionic Acidemia (PCCA-Related)
PCCB	Propionic Acidemia (PCCB-Related)
PCDH15	Usher Syndrome, Type IF
PDHA1	Pyruvate Dehydrogenase E1-Alpha Deficiency
PDHB	Pyruvate Dehydrogenase E1-Beta Deficiency
PEX1	Zellweger Syndrome Spectrum (PEX1-Related)
PEX10	Zellweger Syndrome Spectrum (PEX10-Related)
PEX2	Zellweger Syndrome Spectrum (PEX2-Related)
PEX6	Zellweger Syndrome Spectrum (PEX6-Related)
PEX7	Rhizomelic Chondrodysplasia Punctata, Type 1
PFKM	Glycogen Storage Disease, Type VII
PHGDH	3-Phosphoglycerate Dehydrogenase Deficiency
PKHD1	Polycystic Kidney Disease, Autosomal Recessive
PMM2	Congenital Disorder of Glycosylation, Type Ia
POMGNT1	Muscle-Eye-Brain Disease and Other POMGNT1-Related Congenital Muscular Dystrophy-Dystroglycanopathies
PPT1	Neuronal Ceroid-Lipofuscinosis (PPT1-Related)
PROP1	Combined Pituitary Hormone Deficiency 2
PRPS1	Charcot-Marie-Tooth Disease, Type 5 / Arts syndrome
PSAP	Combined SAP Deficiency
PTS	6-Pyruvoyl-Tetrahydropterin Synthase Deficiency
PUS1	Mitochondrial Myopathy and Sideroblastic Anemia 1
PYGM	Glycogen Storage Disease, Type V
RAB23	Carpenter Syndrome
RAG2	Omenn Syndrome (RAG2-Related)
RAPSN	Congenital Myasthenic Syndrome (RAPSN-Related)
RARS2	Pontocerebellar Hypoplasia, Type 6
RDH12	Leber Congenital Amaurosis 13
RMRP	Car ilage-Hair Hypoplasia
RPE65	Leber Congenital Amaurosis 2 / Retinitis pigmentosa 20
RPGRIP1L	Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome
RS1	X-Linked Juvenile Retinoschisis
RTEL1	Dyskeratosis Congenita (RTEL1-Related)
SACS	Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay
SAMHD1	Aicardi-Goutières Syndrome (SAMHD1-Related)
SEPSECS	Progressive Cerebello-Cerebral Atrophy

Gene	Disease
SGCA	Limb-Girdle Muscular Dystrophy, Type 2D
SGCB	Limb-Girdle Muscular Dystrophy, Type 2E
SGCG	Limb-Girdle Muscular Dystrophy, Type 2C
SGSH	Mucopolysaccharidosis Type IIIA
SLC12A3	Gitelman Syndrome
SLC12A6	Andermann Syndrome
SLC17A5	Salla Disease
SLC22A5	Primary Carnitine Deficiency
SLC25A13	Citrin Deficiency
SLC25A15	Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome
SLC26A2	Sulfate Transporter-Related Osteochondrodysplasia
SLC26A4	Pendred Syndrome
SLC35A3	Arthrogryposis, Mental Retardation, and Seizures
SLC37A4	Glycogen Storage Disease, Type Ib
SLC39A4	Acrodermatitis Enteropathica
SLC4A11	Corneal Dystrophy and Perceptive Deafness
SLC6A8	Cerebral Creatine Deficiency Syndrome 1
SLC7A7	Lysinuric Protein Intolerance
SMARCAL1	Schimke Immunoosseous Dysplasia
SMN1	Spinal Muscular Atrophy
SMPD1	Niemann-Pick Disease (SMPD1-Related)
STAR	Lipoid Adrenal Hyperplasia
SUMF1	Multiple Sulfatase Deficiency
TCIRG1	Osteopetrosis 1
TECPR2	Hereditary Spastic Paraparesis 49
TFR2	Hemochromatosis, Type 3
TGM1	Lamellar Ichthyosis, Type 1
TH	Segawa Syndrome
TMEM216	Joubert Syndrome 2
TPP1	Neuronal Ceroid-Lipofuscinosis (TPP1-Related)
TRMU	Acute Infantile Liver Failure
TSFM	Combined Oxidative Phosphorylation Deficiency 3
TTPA	Ataxia Wi h Isolated Vitamin E Deficiency
TYMP	Myoneurogastrointestinal Encephalopathy
USH1C	Usher Syndrome, Type IC
USH2A	Usher Syndrome, Type IIA
VPS13A	Choreoacanthocytosis
VPS13B	Cohen Syndrome
VPS45	Congenital Neutropenia (VPS45-Related)
VRK1	Pontocerebellar Hypoplasia, Type 1A
VSX2	Microphthalmia / Anophthalmia
WNT10A	Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome

† Please note that GJB2 testing includes testing for the two upstream deletions, del(GJB6-D13S1830) and del(GJB6-D13S1854) (PMID: 11807148 and 15994881)

