Luminex®

xTAG® Cystic Fibrosis (CFTR) 39 kit v2
xTAG® Cystic Fibrosis (CFTR) 60 kit v2

Improved Sensitivity for Hispanic and African American Cystic Fibrosis Mutation Detection Beyond the ACMG/ACOG Panel

The xTAG® Cystic Fibrosis (CF) family of assays offer the utmost flexibility with the ability to test for the 23 CFTR mutations recommended by the American College of Medical Genetics/American College of Obstetricians and Gynecologists (ACMG/ACOG) and an expanded panel of cystic fibrosis mutations providing broad ethnic coverage across populations.[1]

- **Sensitive:** Detects beyond the ACMG/ACOG 23 with broad coverage for ethnic populations
- **Relevant:** Hastens identification of cystic fibrosis causing mutations in a panethnic population
- **Fast:** Complete testing workflow in a single day

Frequencies of Cystic Fibrosis Mutations

Due to the high frequency of mixed ethnicities in the U.S., expanded panels are becoming increasingly significant to improve the detection rate of cystic fibrosis mutations. The carrier detection rate of the ACMG/ACOG 23 mutation panel in a Hispanic population has been estimated to be only 72% and in African American cohorts 64%, which are significantly lower than 88% in Caucasians.[2] (Table 1).

Table 1: CF Mutation detection rate (%)§

Ethnic Group	Incidence of CF§	Carrier Frequency§	ACMG/ACOG§ Recommended Mutation Only
Hispanic Americans	1 in 9,500	1 in 46	71.7
African Americans	1 in 15,300	1 in 65	64.5

§Data collected from the following references: Watson et al. Genet Med 2004;6(5):387-91, Richards et al. Genet Med 2002;4(5):379-391, Bobadilla et al. Human Mutat 2002;19:575-606, Heim et al. Genet Med 2001;3:168-76, Sugarman et al. Genet Med 2004;6:392-99, Organ et al. Genet Testing 2001;5:47-52, Wong et al. Human Mutat 2001;18:296-307, Alder et al. Human Mutat 2004 MIB #752, and Shriver et al. JMD 2005;7:289-99.

Table 2: ACMG/ACOG 23 carrier screening panel genotype frequencies by ethnic ancestry in the genotyped CF population of 2013

Mutations on the ACMG/ACOG 23	White only		Hispanic only		African American	
	N	%	N	%	N	%
2	16,782	76	933	48	454	37
1	4,775	22	712	36	536	44
0	649	3	310	16	224	18
Total	22,206	~100	1955	100	1214	~100
P value*	Reference Group		<0.0001		<0.0001	

Percentages are rounded and may not add up to exactly 100%, indicated where applicable by ~100%.
**Carrying 0 mutations of the ACMG 23 mutation panel.*

Performance

Table 3: Hispanic American

Mutations	ACMG/ ACOG 23	CF 39 v2	CF 60 v2	% of Positive Hispanic Carriers
L206W			X	3.83
3199del6			X	3.48
D1152H			X	6.27
3876delA		X	X	1.39
S549N		X	X	0.7
F508	X	X	X	47.39
R117H	X	X	X	4.88
G542X	X	X	X	4.18
I507	X	X	X	3.83
R553X	X	X	X	2.44
R334W	X	X	X	2.09
3849+10kbC>T	X	X	X	2.09
3120+1G>A	X	X	X	1.74
R1162X	X	X	X	1.74
W1282X	X	X	X	1.39
N1303K	X	X	X	1.39
G85E	X	X	X	1.05
621+1G>T	X	X	X	0.35

16%

The ACMG/ACOG panel includes 13 mutations relevant to the Hispanic American population. The xTAG Cystic Fibrosis (CFTR) 39 kit v2 detects 2 additional targets, while the xTAG Cystic Fibrosis (CFTR) 60 kit v2 detects 5 additional targets, improving the detection rate in Hispanic Americans by 16%.

Table 4: African American

Mutations	ACMG/ ACOG 23	CF 39 v2	CF 60 v2	% of Positive African American Carriers
D1152H			X	3.19
3791delC			X	2.13
G330X			X	1.06
L206W			X	1.06
R1158X			X	1.06
R1066C			X	1.06
A559T		X	X	6.38
S1255X		X	X	1.06
F508	X	X	X	52.13
3120+1G>A	X	X	X	9.57
R117H	X	X	X	5.32
R553X	X	X	X	2.13
3849+10kbC>T	X	X	X	2.13
G542X	X	X	X	1.06
1717-1G>A	X	X	X	1.06
G551D	X	X	X	1.06
I507	X	X	X	1.06
2789+5G>A	X	X	X	1.06

