Advanta Genetics
10935 CR 159 Tyler, TX 75703
Phone: (903) 805-9955 Fax: (903) 839-2494
www.aalabs.com

CLIA: 45D2063134
CAP: 8863194
Laboratory Director: Mary Long, Ph.D., NRCC

Patient: Race Bannon
DOB: 02-05-1960
Gender: Male

Accession: 773933
Specimen: Blood
Provider: Doe, John

Client: Demo Account
Collected Date: 05-09-2022
Report Date: 05-15-2022

Condition	Inheritance	Mutation Detected
	AR	Carrier: Compound Heterozygous Mutantions (Copy the mutations from Col "E") detected in CFTR gene c.1766+5G>T

Interpretation

This individual is a carrier of cystic fibrosis. Carriers generally do not experience symptoms. Disease phenotype is dependent on inherited mutations, but mutations can not accurelty predict the disease menifestation. Genetic counseling and prenatal diagnostic testing are recommended.

Released by Rahul Sharma Ph.D., HCLD (ABB) on 05-15-2022

I. CF Mutation Detection Rate (%) Adopted from ACOG guidelines

Ethnic Group	Detection Rate (%)	Carrier Risk Before Testing	Approximate Carrier Risk After Negative Results*
Ashkenazi Jewish	94	1/24	1/380
Non-Hispanic White	88	1/25	1/200
Hispanic White	72	1/58	1/200
African American	64	1/64	1/170
Asian American	49	1/94	1/180
	Watson MS et al , Genet Med. 2004;6(5):387-391.		Beauchamp et al Genet Med. 2019 Nov;21(11):2569-2576

* Detection rate data based on use of a 64-mutation panel as suggested by ACOG. The lowest detection rates are mentioned above and the actual detection rate will depend on the panel of mutations screened and will be higher for genetic test panels reporting genes.

II. Assay Methodology

DNA was extracted and 65 pathogenic variants in CFTR Gene were amplified using wild-type (WT), or mutant (MUT) allele-specific primers. Genotype and zygosity are determined by allele-specific (MUT or WT) peak size (bp) using the Capillary Electrophoresis (CE).

II. Assay Limitations

This Cystic Fibrosis genetic testing report is intended to facilitate the identification of the disease carrier status. This test should not be used for stand-alone diagnostic purposes, prenatal diagnostic, pre-implantation, or population screening. This assay will not detect all the mutations in the CFTR gene that cause cystic fibrosis or other related conditions. In rare cases of co-localization of two CFTR mutant alleles, one of them will not be detected. This test is designed to cover 93% of mutant allele frequency (MAF) across an ethnically diverse US population. Variant MAF may differ within a specific ethnicity, and population-specific coverage should be determined based on known carrier rates for each specific region as needed. Therefore, the absence of a detectable mutation does not rule out the possibility that an individual is a carrier of or affected by the disease. Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete. Rare polymorphisms in the primer binding region could lead to false-negative or false-positive results. If results obtained are not congruent with clinical findings, additional testing should be considered. Allogeneic bone marrow transplantation will interfere with testing and should be discussed with the laboratory or the ordering physician before testing. These results are only meant to be used by a medical professional or a genetic counselor. This test is not approved or cleared by FDA; the test was designed and validated by Advanta Genetics (CLIA# 45D2063134, CAP# 8863194) as a Laboratory Developed Test (LDT). The laboratory is regulated under CLIA and CAP and is qualified to perform this high-complexity testing.

