

Cystic Fibrosis Transmembrane Conductance Regulator, *CFTR*, Full Gene Analysis, Varies

Test ID: CFTRN

Useful for:

- Follow-up testing to identify variants in individuals with a clinical diagnosis of cystic fibrosis (CF)
- Identifying genetic variants in individuals with atypical presentations of CF (eg, congenital bilateral absence of the vas deferens or pancreatitis)
- Identifying genetic variants in individuals where detection rates by targeted variant analysis are low or unknown for their ancestral background
- Identifying patients who may respond to cystic fibrosis transmembrane conductance regulator (*CFTR*) potentiator therapy

Genetics Information:

- This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in the *CFTR* gene associated with cystic fibrosis (CF).
- Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for CF.

Reflex Tests:

Test ID	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Testing Algorithm:

For prenatal specimens only:

-If amniotic fluid (nonconfluent cultured cells) is received, amniotic fluid culture/genetic test will be added at an additional charge.

-If chorionic villus specimen (nonconfluent cultured cells) is received, fibroblast culture for genetic test will be added at an additional charge.

For any prenatal specimen that is received, maternal cell contamination testing will be performed at an additional charge.

Skin biopsy or cultured fibroblast specimens:

If a skin biopsy is received, fibroblast culture testing will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

Methods:

Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

Reference Values:

An interpretive report will be provided.

Specimen Requirements:

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Submit only 1 of the following specimens:

Specimen Type:	Whole blood
Preferred:	Lavender top (EDTA) or yellow top (ACD)
Acceptable:	Any anticoagulant
Specimen Volume:	3 mL
Collection Instructions:	1. Invert several times to mix blood 2. Send whole blood specimen in original tube. Do not aliquot.
Specimen Stability Information:	Ambient (preferred)/Refrigerated
Minimum Volume:	1 mL
Specimen Type:	Skin biopsy
Supplies:	Fibroblast Biopsy Transport Media (T115)
Container/Tube:	Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.
Specimen Volume:	4-mm punch
Specimen Stability Information:	Refrigerated (preferred)/Ambient
Additional Information:	A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.
Specimen Type:	Cultured fibroblasts
Container/Tube:	T-25 flask

Specimen Volume: 2 Flasks

Collection Instructions: Submit confluent cultured fibroblast cells from a skin biopsy from another laboratory. Cultured cells from a prenatal specimen will not be accepted.

Specimen Stability Information: Ambient (preferred)/Refrigerated (<24 hours)

Additional Information: A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Due to the complexity of prenatal testing, consultation with the laboratory is required for all prenatal testing. Prenatal specimens can be sent Monday through Thursday and must be received by 5 p.m. Central time on Friday in order to be processed appropriately.

Specimen Type: Amniotic fluid

Container/Tube: Amniotic fluid container

Specimen Volume: 20 mL

Specimen Stability Information: Refrigerated (preferred)/Ambient

Additional Information:

1. A separate culture charge will be assessed under CULAF / Culture for Genetic Testing, Amniotic Fluid. An additional 2 to 3 weeks is required to culture amniotic fluid before genetic testing can occur.
2. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Chorionic villi

Container/Tube: 15-mL tube containing 15 mL of transport media

Specimen Volume: 20 mg

Specimen Stability Information: Refrigerated

Additional Information:

1. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 2 to 3 weeks is required to culture chorionic villi before genetic testing can occur.
2. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Confluent cultured cells

Container/Tube: T-25 flask

Specimen Volume: 2 Flasks

Specimen Stability Information: Ambient (preferred)/Refrigerated

Additional Information: **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Stability Information:

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Ordering Guidance:

- This test is not the preferred test for cystic fibrous carrier screening. See CFMP / Cystic Fibrosis, *CFTR* Gene, Variant Panel, Varies.
- Targeted testing for familial variants (also called site-specific or known variants testing) is available for variants identified in the *CFTR* gene. See FMTT / Familial Mutation, Targeted Testing, Varies. To obtain more information about testing option, call 800-533-1710.

Shipping Instructions:

Specimen preferred to arrive within 96 hours of collection.

Interpretation:

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(5) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions:

Clinical Correlations:

- 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.
- If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.
- To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

- Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.
- There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.
- This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

Deletion/Duplication Analysis:

- This analysis targets single and multi-exon deletions/duplications; however, in some instances, single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.

- This test is not designed to detect low levels of mosaicism or to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.
- For detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.
- If the patient has had an allogeneic hematopoietic stem cell transplant or a recent non-leukoreduced blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants:

- Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages health care providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time. Due to broadening genetic knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

Variant Evaluation:

- Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.(5) Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.
- Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.
- Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. These findings will be carefully reviewed to determine whether they will be reported.

CPT Code:

81223
 88233-Tissue culture, skin, solid tissue biopsy (if appropriate)
 88240-Cryopreservation (if appropriate)

Day(s) Performed: Varies

Report Available: 28 to 42 days

Note:

The following referral test code(s) will become obsolete.

Test Name	Test ID	Referral Lab Code	Referral Lab
Cystic Fibrosis (<i>CFTR</i>) Sequencing and Deletion/Duplication	ZW242	3004745	ARUP
GeneSeq PLUS, Prenatal	ZW76	630119	LabCorp

Questions

Contact Michelle Raths, Laboratory Resource Coordinator at 800-533-1710.