

Cystic fibrosis mutations in American Indian population

Shibo Li and Lori L. Williamson

Genetics Section

Department of Pediatrics, OUHSC

CFTR: The Gene Associated with Cystic Fibrosis

- **CRTR, cystic fibrosis transmembrane conductance regulator, gene:** identified in 1989 (Kerem et al; *Science* 245: 1073-1080)
- **Locus:** 7q31.2 - The CFTR gene is found in region q31.2 on the long (q) arm of human chromosome 7.
- **Gene Structure:** The normal allelic variant for this gene is about 250,000 base pairs (bp) long and contains 27 exons.
- **mRNA:** The intron-free mRNA transcript for the CFTR gene is 6129 bp long.
- **Coding Sequence (CDS):** 4443 bp within the mRNA code for the amino acid sequence of the gene's protein product.
- **Protein Function:** The normal CFTR protein product is a chloride channel protein found in membranes of cells that line passageways of the lungs, liver, pancreas, intestines, reproductive tract, and skin. CFTR is also involved in the regulation of other transport pathways.
- **Associated Disorders:** Defective versions of this protein, caused by CFTR gene mutations, can lead to the development of cystic fibrosis (CF) and congenital bilateral aplasia of the vas deferens (CBAVD).

Standards and Guidelines for *CFTR* Mutation Testing

Δ F508	R553X	R1162X	2184delA	3120+1G>A
Δ I507	G542X	G551D	W1282X	N1303K
621+1G>T	R117H	1717-1G>A	A455E	R560T
G85E	R334W	R347P	711+1G>T	1898+1G>A
1078delT	3849+10kbC>T	2789+5G>A	3659delC	I148T

INNO-LiPA *CFTR*

- Please note that the sensitivity of this testing varies in different ethnic populations:
- ~80% detection in the Caucasian/Non-Ashkenazic population
- ~97% detection in the Ashkenazi Jewish population
- ~69% detection in the African-American population

CF mutation analysis by Genzyme

- CFplus™ cystic fibrosis (CF) mutation analysis includes testing for 97 mutations
- With additional mutation testing, CFpuls™ provides highest detection rates for Caucasians, African Americans (78%) and Hispanics (81%)

Analysis of the entire coding region: Sequence analysis:

- Identifies most variations from the wild-type. (In contrast, mutation analysis identifies only specific targeted mutations within a given segment of DNA)
- Identifies novel mutations

CF in Native American

- Native American have the second highest incidence rates of cystic fibrosis
- One in 10,500 Native American has CF
- Compared with one in 3200 whites
- The delta-F508 mutation has not been found in any American Indian CF patients
- The mutation detection rate in American Indian is 94%.

Table 1 Clinical and mutations data of these Native American cystic fibrosis (CF) patients

Patient	Nation	Pancreatic sufficient (PS) Pancreatic insufficient (PI)	Weight (%ile)	Height (%ile)	Haplo-type	Mutations	
021-1	Pueblo Zuni	PI	20	10	CC	R1162X	R1162X
022-1	Pueblo Zuni	PI	7.5	20	CC	R1162X	R1162X
023-1	Pueblo Zuni	PI	75	50	CC	R1162X	R1162X
024-1	Pueblo Zuni	PI	40	10	CC	R1162X	R1162X
028-1	Pueblo Zuni	PI	7.7	5	CC	R1162X	R1162X
029-1	Pueblo Zuni	PS	2	17.5	AC	R1162X	3849+10kbC→T
006-1	Pueblo Jemez	PS	8.5	45	AC	D648V	3849+10kbC→T
008-1	Pueblo Santo Domingo	PS	>95	>95	AB	G542X	3849+10kbC→T

Cystic fibrosis mutations in American Indian population

- Patients with clear diagnosis
- No mutation or only one mutation is found.
- Further information: please contact Lori Williamson at (405)271-8685

American Indian and Alaska Native Populations for the Eight States

- South Dakota 9%(68281)
- North Dakota 5.5%(35228)
- Oklahoma 11.4%(391949)
- Nebraska 1.3%(22204)
- Missouri 1.1%(60099)
- Iowa 0.6%(18246)
- Kansas 1.8%(47363)
- Arkansas 1.4%(37002)