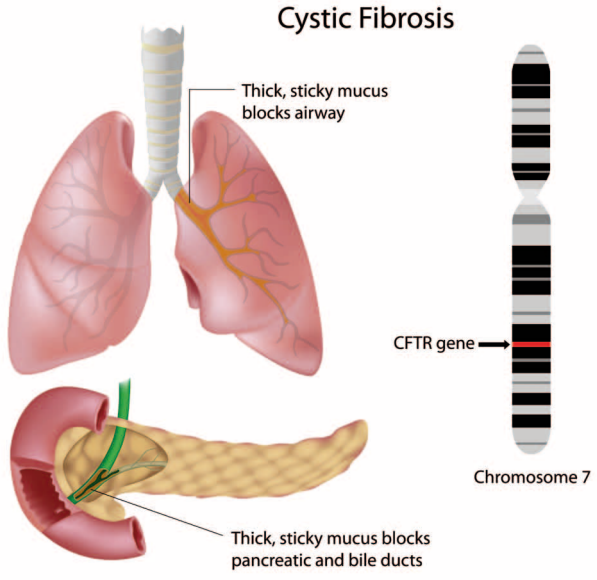
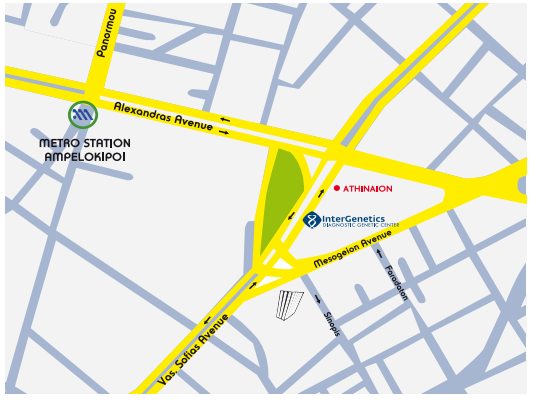
Cystic fibrosis (CF) is the most common genetic disease in the white Caucasian population, with serious consequences for the health and life span of the affected person.

The disease manifests in early infancy, although sometimes it may not be recognized immediately. It affects mostly the mucous glands of the body, resulting in bodily secretions which become thick and thus clog the pores or ducts of many organs, including the lungs, pancreas and liver.

In newborns and young children who are suspected to be affected, a “sweat test” is usually applied and of course full verification is obtained only through molecular genetic testing.

In men, there are specific disease mutations which are associated with infertility.





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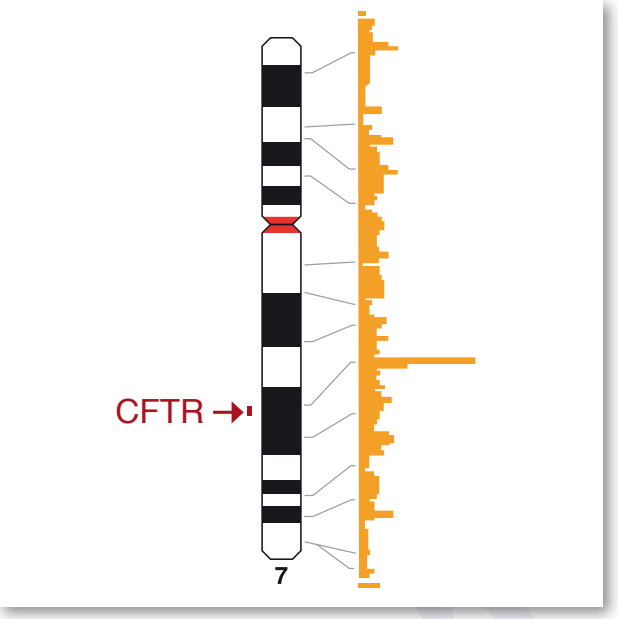
CYSTIC FIBROSIS THE DISEASE AND GENETIC TESTING



- ✓ *specially designed mutation panel for the Greek population, detecting 85% of mutations in carriers of the disease*
- ✓ *extended genetic testing for >99% of mutations in affected individuals and in high-risk cases*
- ✓ *constant and successful participation in external quality control schemes - CF Network*

How is the disease inherited and what is the frequency

The disease is caused by inherited mutations in the CFTR gene and is transmitted as an autosomal recessive disorder.

