Title:
Immune response of polarized cystic fibrosis airway epithelial cells infected with Influenza A virus

Authors:
Aderonke Sofoluwe, Alice Zoso, Marc Bacchetta, Sylvain Lemeille, Marc Chanson

Affiliations:
Faculty of Medicine, University of Geneva, 1211 Geneva, Switzerland

What was your research question?
People with cystic fibrosis (CF) suffer from severe bacterial and viral infections in the lungs. In this study, we asked how the immune response of CF airway cells is abnormally regulated when exposed to the bacterium Pseudomonas aeruginosa or the virus influenza.

Why is this important?
The CF airways are highly susceptible to viral and bacterial infections and the immune response of the body is unable to fight efficiently these infections. We reasoned that there are underlying genetic factors that could explain this reduced function. Understanding why this could lead to the development of therapies that restore the immune system in the lungs.

What did you do?
We monitored gene expression changes in airway cells exposed to either the bacterium or the virus. We compared gene expression in normal cells and in cells where the CF gene (CFTR) was inactivated. When genes are activated, a copy of the gene sequence, called mRNA, is produced. We thus detected mRNAs to identify genes differently activated in CFTR-inactivated and normal airway cells.

What did you find?
We found many different mRNAs in CF airway cells infected by the virus. Most interesting was that a group of genes known to fight viruses were downregulated (scaled down). We could also predict from these findings what factors could link the downregulated genes to CFTR. In summary, we unveiled the signature of CF cells infected with the flu virus.

What does this mean and reasons for caution?
Cystic Fibrosis Research News

Our findings revealed target genes that could contribute to a defective immunity of CF airway cells to viral infection. This is important because this defect may lay the ground for a secondary bacterial infection; a process called superinfection, that is frequently associated with severe pulmonary exacerbations in people with CF. The latter theory remains, however, to be tested.

What’s next?
Genes contain the coding sequence of proteins; we need now to evaluate whether the proteins encoded by the genes identified here are indeed altered in terms of expression and function. This is pre-condition to evaluating the development of strategies to reduce severe inflammation during superinfection of the lungs.

Original manuscript citation in PubMed