



# LABORATORY UPDATE

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## CYSTIC FIBROSIS DESCRIPTION

- Cystic Fibrosis (CF) currently affects approximately 30,000 children and adults in the United States<sup>1</sup>
- CF, one of the most common fatal inherited diseases, is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene<sup>2</sup>
- A child must inherit two such genes, one from each parent, to develop the disease<sup>1</sup>

## CFTR Mutation Description and frequencies

- Mutations in the CFTR gene may result in defective processing of its protein and alter the function and regulation of this channel<sup>2</sup>
- More than 1,000 mutations have been identified within the CFTR gene<sup>3</sup>
- The  $\Delta$ F508 mutation is the most common mutant allele, accounting for approximately 66% of all CF chromosomes worldwide<sup>4</sup>
- The remaining CFTR mutations vary greatly in their frequency and distribution; however, the majority of these mutations are either private or limited to a small number of individuals<sup>5</sup>
- The American College of Medical Genetics (ACMG) and the American College of Obstetrics and Gynecologists (ACOG) recommend a core mutation panel of 25 mutations for pan-ethnic screening in the U.S. population (see table below)<sup>6</sup>

Mutation	Percent of Subjects Carrying this Mutation <sup>7</sup>	Mutation	Percent of Subjects Carrying this Mutation <sup>7</sup>
$\Delta$ F508	2.960	R1162X	0.025
R117H	0.373	711 + 1G>T	0.020
I117H	0.318	1717-1G>A	0.020
W1282X	0.289	A455E	0.020
G542X	0.169	3120_1g>A	0.015
N1303K	0.095	G85E	0.015
3849+10kbC>T	0.090	$\Delta$ 1507	0.015
G551D	0.085	1898+1G>A	0.015
R553X	0.050	3659delC	0.010
R560T	0.040	2184delA	0.010
621+1G>T	0.035	R334W	0.005
2789+5G>A	0.035	R347P	0.005
		1078delT	0.000
		<b>TOTAL</b>	<b>4.711</b>



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## CF Phenotypic Expression

- Affected individuals have a faulty transport of sodium chloride (salt) within cells lining the lung and pancreas to the outer surfaces of those organs, resulting in the production of an abnormally thick mucus<sup>1</sup>
- Of a variety of symptoms associated with CF, the most common include very salty-tasting skin; persistent coughing, wheezing or pneumonia; bulky stools; and poor weight gain despite excessive appetite<sup>1</sup>
- The treatment of CF is determined by the stage of the disease and the organs involved, but include chest physical therapy to dislodge the thick mucus from the lungs, antibiotic treatment for lung infections, and special diets and supplements to increase nutrient absorption<sup>1</sup>
- The current life expectancy for individuals affected with CF is approximately 30 years<sup>8</sup>

## Populations at Risk

- The ACMG/ACOG published recommendations to offer CF screening to non-Jewish Caucasians and Ashkenazi Jews, and to make screening available to other ethnic and racial groups<sup>6,9</sup>
- “ACOG now recommends that ob/gyns make DNA screening for cystic fibrosis available to all couples seeking preconception or prenatal care- not just those with personal or family history of carrying the gene, as previously recommended”<sup>9</sup>

## Relative Risk in Select Populations<sup>10</sup>

<u>Ethnic Group</u>	<u>Carrier Risk</u>
Ashkenazi Jewish	1/25
European Caucasian	1/25
African American	1/65
Hispanic American	1/46
Asian American	1/90

**Specimen Requirements:** 5mL of whole blood (lavender or green top)