Integrated GENETICS
LabCorp Specialty Testing Group

Cystic Fibrosis Mutation Analysis

Patient Name: CB, 481
Referring Physician: David Prescott, MD
Specimen #: [redacted]
Patient ID: [redacted]

Client #: [redacted]
Case #: [redacted]

Cryobiology, Inc.
4830-D Knightsbridge Boulevard
Columbus OH 43214

DOB: [redacted]
Sex: M
SSN: [redacted]

Date Collected: [redacted]
Date Received: [redacted]
Lab ID:
Hospital ID:
Specimen Type: **BLDPER**

Ethnicity: Caucasian

Indication: Carrier test / Gamete donor

RESULTS: Negative for the 97 mutations analyzed

INTERPRETATION

This individual's risk to be a carrier is reduced from 1/25 (4%) to 1/343 (0.3%), based on these results and a negative family history.

COMMENTS:

Mutation Detection Rates among Ethnic Groups

Detection rates are based on mutation frequencies in patients affected with cystic fibrosis. Among individuals with an atypical or mild presentation (e.g. congenital absence of the vas deferens, pancreatitis) detection rates may vary from those provided here.

Ethnicity	Carrier risk reduction when no family history	Detection rate	References
African American	1/65 to 1/338	81%	Genet in Med 3:168, 2001
Ashkenazi Jewish	1/26 to 1/834	97%	Am J Hum Genet 51:951, 1994
Asian		Not Provided	Insufficient data
Caucasian	1/25 to 1/343	93%	Genet in Med 3:168, 2001; Genet in Med 4:90, 2002
Hispanic	1/46 to 1/205	78%	Genet in Med 3:168, 2001;www.dhs.ca.gov/pcfh/gdb/html/PDE/CFStudy.htm
Jewish, non-Ashkenazi		Varies by country of origin	Genet Testing 5:47, 2001, Genet Testing, 1:35, 1997
Other or Mixed Ethnicity		Not Provided	Detection rate not determined and varies with ethnicity

This interpretation is based on the clinical and family relationship information provided and the current understanding of the molecular genetics of this condition.

METHOD / LIMITATIONS:

DNA is isolated from the sample and tested for the 97 CF mutations listed. Regions of the *CFTR* gene are amplified enzymatically and subjected to a solution-phase multiplex allele-specific primer extension with subsequent hybridization to a bead array and fluorescence detection. Some mutations are then specifically identified by bi-directional dideoxysequencing. The assay discriminates between ΔF508 and the following polymorphisms: F508C, I506V and I507V. False positive or negative results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, erroneous representation of family relationships or contamination of a fetal sample with maternal cells.

Integrated Genetics is a business unit of Esoterix Genetic Laboratories, LLC, a wholly-owned subsidiary of Laboratory Corporation of America Holdings.

Under the direction of: Zhaoqing Zhou PhD. FACMG

Date: [redacted]

Zhaoqing Zhou, Ph.D., FACMG

MUTATIONS ANALYZED

ΔF311	3120+1G>A	712-1G>T	Q359K/T360K	S549N
ΔF508	3120G>A	935delA	Q493X	S549R T>G
ΔI507	3171delC	936delTA	Q552X	T338I
1078delT	3199del6	A455E	Q890X	V520F
1288insTA	3659delC	A559T	R1066C	W1089X
1677delTA	3667del4	C524X	R1158X	W1204X
1717-1G>A	3791delC	CFTRdele2,3	R1162X	W1282X
1812-1G>A	3849+10kbC>T	D1152H	R117C	Y1092X C>A
1898+1G>A	3876delA	E60X	R117H	Y1092X C>G
1898+5G>T	3905insT	E92X	R334W	Y122X
1949del84	394delTT	G178R	R347H	
2043delG	4016insT	G330X	R347P	
2055del9>A	405+1G>A	G480C	R352Q	
2105del13ins5	405+3A>C	G542X	R553X	
2108delA	406-1G>A	G551D	R560T	
2143delT	444delA	G85E	R709X	
2183delAA>G	457TAT>G	K710X	R75X	
2184delA	574delA	L206W	R764X	
2184insA	621+1G>T	M1101K	S1196X	
2307insA	663delT	N1303K	S1251N	
2789+5G>A	711+1G>T	P574H	S1255X	
2869insG	711+5G>A	Q1238X	S364P	

The test was developed and its performance characteristics have been determined by Esoterix Genetic Laboratories, LLC. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing. This test must be used in conjunction with clinical assessment, when available.

