CF*plus*®

Cystic Fibrosis Mutation Analysis

Integrated GENETICS
LabCorp Specialty Testing Group

Your Partner for Genetic Testing

Cystic Fibrosis (CF) is a common inherited disease of children and young adults.

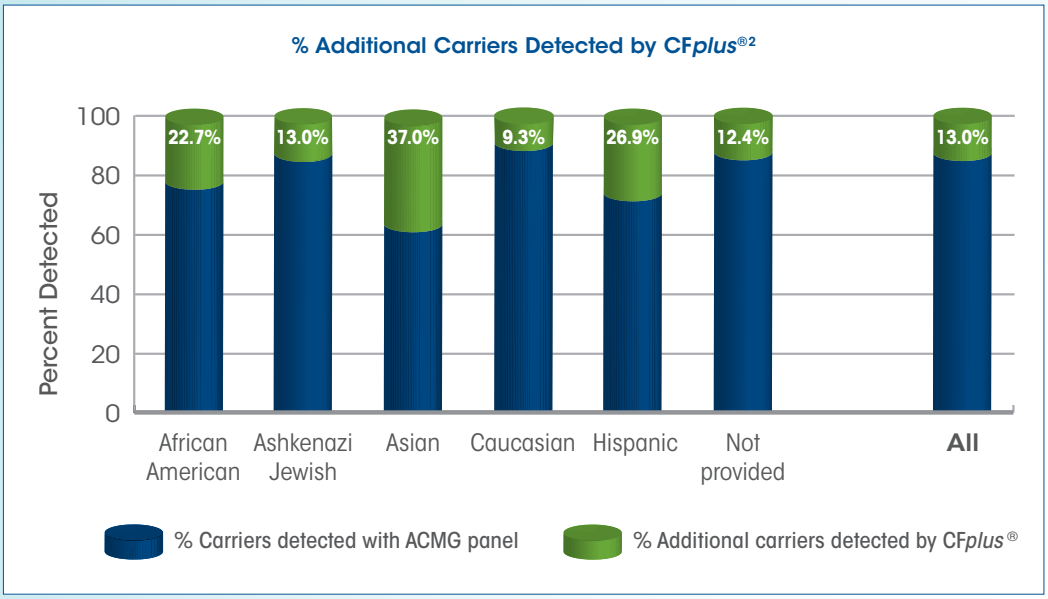
The American College of Obstetricians and Gynecologists recognizes that because it is becoming increasingly difficult to assign a single ethnicity, it is reasonable to offer CF screening to all patients.[1]

CF*plus*®

Cystic Fibrosis Mutation Analysis

CF*plus*® detects more mutations in many ethnic backgrounds.

- Approximately 1 in 8 carriers overall, and specifically 1 in 4 Hispanic or African American carriers and 1 in 11 Caucasian carriers, would otherwise be missed using the ACMG 23-mutation panel.[2]
- Approximately 1 in 9 carriers overall, and specifically 1 in 5 Hispanic or African American carriers and 1 in 13 Caucasian carriers, would otherwise be missed using a 32-mutation panel.[2,3]



Integrated Genetics offers over 25 years of experience with CF Testing

1986 — The first of its kind molecular genetic testing laboratory.

1989 — Cystic fibrosis transmembrane regulator (CFTR) gene is discovered. Testing begins of ΔF508; detection rate (DR) = 72% for Caucasians.

1990 — 4 mutations (added G542X, G551D, and R553X); DR = 77% for Caucasians

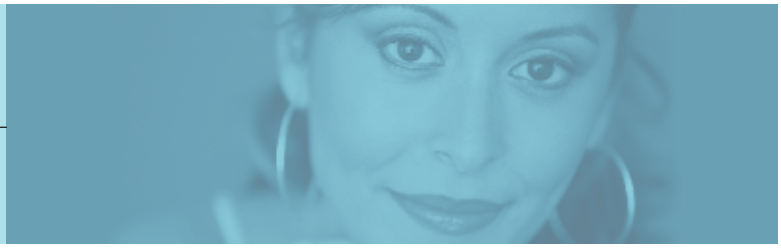
1991 — 12 mutations; DR = 95% for Ashkenazi Jews and 85% for Caucasians.

1993 — 32 mutations; DR = 97% for Ashkenazi Jews and 90% for Caucasians.

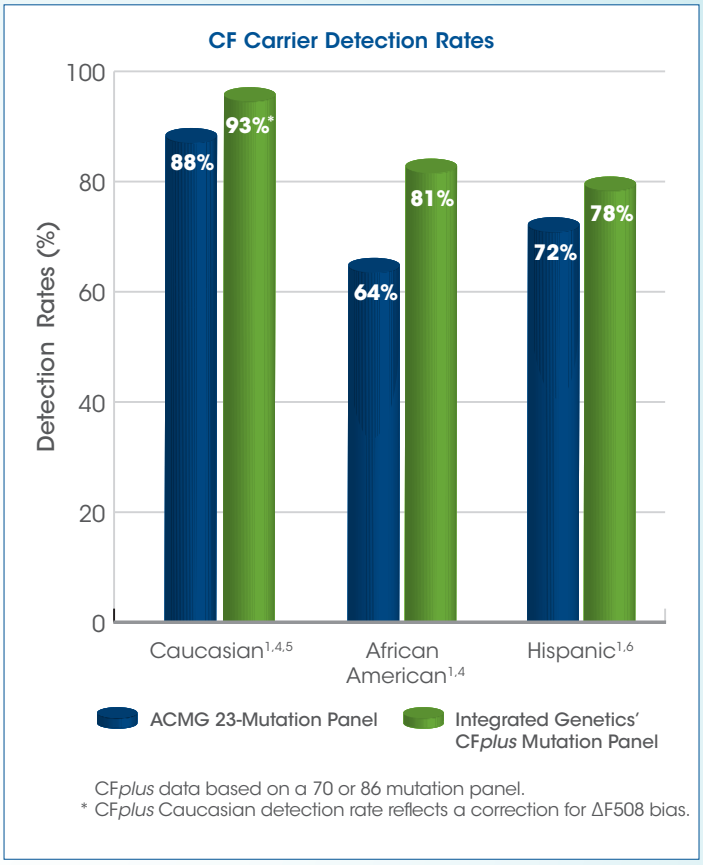
1997 — 70 mutations; DR = 61% for African Americans. Introduction of new high-throughput technology, improving turnaround time to 7–10 days.

