European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

Three small genes are potentially implicated in Cystic Fibrosis

Authors:

Marie-Laure Endale Ahanda[1] , Thierry Bienvenu[2] , Isabelle Sermet -Gaudelus[3] , Laurent Mazzolini[4], Aleksander Edelman[3] , Rima Zoorob[5] and Noélie Davezac[6].

Affiliations:

[1]INRA, UMR 1313 Génétique Animale et Biologie Intégrative, Domaine de Vilver t F-78350 Jouy-en-Josas, France
[2]Inserm U567 - CNRS UMR 8104 - IFR 116 Institut Cochin 22, rue Méchain 75014 PARIS France
[3]Inserm U845 Université Descartes Paris 5 156 rue de Vaugirard 75730, Paris Cedex 15, France
[4]CNRS UMR 5088 LBCMCP Université de Toulouse, 118 route de Narbonne 31062 Toulouse Cedex 09
[5]Inserm UMR-S945 Institut Fédératif de Recherches (IFR) 113 Immunité-Cancer-Infection-Hôpital Pitié-Salpêtrière-83 Bld de l'Hôpital -75651 Paris Cedex 13
[6]CNRS UMR 5547 Université de Toulouse, 118 route de Narbonne 31062 Toulouse Cedex 09

What was your research question?

Even though Cystic Fibrosis (CF) is mainly considered as an inherited disease with only one gene involved, numerous findings argue for a more complicated disease implying other genes also. A region in our DNA (genetic material) is suspected to contain genetic factors that have a relation to the severity of CF: in this region, we encounter genes called microRNA (miRNA). MiRNA are small genes that can regulate the activity of hundreds of genes in the cell and play a role in every aspect of biology. We thus addressed the yet few investigated question: would some microRNA of this region be implicated in Cystic Fibrosis?

Cystic Fibrosis Research News

Why is this important?

The variability of symptoms such as lung dysfunction, obstruction of the bowels or diabetes, exists among patients bearing the DeltaF508 mutation in the CF Transmembrane conductance Regulator gene (CFTR) and has to be explained to understand mechanisms involved in CF. The identification of other genes than CFTR (called modifier genes) implicated in the severity of CF is thus crucial for personalised medicine and the development of novel therapeutic approaches as the products of these genes become immediate targets.

What did you do?

Here we studied a group of patients bearing the DeltaF508 mutation in CFTR for potential other genetic variations. These variations between patients are located in the region predicted to contain genes that could modify CF severity and coding for three miRNA. To analyse the presence of the miRNA, we used cultured cells mimicking CF (with the deviant form of CFTR).

What did you find?

First, we identified three genetic variations in the three miRNA in the genetic material of the CF patients. Second, using cells mimicking CF, we found that the quantity of two of them was increased.

What does this mean and reasons for caution?

Two genetic variations would impact these miRNA and could thus modify the severity of CF. An exciting finding was that the increase in two miRNA induces the same modifications of the biological functions that these observed in CF patients. This analysis places two of the miRNA as important factors in the different mechanisms that are disrupted in CF, suggesting that modifications of their activity would have a real influence on the evolution of the disease.

What's next?

Next, the role of these genetic variations in miRNA function is an important question. The expression of these miRNA in cells from groups of patients bearing the deltaF508 mutation would be helpful in the understanding of the role of these small genes in CF and could eventually become a therapeutic target or a marker of the severity of the disease.

Original manuscript citation in PubMed

cfresearchnews@gmail.com

Cystic Fibrosis Research News

http://ac.els-cdn.com/S1569199315000533/1-s2.0-S1569199315000533-main.pdf?_tid=a7260a84-fee1-11e4-8f5f-00000aab0f6c&acdnat=1432120765_2abfa795627539bdb6e07da06d03937b

cfresearchnews@gmail.com