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Cystic Fibrosis Research News

Title:
Pathological remodeling of distal lung matrix in end-stage cystic fibrosis patients

Lay Title:
Breakdown of lung proteins causes structural damage in cystic fibrosis lungs

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What was your research question?

The lungs are made up of many cell types that are supported by a 3D protein network called the matrix. The matrix serves as scaffolding on which cells grow. In our study, we wanted to understand how proteins in the matrix are altered in people with cystic fibrosis.

Why is this important?

The lung matrix supports the function of the lung and gives them elasticity allowing the lung to stretch when inhaling and return to their normal size after exhaling. The lung matrix also provides cues to the cells in the lung telling them how to behave. These cues can include the number and types of proteins found in the matrix, as well as their 3D architecture, shape, and stiffness of the proteins. The communication between cells and the matrix impacts inflammation, the response to injury, and tissue healing in the lung. We wanted to understand the role that the lung matrix plays in these processes in people with cystic fibrosis.

What did you do?

When people with cystic fibrosis had undergone lung transplantation, we obtained a portion of their diseased lungs which had been removed. We then looked for the supporting lung proteins found in the matrix and recorded the number and types of proteins. We also used imaging techniques to analyse the structure of these proteins.

What did you find?

We found that in people with cystic fibrosis most supportive lung matrix proteins are broken down, including elastic proteins that allow the lungs to stretch and structural proteins that serve as a thin barrier between inhaled air and circulating blood. We also observed decreased amounts of proteins that allow the matrix to communicate with the lung cells. These proteins regulate responses to infection and healing of lung tissue.

What does this mean and reasons for caution?

Our findings show that cystic fibrosis causes changes to the lung matrix, which is the lung environment outside of the cells. Today's CFTR modulator therapies work really well in correcting the underlying cause of cystic fibrosis in the cells; however, they do not directly act on the lung environment which includes the supporting lung matrix. Therefore, it is important to understand how cystic fibrosis leads to changes in the lung matrix, especially for adults with cystic fibrosis who had a lot of lung damage before they started CFTR modulator therapy.

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We may be able to repair the supporting lung matrix with drugs, and our study identified proteins that could be targets for these drugs and inform future studies.

What's next?

Now that we know that the supporting lung matrix proteins in cystic fibrosis are largely broken down, it is important to understand how these changes affect cells in the lung. Our study only analysed *end-stage* cystic fibrosis lungs. To identify treatments that can prevent the breakdown of the lung matrix, it is important to analyse lung matrix proteins in tissue biopsies at early stages of disease. Finally, whether CFTR modulators and other drugs are able to allow the lung matrix to repair and heal itself should be studied in the future.

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