



Cystic Fibrosis Research News

Title:

COMPARISON OF EX VIVO AND IN VITRO INTESTINAL CYSTIC FIBROSIS MODELS TO MEASURE CFTR-DEPENDENT ION CHANNEL ACTIVITY

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What was your research question?

Can we develop new test models for cystic fibrosis (CF) using cells from patients which have been grown in the laboratory? CF is caused by mutations in a protein called CFTR that affects how cells transport salts (ions) and fluids. The transport of salt and fluid in cells freshly taken from patients (ex vivo) was compared to salt and fluid transport in the same cells after they had been grown in the laboratory for a period of the time (in vitro).

Why is this important?

Laboratory tests on cells from patients play an important role in the development of new drugs and in studying individual characteristics of the disease. Tests that can be performed on freshly isolated patient cells are limited as only a small number of cells can be safely taken from the patient. If we use new technology that allows us to greatly expand the number of cells in the laboratory, the number of tests is virtually unlimited. These laboratory-grown cells can be stored in frozen containers and thawed when needed. These cells can be a very important resource for CF research, provided that the patient-specific properties of the cells do not change by the laboratory process.

What did you do?

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We first compared salt transport in fresh gut tissue taken from the rectum of 12 people with severe to milder forms of CF, or healthy people. Next, we grew the cells of the gut tissue in the laboratory as three-dimensional (3D) miniature guts. We then studied how fluid transport was different between cells from the healthy controls and the people with CF. We also studied salt transport in the miniature guts we grew in the laboratory using a newly developed test. We compared the results from the three models to see how differences between healthy controls and people with CF were represented.

What did you find?

We found that the properties of the cells grown in the laboratory were essentially similar to those of freshly isolated cells.

What does this mean and reasons for caution?

Our findings imply that cells grown in the laboratory can copy the CF defect that is observed in freshly isolated cells. This means that these laboratory-grown cells can play an important role in studying the individual characteristics of CF, such as how much function of the CFTR protein is affected and can the CFTR function be restored by drugs. As this is a first proof-of-concept study, these observations need further testing in new studies.

What's next?

The laboratory models can be used to further characterize salt and fluid transport in the intestine, and to study other cell properties that are affected by CF such as mucus or bacterial interactions. In addition, we can compare how the CF defect in the intestine compares to the defect in the airways.

Original manuscript citation in PubMed

<https://www.ncbi.nlm.nih.gov/pubmed/?term=COMPARISON+OF+EX+VIVO+AND+IN+VITRO+INTESTINAL+CYSTIC+FIBROSIS+MODELS+TO+MEASURE+CFTR-DEPENDENT+ION+CHANNEL+ACTIVITY>

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