MAYO CLINIC LABORATORIES

Test Definition: CFMP

Cystic Fibrosis, CFTR Gene, Variant Panel, Varies

Overview

Useful For

Confirmation of a clinical diagnosis of cystic fibrosis

Reproductive risk refinement via carrier screening for individuals in the general population

Reproductive risk refinement via carrier screening for individuals with a family history when familial variants are not available

Identification of patients who may respond to cystic fibrosis transmembrane conductance regulator (*CFTR*) potentiator therapy

Genetics Test Information

This test includes targeted testing to evaluate over 500 genetic variants including 23 disease-causing variants recommended by the American College of Medical Genetics and Genomics.

For details regarding the specific variants identified by this test see Targeted Variants Interrogated by Cystic Fibrosis Variant Panel.

Testing Algorithm

For more information see Cystic Fibrosis Molecular Diagnostic Testing Algorithm.

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Cystic Fibrosis Molecular Diagnostic Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)
- Targeted Variants Interrogated by Cystic Fibrosis Variant Panel

Highlights

A targeted genotyping array is utilized to detect more than 500 genetic targets associated with cystic fibrosis or cystic fibrosis-related disorder for the purpose of carrier screening or first-tier diagnostic testing.

Method Name

Targeted Genotyping Array

NY State Available

Yes

Specimen

Specimen Type
Varies

Ordering Guidance
If testing is negative, and a diagnosis of cystic fibrosis is still suspected, consider CFTRN / Cystic Fibrosis Transmembrane Conductance Regulator, *CFTR*, Full Gene Analysis, Varies.

Targeted testing for familial variants (also called site-specific or known mutation testing) is available for all genes on this panel under FMTT / Familial Variant, Targeted Testing, Varies. Call 800-533-1710 to obtain more information about this testing option.

Necessary Information
If there is a family history of cystic fibrosis, the known variant in the family should be supplied for best interpretation of results.

Specimen Required
Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: None
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

Forms
1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521)

Specimen Minimum Volume
See Specimen Required

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		
	Frozen		

Clinical & Interpretive

Clinical Information

Cystic fibrosis (CF), in the classic form, is a severe autosomal recessive disorder characterized by a varied degree of chronic obstructive lung disease and pancreatic enzyme insufficiency. The incidence of CF varies markedly among different populations, as does the genetic variant detection rate for the variant screening assay. To date, over 1500 variants have been described within the gene that causes CF, named cystic fibrosis transmembrane conductance regulator (*CFTR*). The most common variant, deltaF508, accounts for approximately 67% of the variants worldwide and approximately 70% to 75% in the North American White population. Most of the remaining variants are rare, although some show a relatively higher prevalence in certain ethnic groups or in certain atypical presentations of CF, such as congenital bilateral absence of the vas deferens (CBAVD). Genetic variants detected by this assay include the 23 variants recommended by the American College of Medical Genetics and Genomics as well as over 450 other variants.

Of note, *CFTR* potentiator therapies may improve clinical outcomes for patients with a clinical diagnosis of CF and at least one copy of a select subset of variants.

See the CF Detection rates table for several ethnic and racial group carrier frequency and variant detection rate. Note that interpretation of test results and risk calculations are also dependent on clinical information and family history.

Table. CF Detection Rates

Racial or ethnic group	Carrier frequency	Variant detection rate*
European American	1/25	94%
Ashkenazi Jewish	1/25	95%
African American	1/65	87%
Hispanic American	1/46	87%
Asian American**	1/90	65%
General US population	1/35	86%

*Rates are for classic CF. Rates are lower for atypical forms of CF and for CBAVD.
**Does not apply to individuals of Japanese ancestry.

A list of *CFTR* variants included in the panel can be found in Targeted Variants Interrogated by Cystic Fibrosis Variant Panel.

Reference Values

An interpretive report will be provided.

Interpretation

All reported alterations are evaluated according to American College of Medical Genetics and Genomics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

This assay will not detect all known disease-associated variants that cause cystic fibrosis or *CFTR*-related disorders. Therefore, the absence of a detectable variant does not rule out the possibility that an individual is a carrier of or affected with this disease.

