# CYSTIC FIBROSIS

## " YOU BREATH WITHOUT THINKING... I ONLY THINK ON BREATHING

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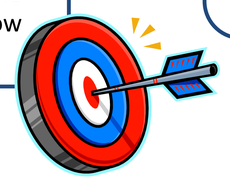
### Objective:

Make informative work on cystic fibrosis (CF), giving a general view of the most important aspects of the disease and new lines of research in order to cure the different problems that arise with CF.

I decided to do this work because during the degree we have constantly made literature review jobs, in which we showed what we have learned about a topic, by consulting various sources of information. In contrast, with informative work I think that you have to show not only the knowledge acquired during the execution of the work, but also the ability to convey this information to an audience with a low knowledge about the topic.



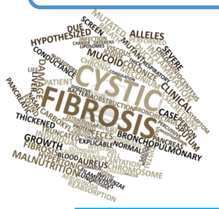
### Materials and Methods:

To carry out this work I mainly took information from articles and doctoral theses and although I have consulted various informative websites, related both to CF and other diseases, to get an idea of how it should be the best way of communicating information as clearly as possible to an audience with little knowledge about this topic. In addition, I have also based my search for information on online videos and I have done a course that allowed me to make an informative website about CF.

### Results:

As a result, I have made an informative website (http://victorsanchezclares.wix.com/fibrosisquistica) with the aim to allow anyone to learn about the pathogenesis of CF or how are currently investigations on treatments for the disease and I have made a informative class in a High School for scientific students.
In this section I summarize the most important aspects of the work, which are explained widely on the web.

#### Introduction:

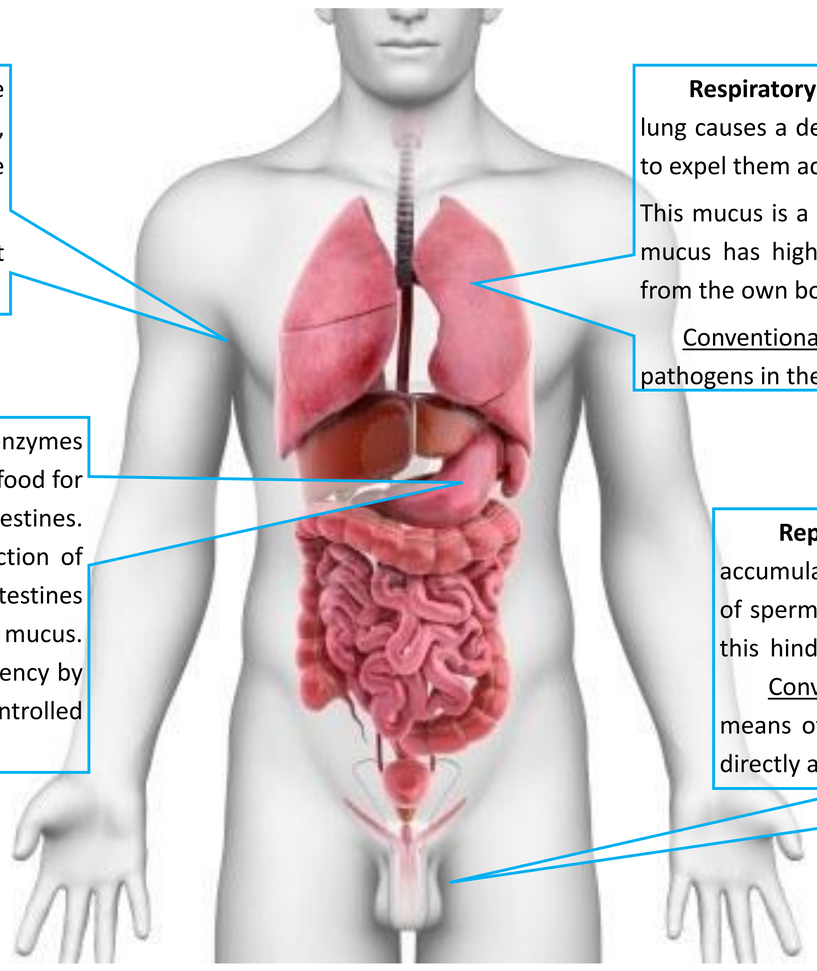



CF is a inherited disease, autosomal recessive, with an incidence of 1:2500. Is caused by a mutation in the CFTR gene which encodes a transmembrane transporter that acts as a channel of chlorine ($Cl^-$) in the membranes of epithelial cells. Its gene product also acts as a regulator of other channels, such as sodium ($Na^+$).

