Easy, Cost-Effective Solutions for Targeted Cystic Fibrosis Mutation Analysis

INTRODUCTION

Cystic fibrosis (CF) is one of the most common life-threatening genetic diseases affecting children and young adults, with as high as one in 25 serving as a carrier for the autosomal recessive condition.[1, 3]

CF is characterized by chronic lung disease, pancreatic and gastrointestinal insufficiency, failure to thrive, and infertility. Mutations in the CF transmembrane conductance regulator (*CFTR*) gene on Chromosome 7 have been linked to the disease.[2] SNP genotyping is extremely accurate at detecting prevalent CF mutations, providing an ideal method for cost-effective identification of CF carriers.[3,4,5]

HIGHLIGHTS OF THE MASSARRAY® SYSTEM

- ✓ Flexible, scalable, and cost-effective variant detection
- ✓ Fast, simplified workflow using multiplexed primer sets and universal cycling conditions
- ✓ Rapid interrogation of over 250 samples per day
- ✓ Open platform for custom content

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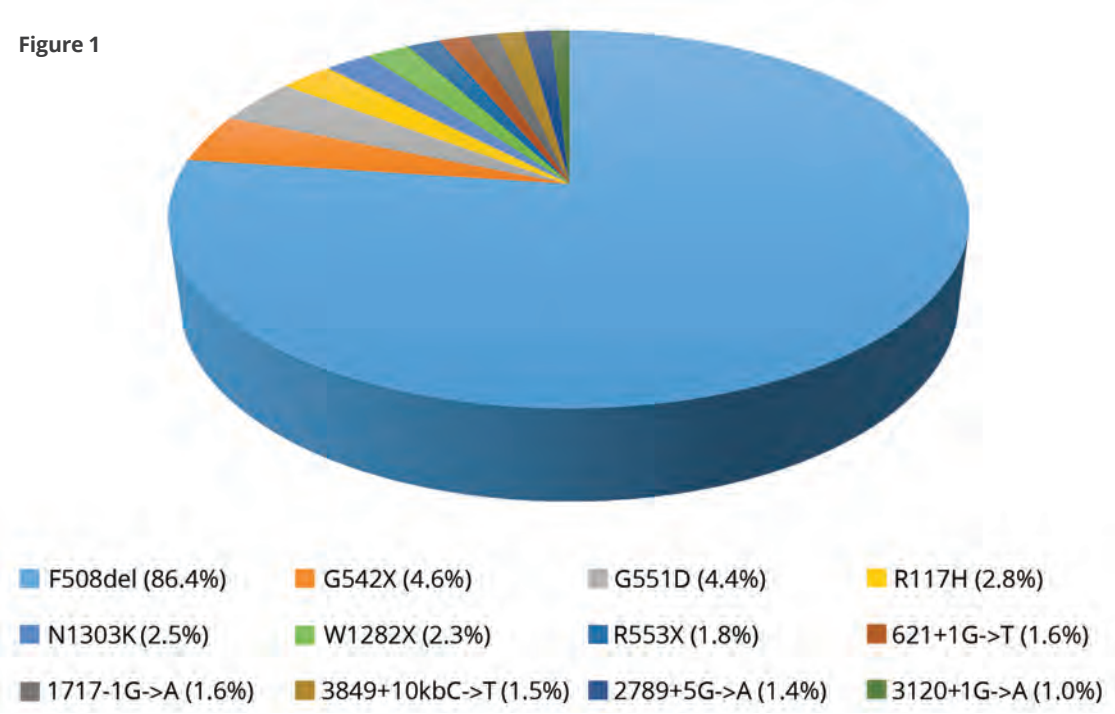
Highly Penetrant Cystic Fibrosis Mutations

The American College of Medical Genetics (ACMG) and the American Congress of Obstetricians and Gynecologists (ACOG) currently recommend routine screening of the most prevalent *CFTR* mutations for all couples who are pregnant or considering pregnancy.[3] Additional mutations provide enhanced coverage for various ethnic groups (allele frequency >0.1% in the general population) and are necessary for effectively screening carriers of non-Northern European descent.[1,7]

Although over 1,700 *CFTR* mutations have been identified, only a few occur at a frequency ≥1%. Studies both in the United States and Europe indicate that >86% of CF carriers have the F508del mutation (Figure 1).