19 — CFTR poly T t for individual pancreatitis, R117H positi

CF*plus*® tests for 97 clinically relevant mutations.



CF*plus*® provides higher detection rates for the pan-ethnic U.S. population.



CF*plus* data based on a 70 or 86 mutation panel.
* CF*plus* Caucasian detection rate reflects a correction for ΔF508 bias.

Additional CF*plus* Detection Rates	
Ashkenazi Jewish[7]	97%
Native American[4]	81%*
Asian[4,8]	37–55%**

*Based on 21 self-identified individuals
**Based on 8 self-identified individuals

Ethnicity	CF Carrier Risk*[1]
Caucasian	1 in 25
Ashkenazi Jewish	1 in 24
Hispanic	1 in 58
African American	1 in 61
Asian	1 in 94

*CF carrier risk in individuals with no known family history of CF.

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98

1999

86 mutations, additions specific to African Americans, Caucasians and Hispanics; DR = 75% for African Americans.

2001

- Data published in Genetics in Medicine: *Improved Detection of Cystic Fibrosis Mutations in the Heterogeneous U.S. Population Using an Expanded, Pan-Ethnic Mutation Panel.*
- ACMG/ACOG publish initial guidelines for CF carrier screening. Katherine Klinger was a contributing author.

2003

D1270N removed after careful review of data shows frequency much higher in carriers than in affected patients, i.e. should be redefined as variant.

2004

- Data published in Genetics in Medicine – *CFTR Mutation Distribution Among U.S. Hispanic and African American Individuals: Evaluation in Cystic Fibrosis Patient and Carrier Screening Populations.* AND *Analysis of 3208 Cystic Fibrosis prenatal diagnoses: Impact on carrier screening guidelines on distribution of indications for CFTR mutation and IVS-8 poly(T) analyses.*
- Data show that 3199del6 and I148T are linked, but that 3199del6 is the disease-causing mutation. 3199del6 replaces I148T in the panel.

2005

- 97 mutations; DR = 78% for Hispanics, turnaround reduced time to 5–8 days.
- ACOG publishes updated Committee Opinion stating "it is reasonable to offer CF carrier screening to all couples regardless of race or ethnicity."[9]

2011

Publication: *Cystic Fibrosis Carrier Screening in an Ethnically Diverse US Population* appears in Clinical Chemistry.

Indications for testing include:

Carrier Screening	Prenatal Diagnostic Testing	Diagnostic Testing

■ Pregnant and preconception couples
■ Individuals with a family history of CF
■ Individuals who are negative on a lesser mutation panel when:
  ● There is a family history of CF
  ● Their partners are positive
■ Gamete donors
■ Partners of men with Congenital Bilateral Absence of Vas Deferens(CBAVD)
	■ Pregnancies where both parents are CF carriers
	■ Pregnancies where echogenic bowel is found on fetal ultrasound
		■ Symptomatic or screen-positive infants too young for sweat testing
		■ Symptomatic individuals with negative or equivocal sweat test
		■ Men with CBAVD
		■ Individuals with idiopathic chronic pancreatitis

ACOG recognizes that because it is becoming increasingly difficult to assign a single ethnicity, it is reasonable to offer CF screening to all patients.[1]

Integrated Genetics also offers:

- Result interpretation provided by board-certified clinical molecular geneticists and access to these genetic professionals to help with any questions
- Full and partial CF sequencing for those patients with a family history of mutations not found on CF*plus*®
- Rapid 5-8 day turnaround time allowing you to provide your patients with quick answers
- Multiple specimen types to meet your clinic's and patients' needs

REFERENCES

1) Update on Carrier Screening for Cystic Fibrosis. ACOG Committee Opinion, Number 486, April 2011.
2) Rohlfs, E, et al., Cystic Fibrosis Carrier Testing in an Ethnically Diverse US Population. *Clinical Chemistry* 2011; 57(6):841–848.
3) LabCorp Technical Review: Genetic Testing for Cystic Fibrosis. 2010.
4) Heim, RA. et al., Improved detection of cystic fibrosis mutations in the heterogeneous U.S. population using an expanded, pan-ethnic mutation panel. *Genet Med* 2001; 3:168–176.
5) Palomaki, G.E., et al., Updated assessment of cystic fibrosis mutation frequencies in non-Hispanic Caucasians. *Genet Med* 2002; 4:90–94.
6) Sugarman, EA, et al. CFTR mutation distribution among U.S. Hispanic and African American individuals: Evaluation in cystic fibrosis patient and carrier screening populations. *Genet Med* 2004; 6(5):392–399.
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8) Watson, M.S., et al., Cystic fibrosis population carrier screening: 2004 revision of American College of Medical Genetics mutation panel. *Genet Med* 2004; 6:387–391.
9) Update on Carrier Screening for Cystic Fibrosis. ACOG Committee Opinion, Number 325, December 2005.

Integrated Genetics Client Services (800) 848-4436

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