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Cystic Fibrosis Research News

Title:

***FAM13A* is a modifier gene of cystic fibrosis lung phenotype regulating rhoa activity, actin cytoskeleton dynamics and epithelial-mesenchymal transition**

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What was your research question?

Although cystic fibrosis (CF) is due to mutations in the *CFTR* gene, considerable disease variability among patients suggests the influence of other genes called "modifier genes". In this study, we ask if the *FAM13A* gene influences lung disease severity of CF patients and what is its function in the lung.

Why is this important?

It is estimated that modifier genes could contribute up to 50% of the lung function variability. Previous genetic studies have already identified the location of several of these modifier genes, but few have evaluated their functions. The characterization of modifier genes, such as *FAM13A*, will offer not only a better understanding of their function in the lung but may also help to discover new therapeutics targets.

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What did you do?

To determine if *FAM13A* influences the lung function of CF patients, we performed a genetic analysis in a large cohort of 1,222 French CF patients. Next, we performed *in vitro* studies in order to understand the presumptive biological role of FAM13A in the lung. These studies were done with epithelial cells isolated from the lung and inflammatory molecules known to be important in CF disease. To understand the function of FAM13A, we decreased its expression in lung cells and examined the consequences on the cell behaviour such as the epithelial cell morphology.

What did you find?

We found that *FAM13A* was indeed a modifier gene of CF lung function. We observed that the FAM13A protein was expressed in lung epithelial cells and that the inflammatory context of CF induced a decrease of its expression. Finally, we observed that lung epithelial cells exhibited a change in their morphology when the expression of FAM13A was reduced.

What does this mean and reasons for caution?

This work indicates that FAM13A plays a role in the lung function of CF patients. The contribution of this gene to lung function is however relatively small and more work is needed to explain how *FAM13* may influence the lung function of CF patients. Our *in vitro* experiments suggest that FAM13A protein is important for the cell architecture and possibly to the lung tissue integrity. The limitations are the use of isolated cells from the lung, which may not reflect the role of FAM13A in the lung in vivo.

What's next?

In order to have a better understanding of the role of FAM13A on the lung function of CF patients, further studies will decipher if FAM13A has an impact on CFTR function *in vitro* and *in vivo*.

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