Figure 1



Custom Cystic Fibrosis Analysis with the MassARRAY System

To date, independent laboratories have developed and tested over 100,000 *CFTR* samples using the MassARRAY System.

Agena Bioscience™ now offers custom services to aid in assay design for cystic fibrosis mutation analysis. Table 1 shows examples of *CFTR* mutations which have been tested against well-characterized *CFTR* HapMap samples from the Coriell Biorepository (MUTCF-2) plus additional Coriell samples known to harbor *CFTR* mutations, and showed 100% concordance with the Coriell data.[6]

EXAMPLES OF COMMON *CFTR* MUTATIONS ON THE MASSARRAY SYSTEM					
F508del	I507del	G542X	G85E	R117H	621+1G->T
711+1G->T	R334W	R347P	A455E	1717-1G->A	R560T
R553X	G551D	1898+1G->A	2184delA	2789+5G->A	3120+1G->A
R1162X	3659delC	3849+10kbC->T	W1282X	N1303K	T5/T7/T9
1078delT	394delTT	Y122X	R347H	M1101K	S1255X
1898+5G->T	2183AA->G	2307insA	Y1092X	3876delA	3905insT
S549N	S549R_1645A->C	S549R-1647T->G	V520F	A559T	1677delTA
2055del9->A	2143delT	3199del6	3791delC	406-1G->A	935delA
D1152H	CFTRdele2,3_3′	CFTRdele2,3_5′	E60X	G178R	G330X
K710X	L206W	Q493X	Q890X	R1066C	R1158X
R75X	S1196X	W1089X	G1244E	G1349D	G551S
R560KT	S1251N	S1255P	F508C	I507V	I506V

Table 1

23 ACMG/ACOG-recommended mutations

49 of the other most common variants (allele frequency >0.1%) with known *CFTR* relevance

Additional mutations are also offered through Assays by Agena Custom Laboratory Services.

WORKFLOW

Each sample is subjected to multiplexed PCR using 10 ng genomic DNA, followed by iPLEX® Pro single base primer extension. The extension products are dispensed onto a SpectroCHIP® Array and detected via mass spectrometry using the MassARRAY System.

THROUGHPUT

The MassARRAY System is offered in 24-, 96-, and 384-format configurations and enables sample processing in under 8 hours. Tens to hundreds of samples can be processed per day, providing flexibility in sample throughput and batching requirements

Contact Agena Bioscience for additional information.

REFERENCES

1. Grody WW, Cutting GR, Klinger KW, Richards CS, Watson MS, et al. (2001) Laboratory standards and guidelines for population-based cystic fibrosis carrier screening. *Genet Med* 3(2):149-54.
2. Langfelder-Schwind E, Kloza E, Sugarman E, Pettersen B, Brown T, et al. (2005) Cystic fibrosis prenatal screening in genetic counseling practice: recommendations of the National Society of Genetic Counselors. *J Genet Couns* 14(1):1-15.
3. Update on carrier screening for cystic fibrosis. www.acog.org.
4. Farkas DH, Miltgen NE, Stoerker J, van den Boom D, Highsmith WE, et al. (2010) The suitability of matrix assisted laser desorption/ionization time of flight mass spectrometry in a laboratory developed test using cystic fibrosis carrier screening as a model. *J Mol Diagn* 12(5):611-9.
5. 2013 Cyctic Fibrosis Foundation patient registry annual data report to the center directors. www.cff.org.
6. MUTCF-2 gene mutation panel. www.catalog.coriell.org.
7. Heim RA, Sugarman EA, Allitto BA. (2001) Improved detection of cystic fibrosis mutations in the heterogeneous U.S. population using an expanded, pan-ethnic mutation panel. *Genet Med* 3(3):168-76.

RESEARCH USE NOTIFICATION

While research tests may be performed using either clinical or nonclinical materials, research use devices have no intended clinical use and the testing performed is not designed to provide data addressing or demonstrating safety and effectiveness.

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