

Cystic Fibrosis Research News

Title:

Cell signaling and regulation of CFTR expression in cystic fibrosis cells in the era of high efficiency modulator therapy

Lay Title:

What happens with CFTR inside human cells affected by cystic fibrosis and how the latest CF drugs change the effects.

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What was your research question?

Cystic fibrosis (CF) is a chronic disease, which causes thick mucus build up in lungs and dysfunction of other body parts because of the absence or malfunction of a protein called CFTR. In this review, we aim to describe some of the ways CFTR function is governed in human cells (i.e. 'regulatory mechanisms').

Why is this important?

Understanding how CFTR is regulated is very important because it can help to develop novel therapies to restore its function even in those CF patients who do not respond to the current CF drugs. Understanding whether the current CF medications work through these regulatory mechanisms may explain why some people do not respond to the available therapy. It may also inform how to use these mechanisms to make the drugs more effective.

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What did you do?

Based on our unique expertise, each of us described a specific mechanism of CFTR regulation. We reviewed the most up-to-date information published in scientific journals and summarised our findings in a brief paragraph. We also prepared an image to help understanding how the different mechanisms work all together to govern CFTR.

What did you find?

We found that CFTR is very finely regulated in different ways inside human cells. There are very precise mechanisms that control how new CFTR channels are “produced” by the cell, while others regulate CFTR function. For example, we described that CFTR protein needs some modifications called ‘phosphorylation’ to work in our cells. Studies done in a research laboratory suggest that helping the phosphorylation of CFTR can make the latest triple combination CF therapy more effective. However, we found that still little is known about how these CF therapy affects all of the CFTR regulatory mechanisms.

What does this mean and reasons for caution?

This means that, while we understand at a basic level how CFTR is governed in human cells, we do not know the exact impact of the CF drugs on these mechanisms. Although we improved the efficacy of the triple combination therapy when we acted on one of the CFTR regulatory mechanisms in the lab, more studies are needed to translate this finding and determine whether it benefits people with CF.

What’s next?

More research will be done on these regulatory mechanisms in presence of the triple combination therapy, first in the lab and then eventually in clinical trials to translate lab-based findings into clinical practice.

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