III. List of CFTR Mutations Tested

1717-1G>A* (c.1585-1G>A)	F508del* (c.1521_1523del)	R117H* (c.350G>A)	1811+1.6kbA>G (c.1680-886A>G)	Q493X (c.1477C>T)
1898+1G>A* (c.1766+1G>A)	G542X* (c.1624G>T)	R334W* (c.1000C>T)	1898+5G>T (c.1766+5G>T)	Q890X (c.2668C>T)
2184delA* (c.2052del)	G551D* (c.1652G>A)	R347H (c.1040G>A)	2789+2insA (c.2657+2_2657+3insA)	R1066C (c.3196C>T)
2184insA (c.2052dup)	G622D (c.1865G>A)	R347P* (c.1040G>C)	3876delA (c.3744del)	R1070W (c.3208C>T)
2789+5G>A* (c.2657+5G>A)	G85E* (c.254G>A)	R553X* (c.1657C>T)	3905insT (c.3773dup)	R1158X (c.3472C>T)
3120+1G>A* (c.2988+1G>A)	I507del* (c.1516_1518del)	R560T* (c.1679G>C)	394delTT (c.262_263del)	R117C (c.349C>T)
3272-26A>G (c.3140-26A>G)	L206W (c.617T>G)	S945L (c.2834C>T)	A559T (c.1675G>A)	R352Q (c.1055G>A)
3659delC* (c.3528del)	N1303K* (c.3909C>G)	W1282X* (c.3846G>A)	E60X (c.178G>T)	R75X (c.223C>T)
3849+10kbC>T* (c.3718-2477C>T)	P5L (c.14C>T)	2183AA>G (c.2051_2052delAAinsG)	F311del (c.935_937del, c.933_935del)	S549N (c.1646G>A)
621+1G>T* (c.489+1G>T)	PolyT (c.1210-12T[5_9])	1078delT (c.948del)	G970D (c.2909G>A)	V456A (c.1367T>C)
711+1G>T* (c.579+1G>T)	PolyTG (c.1210-34TG[10_12])	1154insTC (c.1019_1020dup)	I618T (c.1853T>C)	V520F (c.1558G>T)
A455E* (c.1364C>A)	R1070Q (c.3209G>A)	1548delG (c.1418del)	M1101K (c.3302T>A)	Y1092X (c.3276C>A, c.3276C>G)
D1152H (c.3454G>C)	R1162X* (c.3484C>T)	1677delTA (c.1545_1546del)	P67L (c.200C>T)	Y122X (c.366T>A)

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CLIA: 45D2063134
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Laboratory Director: Mary Long, Ph.D., NRCC

Patient: Race Bannon
DOB: 02-05-1960
Gender: Male

Accession: 767866
Specimen: Blood
Provider: Doe, John

Client: Demo Account
Collected Date: 03-16-2022
Report Date:

Final Results

Carrier Premutation(s) Identified
Premutation (55-200 CGG repeats on FMR1 gene)

Condition and Gene	Inheritance	Genetic Alteration
Fragile X Syndrome (FMR1)	X-linked	Premutation (55-200 CGG repeats on FMR1 gene) 69, 100, 116 mutation

Interpretation

Individual is carrier for the altered FMR1 gene. This individual has one FMR1 allele in the premutation range. Although males with premutation are not affected with fragile X syndrome, they are at risk for developing fragile X-associated tremor/ataxia syndrome (FXTAS); Approximately 40-45% of males with a premutation develop FXTAS after age 50 (Am J Hum Genet. 2004; 74:805-816). All your daughters will be premutation carriers. Your sons will not be premutation carriers. A man with a premutation will not pass on a full mutation to any of his children. Genetic counseling and prenatal diagnostic testing are recommended.

I. Fragile X Syndrome Risk

Negative	< 44 CGG repeats
Intermediate	45-54 CGG repeats
Premutation	55-200 CGG repeats
Full Mutation	>200 CGG repeats

Released by Rahul Sharma Ph.D., HCLD (ABB) on

II. Assay Methodology

DNA was extracted and CGG repeat region of FMR gene was amplifed using triplet repeat-primed polymerase chain reaction (PCR). Number of the CGG repeat is determined using capillary electrophoresis.

III. Assay Limitations

The analytical sensitivity of PCR analysis is 99% for expansion mutations in the FMR1 gene. Reported CGG trinucleotide repeat unit report sizes may vary: CGG repeats 120 ≥ 10%. Diagnostic errors can occur due to rare sequence variations. This test should not be used for stand-alone diagnostic purposes, prenatal diagnostic, pre-implantation, or population screening. If >55 trinucleotide repeat units are detected, targeted Next Generation Sequencing is performed by Fulgent Genetics (CLIA# 05D2043189, CAP# 8042697). This test is not approved or cleared by FDA; the test was designed and validated by Advanta Genetics (CLIA# 45D2063134, CAP# 8863194) as a Laboratory Developed Test (LDT). The laboratory is regulated under CLIA and CAP and is qualified to perform this high-complexity testing.