A negative result does not eliminate the risk of carrier status for any of the included conditions, due to the possibility that the patient carries a variant that is not interrogated with this assay or the rare chance of a false-negative result for a tested variant. For tested variants, the negative predictive value of this screen is greater than 98%. The patient's residual risk to be a carrier after a negative screen is dependent on ethnic background and family history.

A positive control was not available for all variants targeted on this panel. For more information regarding availability of a positive control for each variant see Targeted Variants Interrogated by Cystic Fibrosis Variant Panel. The negative predictive value of these targets is unknown.

Rare variants (ie, polymorphisms) exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(1) This assay was designed to specifically target known disease-causing or likely disease-causing variants. In rare cases, DNA variants of undetermined significance may be identified. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

Multiple in-silico evaluation tools may have been used to assist in the interpretation of these results. Of note, the sensitivity and specificity of these tools for the determination of pathogenicity is currently unvalidated.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Bone Marrow transplants from allogenic donors will interfere with testing. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

An online research opportunity called GenomeConnect (genomeconnect.org), a project of ClinGen, is available for the recipient of this genetic test. This patient registry collects deidentified genetic and health information to advance the knowledge of genetic variants. Mayo Clinic is a collaborator of ClinGen. This may not be applicable for all tests.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus

recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-424. doi: 10.1038/gim.2015.30
2. Quint A, Lerer I, Sagi M, Abeliovich D. Mutation spectrum in Jewish cystic fibrosis patients in Israel: implication to carrier screening. Am J Med Genet A. 2005;136(3):246-248
3. Bobadilla JL, Macek M Jr, Fine JP, Farrell PM. Cystic fibrosis: a worldwide analysis of CFTR mutations-correlation with incidence data and application to screening. Hum Mutat. 2002;19(6):575-606
4. Sugarman EA, Rohlfs EM, Silverman LM, Alitto BA. 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
5. Watson MS, Cutting GR, Desnick RJ, et al. Cystic fibrosis population carrier screening: 2004 revision of American College of Medical Genetics mutation panel. Genet Med. 2004;6(5):387-391
6. Heim RA, Sugarman EA, Allitto BA. Improved detection of cystic fibrosis mutations in the heterozygous U.S. population using an expanded, pan-ethnic mutation panel. Genet Med. 2001;3(3):168-176
7. De Boeck K, Munck A, Walker S, et al. Efficacy and safety of ivacaftor in patients with cystic fibrosis and a non-G551D gating mutation. J Cyst Fibros. 2014;13(6):674-680
8. Carrier Testing for Cystic Fibrosis. Cystic Fibrosis Foundation; Accessed November 14, 2024. Available at www.cff.org/What-is-CF/Testing/Carrier-Testing-for-Cystic-Fibrosis/

Performance

Method Description

The targeted genotyping assay utilizing the ThermoFisher GeneTitan platform is used to detect 500 plus genetic targets, including the 23 disease-causing variants specified in the American College of Medical Genetics standards for population-based carrier screening. For details regarding the targeted disease-causing variants identified by this test see Targeted Variants Interrogated by Cystic Fibrosis Variant Panel. Confirmatory testing of homozygous results is performed as reflex tests when appropriate.

Multiplex ligation-dependent probe amplification, polymerase chain reaction (PCR), relative quantitative PCR, and Sanger sequencing are used to confirm alterations detected by array when appropriate.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday, Wednesday, Friday

Report Available

7 to 21 days

Specimen Retention Time

Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81220
81222

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CFMP	Cystic Fibrosis (CF) Mutation Panel	38404-0

Result ID	Test Result Name	Result LOINC® Value
606027	Result Summary	50397-9
606028	Result	82939-0
606029	Interpretation	69047-9
606030	Additional Information	48767-8
606031	Method	85069-3
606032	Specimen	31208-2
606033	Source	31208-2
606034	Released By	18771-6