European Cystic Fibrosis Society

Journal of Cystic Fibrosis
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Cystic Fibrosis Research News

Title:
Forskolin induced swelling (FIS) assay in intestinal organoids to guide eligibility for compassionate use treatment in a CF patient with a rare genotype

Lay Title:
Use of swelling tests in mini-guts to help determine eligibility for treatment with Trikafta for a CF patient with a rare mutation

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What was your research question?
Can we use a swelling test in mini-guts to confirm a patients' eligibility for start of a new CF therapy?

Why is this important?
The fact that the swelling test in mini-guts was in this case convincing to confirm eligibility for start of new medication may mean that we can use this technique in the future to determine eligibility in other patients with rare mutations, who do not have access yet to new therapies for their CF.

What did you do?
To test if a new drug can be effective for a cystic fibrosis (CF) patient, cells of the patients' intestine can be grown out in the laboratory. The cells form small spheres: mini-guts, which start to swell when stimulated, if the CF protein (also called CFTR protein) is functioning (figure 1). The more these mini-guts grow, the better the protein function. We used this test to assess protein function in our patient who has a rare mutation, with unknown effect to the CF protein.

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What did you find?

We confirmed that our patients' mutation leads to a severely impaired CF protein function, and that already available medication would have no effect. Based on this test result and her clinical condition, she was accepted to the compassionate use program for Trikafta, a new CF medicine that can improve CF protein function (also called a CFTR modulator). After the start, she improved very well in lung function, weight, CT scan of the lungs (figure 2) and quality of life.

What does this mean and reasons for caution?

This method has helped confirm suitability of new CF medication for our patient, which has worked very well for her. We hope this may work for more individual patients in the future. Reasons to be cautious are that we cannot guarantee that this technique will always be accepted as it is different from the standard criteria to determine suitability, and also that there is no defined cut-off point yet when we can say that protein function loss should be called severe. In this specific case severity was quite clear as no swelling occurred entirely, but this is not always the case.

What's next?

We will have to see if the swelling test is accepted in future cases to confirm that a patient will benefit from new treatment, and what the cut-off point for this test should be for severely impaired CF protein function.

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Figure 1: Images of swelling test on mini guts of our patient: no swelling in any condition. A: Before stimulation. B: Without treatment, after maximum stimulation. C: With Orkambi, after maximum stimulation. D: With Symkevi, after maximum stimulation.

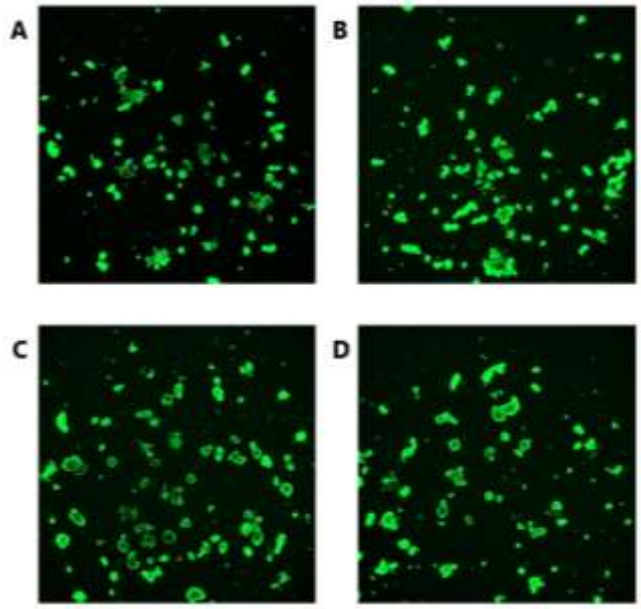

Figure 3: CT scan images of our patient 1 month before start (left) and 3 months after start of treatment (right).