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CLIA: 45D2063134
CAP: 8863194
Laboratory Director: Mary Long, Ph.D., NRCC

Patient: Bannon Race
DOB: 02-05-1960
Gender: Male

Accession: 775088
Specimen: Blood
Provider: Doe, John

Client: Demo Account
Collected Date: 05-18-2022
Report Date:

Final Results

Carrier mutation(s) detected
Absence of SMN1 gene detected

Condition and Gene	Inheritance	Mutation Detected
Survival of motor neuron (SMN1)	AR	SMN1 deletion c.*211_*212del mutation

Interpretation

Patient Likely Affected with SMA: Homozygous loss of SMN1 (0 copies of SMN1) is consistent with a diagnosis of SMA.

I. Spinal Muscular Atrophy (SMA) Risk

Ethnicity	Detection rate (Copy number + SNP)	Pre-test carrier	Post-test carrier risk with 2 copies (c.*3+80T>G or c.*211_*212del)		Post-test risk of being a carrier with 3 copies
			Positive	Negative	
African American	90.30%	1 in 72	1 in 34	1 in 375	1 in 4200
Ashkenazi Jewish	92.80%	1 in 67	High risk	1 in 918	1 in 5400
Asian	93.60%	1 in 59	High Risk	1 in 907	1 in 5600
Caucasian	95.00%	1 in 47	1 in 29	1 in 921	1 in 5600
Hispanic	92.60%	1 in 68	1 in 140	1 in 906	1 in 5400

Feng, Y et al. Genet Med 2017; 19, 936-944. Sugarman et al Eur J Hum Genet. 2012; 20(1): 27-32. Luo et al Genet Med. 2014;16(2):149-156

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II. Assay Methodology

DNA was extracted and the SMN1 gene fragment was amplified via polymerase chain reaction (PCR). Genomic copies of exon 7 for SMN1 were enumerated and reported as 0, 1, 2, 3, or ≥ 4 by capillary electrophoresis (CE). Variant-specific primers were used for determining the gene duplication variants (SMN1 c.*3+80T>G and SMN1 c.*211_*212del). If less than 2 copies of SMN1 gene or disease modifier variants are detected, targeted Next Generation Sequencing is performed by Fulgent Genetics (CAP #8042697; CLIA #05D2043189).

III. Assay Limitations

This test should not be used for stand-alone diagnostic purposes, prenatal diagnostic, pre-implantation, or population screening. SMA carrier screening test is validated only to quantify exon 7 of the SMN1 gene. Samples with two copies of SMN1 on one chromosome and zero copies on the other (2+0 or silent carriers) may not be distinguished from samples with one genomic SMN1 copy on each chromosome (1+1) based on the genotype of the gene duplication variants in some populations (Luo et Al. 2014; Alias et al., 2018). This test detects three variants related to SMN1 and SMN2 gene structure and function, including the gene duplication markers c.*3+80T>G and c.*211_*212del (Luo et al. 2014), and the disease modifier c.859G>C (Vezain et al. 2010, Prior et al. 2009). Variants detected by this test are not gene-specific; variants in the SMN1 or SMN2 gene will be reported. SMN2 copy number is not reported. The higher SMN2 copy number may correlate with milder disease severity in affected individuals. The binding sites for the primers used in this test are free of polymorphic sites with minor allele frequencies (MAF) above 0.005 (The Single Nucleotide Polymorphism database dbSNP build 152); however, very rare polymorphisms located within the primer binding sites may affect SMN1 copy number quantification (Prior et al. 2011). False-positive or false-negative results may occur because of genetic variants in the primer binding region, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships. This test is not approved or cleared by FDA; the test was designed and validated by Advanta Genetics (CLIA# 45D2063134, CAP# 8863194) as a Laboratory Developed Test (LDT). The laboratory is regulated under CLIA and CAP and is qualified to perform high-complexity testing.