

1. [How is each mutation listed in CFTR2 characterized?](#)

Each mutation listed in CFTR2 has been evaluated in several different ways. Using all of the information collected, the CFTR2 team has labeled each mutation as one of the following:

- CF-causing mutation
- Non CF-causing mutation
- Mutation of varying clinical consequence
- Mutation of unknown significance

For more information about these categories and to learn how mutations were evaluated, please click [here](#) .

2. [What is the source of the information included on the website?](#)

The clinical data for the CFTR2 database was assembled by collecting information about CF patients from national CF registries and large CF clinics from around the world. We will be collecting additional clinical information from other large CF centers throughout the world that will be incorporated into the database as the information becomes available. Please see the section "CFTR2 Contributors" under the Quick Links to view a list of registries that have contributed information to the CFTR2 database.

3. [What is done to protect the privacy of the patients whose clinical information is included in the CFTR2 database?](#)

Patient names are not included in the CFTR2 database, and all patient information in the database is de-identified. This means that we have no way to link the information in the database back to any individual patient. The CFTR2 project was approved by the Institutional Review Board at the Johns Hopkins University Hospital, the Patient Registry review committee of the US Cystic Fibrosis Foundation, and the Canadian CF Patient Registry oversight committee.

4. [Do all CFTR mutations cause CF?](#)

No, not all mutations of the CFTR gene cause CF. Most of the mutations included in the CFTR2 database cause CF, but some of the mutations included in the database do not cause CF. (These mutations are called "non CF-causing mutations," meaning that they do not cause disease.) Typically, the term "mutation" refers to **any** genetic difference, not just the ones that cause disease. Sometimes the terms "polymorphism" or "neutral variant" are used for mutations that do not cause disease. Only patients who have been diagnosed clinically with CF are included in the CFTR2 database. The cause of CF in some of these patients is not clear.

5. [How can you determine whether a particular CFTR mutation causes CF?](#)

To determine whether a particular mutation causes CF, we can use 3 different criteria:

- a. Clinical Characteristics of patients who have one copy of the mutation in question and one copy of another mutation that is known to cause CF. In these patients, we have analyzed the sweat chloride, lung function, pancreatic function and sputum microbiology (all major clinical characteristics abnormal in CF patients) to determine whether individuals with the mutation in question have clear evidence of CF. If the evaluation of

the clinical criteria is not sufficient to determine whether or not a particular mutation causes CF, we then review the functional testing and/or prediction algorithms to help determine whether the mutation causes CF.

- b. Functional testing. By looking at cells that have had the mutation in question inserted into them, we can characterize the degree of dysfunction caused by the mutation. We have reviewed previously published experiments, and in cooperation with Vertex Pharmaceuticals (Cambridge, MA, USA), are conducting experiments to assess the disease liability of a broad range of mutations.
- c. Mutation prediction algorithms. We also can use mathematical models to predict whether or not a given mutation will cause disease.

6. [What if the mutation for which I am searching is not shown on CFTR2.org?](#)

A CFTR mutation may not be shown on the CFTR2.org website for two reasons. First, the mutation may not have been seen in any of the 35,000 patients whose information is contained in the CFTR2 database. Therefore, the mutation would not be included in the database. Second, only the 160 most common CFTR mutations are included on the CFTR2 website at the current time. The mutation for which you are searching may be so rare that it is not included at this time. To find out whether the mutation has been described in CFTR1, [click here](#). We will continue to add mutations to CFTR2 to increase the list of mutations that are described. We encourage you to check back in the future to see if the mutation for which you are searching has been added.

7. [Why is the mutation for which I am searching referred to by a different name in CFTR2?](#)

Many commonly-known mutation names have changed in accordance with the Human Genome Variation Society (HGVS), which sets standards for describing genetic changes in all diseases. CFTR2 includes both the traditional (or "legacy" name) as well as the most up-to-date naming system for CFTR mutations.