17%

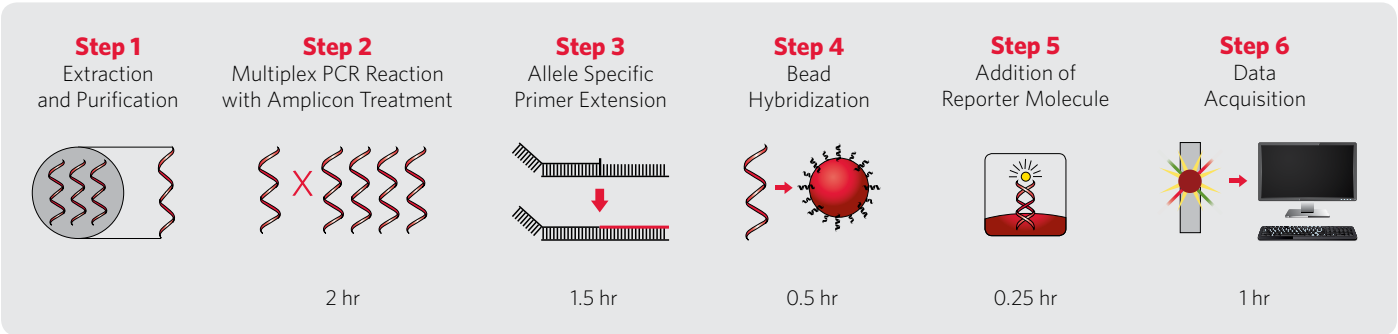
The ACMG/ACOG panel includes 10 mutations relevant to the African American population. The xTAG Cystic Fibrosis (CFTR) 39 kit v2 detects 2 additional targets, while the xTAG Cystic Fibrosis (CFTR) 60 kit v2 detects 8 additional targets, improving the detection rate in African Americans by 17%.

Table 5: Improved detection rates and decreased residual risk

Ethnic Group	ACMG/ ACOG 23 Detection Rate	CF 39 Detection Rate[3]	Ethnic Frequency (Table 1)	Estimated Ethnic Carrier Risk after Negative CF 39 Test		CF 60 Detection Rate[3]	Estimated Ethnic Carrier Risk after Negative CF 60 Test	
Formula		A	B	C=(100-A)*B	D= 1/(1/C)	E	F = (100-E)*B	G = 1/(1/F)
Hispanic	71%	73%	1/46	0.0059	1/170	87%	0.0028	1/354
African American	64%	71.5%	1/65	0.0044	1/228	81%	0.0029	1/342

The spectrum and frequency of individual CFTR alleles vary by ethnic group and geography.[4] Expanded panels increase sensitivity when testing a diverse population, and similar sensitivities can be achieved for all races (except Asian Americans) when using a 50-70 mutation panel.[5] The xTAG Cystic Fibrosis kits incrementally improve detection rates of relevant and frequent Hispanic and African American alleles, with a single day workflow.

Workflow



Total hands-on time ~50 minutes | Total elapsed time ~5.25 hours after extraction

Assay Description

The xTAG Cystic Fibrosis kits are used to simultaneously detect and identify a panel of mutations and variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene in human blood specimens. The panels include mutations and variants currently recommended by the American College of Medical Genetics and American College of Obstetricians and Gynecologists (ACMG/ACOG), plus some of the world's most common and North American-prevalent mutations. The kits are qualitative genotyping tests which provide information intended to be used for carrier testing in adults of reproductive age, as an aid in newborn screening, and in confirmatory diagnostic testing in newborns and children.

The kits are not indicated for use in fetal diagnostic or pre-implantation testing. The kits are is also not indicated for stand-alone diagnostic purposes.

Ordering Information

Product Name	Part Number
xTAG® Cystic Fibrosis (CFTR) 39 kit v2 (IVD)	I027C0231
xTAG® Cystic Fibrosis (CFTR) 60 kit v2 (IVD)	I024C0181

References

1. Luminex Corporation. Kit Brochure | IVD xTAG® Cystic Fibrosis 60 Kit v2.
2. Brennan ML, Schrijver I. Cystic fibrosis: A review of associated phenotypes, use of molecular diagnostic approaches, genetic characteristics, progress, and dilemmas. J Mol Diagn 2016 Jan:18(1):3-14.
3. Sugarman EA, Rohlfs EM, Silverman LM, Allitto BA. CFTR mutation distribution among U.S. Hispanic and African American individuals: evaluation in cystic fibrosis patient and carrier screening populations. Genet Med 2004 Sep-Oct;6(5):392-9.
4. Schrijver, et. al. The spectrum of CFTR Variants in nonwhite cystic fibrosis patients. J Mol Diagn 2016 January;18 (1):39-50.
5. Grody WW, Cutting GR, Klinger KW, et.al. Laboratory standards and guidelines for population-based cystic fibrosis carrier screening. Genet Med 2001 Mar-Apr;3(2):149-54.

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