Individuals who have a mutation in one of the two chromosomes-copies of the gene are carriers and are not affected. The frequency of carriers of the disease in the Greek population is about 1/25.

If both parents are proven to be carriers of the same or (more often) different mutations, then they have a 25% chance to transmit both mutations to their children, which in this case will be affected.

The incidence of the disease in Greece is about 1/2,500 newborns.

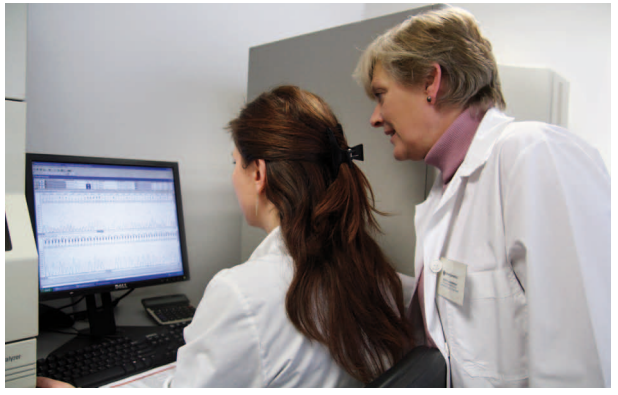
Diagnostic issues

Carriers of the disease are perfectly healthy, with no recognizable clinical symptoms and therefore without some way to identify them, while the gene is relatively large in size with many possible mutations (>1,500).

Furthermore, mutations in the gene are encountered with varying frequency in different ethnic groups, with very significant differences, for example, among the Northern European population and the Mediterranean population.

The only way to identify carriers of the disease is by molecular genetic testing (detection of mutations in the CFTR gene) in the general population (carrier detection).

In many countries, specific guidelines have been issued concerning recommendations for molecular genetic testing for cystic fibrosis in all couples. Typically, genetic testing starts with the mother, before or very early in pregnancy.



A key element of carrier testing concerns the proportion of mutations which are detected in the specific population. Due to the large number, but also the different frequencies of mutations in different ethnic populations, it is almost impossible to design a specific panel of mutations to be tested worldwide. For this reason we apply, in accordance with international guidelines, carrier testing for gene mutations, covering at least 85% of all CF mutations in the Greek population.

In special high risk cases, we apply extended mutation testing of all exons of the CFTR gene and splice sites, through DNA sequence analysis (automated bi-directional fluorescent DNA sequencing), covering >99% of the mutations for the disease.

Important note: as for most recessive genetic disorders (e.g. thalassemia) we never perform direct testing of the fetus.

Genetic testing during pregnancy

In prenatal testing, especially in high-risk cases, such as embryo carrier of the F508del mutation or embryo with echogenic bowel, it is desirable to immediately test the parents (and not the fetus), covering the largest possible proportion of mutations.
In case both parents are found to be carriers, it is necessary (and relatively simple) to test the fetus, which in this case has a 25% chance of being affected

We wish to stress once more that genetic testing of cystic fibrosis should not be directed to the fetus but primarily to the parents (carrier detection).

Some useful facts and figures

- 1/700 couples are both carriers of the disease, with a 25% chance of having affected children
- if a mutation is not detected in the mother (85% detection), then the risk of having an affected child (without testing the father) is ~ 1/17,000
- if a mutation is detected in the mother (heterozygous carrier), then the risk of having an affected child (without testing the father) is ~1/100. If the father is tested for 85% of mutations and is negative, the above risk is reduced to ~1/700
- if the mother is a carrier and if the father is tested with >99% mutation detection and is found negative, then the risk is further reduced to ~1/4,000

Knowledge of the genetic lesion which leads to the manifestation of cystic fibrosis is an invaluable (if not necessary) tool for further management of the affected individual by the referring physician.

Without this knowledge, it is also extremely difficult to offer genetic counseling for disease progression, for reproductive options of the couple but also for assessing the overall impact in the family.