Integrated GENETICS
LabCorp Specialty Testing Group

SMN1 Copy Number Analysis

Patient Name: 481 CB
DOB: [redacted] Age: [redacted]
SSN #: Gender: Male

Specimen #: [redacted]
Case #: [redacted] Patient ID #: [redacted]
Date Collected: [redacted] Date Received: [redacted]

[redacted]
Cryobiology, Inc.
4830-D Knightsbridge Boulevard
Columbus, OH 43214

Referring Physician: David Prescott
Genetic Counselor:

Specimen Type: Peripheral blood

Clinical Data: Carrier Test/Gamete donor

Client Lab ID #:
Hospital ID #:
Specimen ID #:
Specimen(s) Received: 1 - Lavender 7 ml round bottom tube(s)
Ethnicity: Caucasian

RESULTS: SMN1 copy number: 2 (Reduced Carrier Risk)

INTERPRETATION:

This individual has an SMN1 copy number of two. This result reduces but does not eliminate the risk to be a carrier of SMA. Ethnic specific risk reductions based on a negative family history and an SMN1 copy number of two are provided in the Comments section of this report.

COMMENT:

Spinal muscular atrophy (SMA) is an autosomal recessive disease of variable age of onset and severity caused by mutations (most often deletions or gene conversions) in the survival motor neuron (SMN1) gene. Molecular testing assesses the number of copies of the SMN1 gene. Individuals with one copy of the SMN1 gene are predicted to be carriers of SMA. Individuals with two or more copies have a reduced risk to be carriers. (Affected individuals have 0 copies of the SMN1 gene.)

This copy number analysis cannot detect individuals who are carriers of SMA as a result of either 2 (or very rarely 3) copies of the SMN1 gene on one chromosome and the absence of the SMN1 gene on the other chromosome or small intragenic mutations within the SMN1 gene. This analysis also will not detect germline mosaicism or mutations in genes other than SMN1. Additionally, de novo mutations have been reported in approximately 2% of SMA patients.

Carrier Frequency and Risk Reductions for Individuals with No Family History of SMA				
Ethnicity	**Detection Rate**[1]	**Prior Carrier Risk**[1]	**Reduced Carrier Risk for 2 copy result**	**Reduced Carrier Risk for 3 copy result**
Caucasian	94.8%	1:47	1:834	1:5,600
Ashkenazi Jewish	90.5%	1:67	1:611	1:5,400
Asian	93.3%	1:59	1:806	1:5,600
Hispanic	90.0%	1:68	1:579	1:5,400
African American	70.5%	1:72	1:130	1:4,200
Asian Indian	90.2%	1:52	1:443	1:5,400
Mixed or Other Ethnic Background	For counseling purposes, consider using the ethnic background with the most conservative risk estimates.			

METHOD/LIMITATIONS: Specimen DNA is isolated and amplified by real-time polymerase chain reaction (PCR) for exon 7 of the SMN1 gene and the internal standard reference genes. A mathematical algorithm is used to calculate and report SMN1 copy numbers of 0, 1, 2 and 3. Based upon this analysis, an upper limit of 3 represents the highest degree of accuracy in reporting SMN1 copy number with statistical confidence. Sequencing of the primer and probe binding sites is performed on all fetal samples and samples with one copy of SMN1 by real-time PCR to rule out the presence of sequence variants which could interfere with analysis and interpretation. False positive or negative results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, erroneous representation of family relationships or contamination of a fetal sample with maternal cells.

REFERENCES:
1. Sugarman EA, Nagan N, Zhu H, et al. Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of >72,400 specimens. Eur J Hum Genet 2012; 20:27-32. 2. Prior TW, et al. Technical standards and guidelines for spinal muscular atrophy testing. Genet Med 2011; 13(7): 686-694.

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Electronically Signed by: Jane W. Thuo, Ph.D., FACMG, on [redacted]

Reported by: /

BCM
lor College of Medicine

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KLEBERG CYTOGENETICS LABORATORY

Name: DONOR CB481
Date of birth: [redacted]
Gender: M
Hospital/MR #:
Accession #:
Sample Type: BLOOD
Test Code: 8600
Indication: Sperm Donor

Lab Number: [redacted]
Family #:
Date Collected:
Date Received:
Date Reported:

Sendouts
Cryobiology
Tel. No.: 614-451-4375
Fax No: 614-451-5284

Chromosome Analysis - Blood

METHOD OF ANALYSIS:
GTG-Banding

[redacted]

Cultures:	2	***No. of images:***	9
Cells counted:	50	***Cells karyotyped:***	4
Cells analyzed:	5	***Band resolution:***	525

RESULTS:
46,XY

I... ERPRETATION :
Normal male chromosome analysis.

DISCLAIMER:
The resolution of analysis for this standard cytogenetic methodology does not routinely detect subtle rearrangements (<5Mb) or low-level mosaicism. Standard cytogenetic analysis cannot detect microdeletions/microduplications that might be diagnosed with Chromosomal Microarray Analysis. These results do not rule out the possibility of genetic conditions not detectable by cytogenetic analysis. Depending upon the clinical indication, additional testing may be warranted.

Carlos A. Bacino, M.D., FACMG
ABMG Certified Cytogeneticist and Molecular Geneticist
Medical Director

Janice L. Smith, Ph.D.
ABMG Certified Clinical Cytogeneticist
Assistant Laboratory Director

[redacted]