These transporters CFTR play an important role in the functional regulation of secretory tissues organs and/or absorptive. Its functional loss causes:

**Sweat glands:** The inability to reabsorb $Cl^-$ at the same time prevents the capacity of this channel to regulate the $Na^+$ channel, causing an incontrollable entrance of $Na^+$ in the ducts of the sweat glands.

This will generate a very salty sweat that is irrelevant pathologically, but is very useful for diagnosis.



**Respiratory system:** The uncontrolled entrance of $Na^+$ and water within the cells of the lung causes a densification and solidification of the outer mucus that produce the inability to expel them across the airways.

This mucus is a suitable nest for selected pathogens that cause respiratory infections. This mucus has high concentrations of other ions that remain defensins inactive (antibiotics from the own body), thus hindering the removal of these infections.

Conventional treatment: Targeted mainly to clear the airways and eliminating pathogens in them.

**Digestive System:** Pancreatic insufficiency due to digestive enzymes secreted by the pancreas, which are proteins responsible for slicing food for being absorbed, are retained in the ducts before they reach the intestines. These enzymes will be activated prematurely, causing the destruction of the pancreas and a serious state of malnutrition. Bile ducts and intestines are also affected, which also generate an accumulation of thick mucus.

Conventional treatment: Targeted to combat pancreatic insufficiency by administering synthetic pancreatic enzymes, combined with a controlled and plenty diet , rich in fiber and water.

**Reproductive System:** Infertility, in 98% of male patients, due to the accumulation of mucus in the tubes that carry sperm, causing azoospermia (lack of sperm in the semen). In women, the cervical mucus is usually more thick and this hinders the progress of the spermatozoa, but it does not cause infertility.

Conventional Treatment: There is no treatment for this problem, although by means of biopsies or aspirations it is possible to obtain sperm from the testes directly and subsequently use them for insemination or in vitro fertilization.

#### Research in new therapies:

**Animal model:**

The experimental animal is one of the fundamental parts in the biomedical sciences.

Animal models used in the study of diseases are animals that have been genetically modified to express a particular disease, so they can act as models to study various treatments before using them in humans. The main animal model is the mouse.

In the CF research, they used mouse as animal model, but it was not good because it does not develop the typical respiratory and pancreatic problems from patients with CF. Finally, in 2008-2009, new animal models were developed, as ferret and pig, which are considered good models of CF due to its similarity to human in terms of the respiratory system biology. Getting better animal models has allowed much progress in the study of these diseases.

The technology used for obtaining these animals is known as somatic cell nuclear transfer (SCNT).

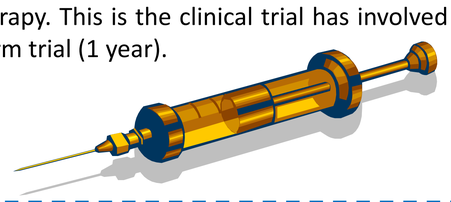
**Gene Therapy:**


One of the most promising line of research for the future treatment of CF is gene therapy, that pretend to replace the use of medicines by gene delivery using viral or non-viral vectors. These will replace the lack of proteins and functions that for some reason patients do not have.

CF is a good candidate for gene therapy because it has a very favorable number of features for this treatment: it does not require a recovery of all the CFTR and the target tissue to treat (airways) is easily accessible.

Despite all these benefits, today there is no drug for CF patients obtained by gene therapy. This is mainly due to sophisticated physical and immunological barriers presented by the lungs.

Actually, the Gene Therapy Consortium for Cystic Fibrosis in the UK have begun a new clinical trial for treating respiratory problems by using non-viral gene therapy. This is the clinical trial has involved more patients (130 patients) and it going to be the longest term trial (1 year).



### Conclusions:

1. Despite the apparent facilities that present this disease to be treated by gene therapy, it has not been possible yet to obtain an effective drug.
2. Obtaining a good animal model when studying and researching about human disease is very important.
3. It is surprisingly the large amount of people and associations that are dumped on this issue and that support both patients and family members.

### Bibliography:

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3. Alton EW, et al. (2013). *A randomised, double-blind, placebo-controlled phase IIB clinical trial of repeated application of gene therapy in patients with cystic fibrosis.* Thorax. doi: 10.1136/thoraxjnl-2013-203309.