

Cystic Fibrosis Testing

At the

The Johns Hopkins University DNA Diagnostic Laboratory

History and Experience

The DNA Diagnostic Lab (DDL) at Johns Hopkins was established in 1978 and has served as the clinical component of the CF Foundation Genotyping Center at Hopkins since 1999. Through our clinical and research testing we have provided CF testing to more than 800 families.

Technology

We use direct DNA sequencing which allows each nucleotide to be examined in both the forward and reverse directions. This offers the ability to detect rare and/or novel mutations, thereby increasing the sensitivity of the test. Sequence based testing has an inherent flexibility that allows the lab to use the same accurate methodology while adapting the test to a mutation identification screening test, or a targeted carrier test, as dictated by each clinical situation. The use of dye-primer sequencing chemistry maximizes our ability to detect heterozygotes over other chemistries available for DNA sequencing.

Laboratory Services

The DDL at Hopkins has 2 genetic counselors available for pre- and post-test consultation to aid referrers in all aspects of the molecular testing process. We are a small academic laboratory specializing in complex genetic testing, and are dedicated to providing diagnostic molecular testing of the type and quality not available elsewhere.

5T/TG Typing

A recent Johns Hopkins study has provided evidence that the TG repeat sequence adjacent to the 5T variant in intron 8 significantly alters its penetrance and allows for revised risk assessment according to the various 5T/TG combinations. You may also find additional information on our web site: (www.hopkinsmedicine.org/dnadiagnostic).

Cystic Fibrosis Related Tests

CFTR sequencing (for mutation identification)

The lab sequences and analyzes the entire coding region, intron-exon boundaries, a portion of the 5' and 3' untranslated DNA, and two deep intronic mutations. This test will detect ~98% of published CFTR mutations as well as novel sequence variations that may be deleterious. Because this test will detect novel changes of unknown clinical significance, it should be used for confirmatory/diagnostic purposes only, and not as a carrier test.

Prenatal Diagnosis

The DDL's direct sequence based approach allows prenatal diagnosis for almost any reported mutation, including rare mutations not included on most American CF panels.

Targeted Mutation testing

The targeted test is ideal for carrier testing in families with known mutations or clinical confirmation of a mutation identified in a research setting, clinical laboratory outside the US or any other non-CLIA certified environment.

Combined 5T-TG Tract Analysis ****NEW****

The newest CF test offered by the DDL is a combined 5T-TG tract analysis. It is well established that 5T is a variably penetrant mutation that can lead to abnormal splicing of exon 9. The presence of 5T plus another CF mutation in *trans* can cause a spectrum of phenotypes: male infertility (~60%), normal phenotype (~40%), atypical CF (<1%). Combined testing of 5T and TG tract length provides more accurate assessment of pathogenic versus benign alleles, thereby influencing disease risk. Situations for 5T-TG tract analysis:

- 5T positive patients with nonclassic CF
- Males with CBAVD
- Other individuals known to carry a 5T

Laboratory Information

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