European Cystic Fibrosis Society

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Cystic Fibrosis Research News

Title:

AP2 α modulates cystic fibrosis transmembrane conductance regulator function in the human intestine

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What was your research question?

We aimed to identify a factor specifically in the intestine that controls the function of the cystic fibrosis transmembrane conductance regulator (CFTR). CFTR helps to regulate fluid and electrolyte balance in cells and contributes to the proper function of certain organs by maintaining a proper balance of salt and water across the cell surfaces.

Why is this important?

We examined a specific factor (AP2-alpha) that binds to CFTR only in the intestine, to determine whether it can modulate CFTR function. We found that inhibition of this factor increased CFTR ion transport on the surface of the intestine. It is possible that inhibition of this factor may also increase CFTR mediated salt and water transport in the CF intestine and thus would be helpful in ameliorating the constipation in CF.

What did you do?

In laboratory tests we examined a specific factor (AP2-alpha) that binds to CFTR only in the intestine, to determine whether it can affect CFTR function.

What did you find?

We found that when we depleted AP2-alpha in intestinal cells expressing CFTR, that CFTR function was increased because less CFTR entered the cells. AP2-alpha binds to CFTR.

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What does this mean and reasons for caution?

It is likely that a "small molecule" drug can be developed to increase CFTR function in the intestine by blocking AP2-alpha. We will need to examine whether this could work in del F508 mutation or others. Of course the ideal situation would be if we could increase or rescue del F508 CFTR by increasing its abundance and fluid transport on the surface of the intestine.

What's next?

We are partnering with companies to develop a treatment that would inhibit AP2-alpha in the intestine to treat obstruction in CF intestinal disease.

Original manuscript citation in PubMed

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