8. [How long do people with a given pair of mutations \(sometimes referred to as "genotype"\) live?](#)

There is a great range of life expectancy in patients with CF. In general, the life expectancy of CF patients is improving every day as a result of better CF care. Many different factors contribute to determining how long a person with CF will live. Genotype, or an individual's specific combination of mutations, is a poor predictor of survival, so we cannot predict how long people with a given pair of mutations will live.

9. [Does my genotype make me more likely to become infected with Burkholderia cepacia, to get diabetes, or to become pancreatic insufficient?](#)

In general, we can predict whether a patient will be pancreatic insufficient or pancreatic sufficient based upon the patient's genotype (the patient's specific combination of mutations). However, our ability to make this prediction accurately becomes less reliable as the patient ages. For nearly all other clinical traits (such as infection with Burkholderia cepacia, developing diabetes, or lung function), genotype is NOT predictive, meaning that we cannot predict these traits accurately based upon a person's genotype. The possible exception to this rule is male infertility. Nearly all males with CF-causing mutations will be infertile.

10. [Are any particular genotypes amenable to gene therapy?](#)

Gene therapy is a treatment in which the mutated copy of the CFTR gene is replaced or supplemented by a healthy copy of the gene. Research continues into this therapy, but it is not currently available in the United States outside of a research setting. Mutation specific therapy is an alternative to gene therapy that also is under investigation. Different mutations of the CFTR gene cause CF in different ways. In mutation specific therapy, medication is used to correct the defect caused by a particular CFTR mutation. There are clinical trials underway for certain mutation specific therapies, but these therapies have not yet been approved by the U.S. or European regulatory agencies. We will add information about mutation specific therapies to the CFTR2 website when they are approved.

11. [Will new drugs work for my mutation?](#)

There are several promising new medical therapies being developed that may help patients with CF. Some of these medicines work only for patients who carry at least one copy of certain mutations. The drug ivacaftor (Kalydeco) was recently approved by the U.S. Food and Drug Administration for people with cystic fibrosis ages 6 years and older who have at least one copy of the mutation G551D. In people with this mutation, ivacaftor helps the defective CFTR protein work at the surface of the cell. This is the first example of a CF drug that works for a specific mutation. Research is being conducted to find new therapies that will work for other CFTR mutations. We will add information about other therapies for specific mutations to the CFTR2 website as they are approved. For information about enrolling in CF clinical trials, please visit the U.S. CF Foundation or the European CF Society website. See also the glossary entries on "Mutation Specific Therapeutics" and "Mutation Classes".

12. [Why is the website called CFTR2?](#)

"CFTR" is the abbreviation for the "Cystic Fibrosis Transmembrane Conductance Regulator" gene. This is the gene that causes cystic fibrosis. The CFTR2 website is designed to provide information about the Clinical and Functional Translation of specific CFTR mutations. This means that the website provides information about what is currently known about the clinical signs and symptoms associated with specific CFTR mutations. It is called CFTR2 because it links to the Cystic Fibrosis Mutations Database (now called CFTR1), the original website devoted to the collection of mutations in the CFTR gene for the international cystic fibrosis genetics research community. For more information about CFTR1, click [here](#).

13. [How does the mutation R117H work?](#)

R117H is a fairly common CFTR mutation. The severity of the R117H mutation is influenced by a region of the CFTR gene called the poly-T tract. Depending on which form of the poly-T tract is present (5T, 7T, or 9T), different individuals with R117H and another CF-causing mutation may have very different clinical features.

For more detailed information about how R117H and the poly-T tract work, click [here](#).

14. [Why are only some of the published articles about specific mutations listed under the "Literature Review" section?](#)

In the "Literature Review" section, we provide references for research publications that demonstrate how a particular mutation causes the CFTR protein to function improperly. The list of publications we have included is not intended to be a comprehensive list. We have not

included publications that describe the clinical findings associated with particular mutations.