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Cystic Fibrosis Research News

Title:

The CF Canada-Sick Kids Program in Individual CF Therapy: A Resource for the Advancement of Personalized Medicine in CF

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What was your research question?

We are developing a resource of stem cells from 100 people with cystic fibrosis (CF), with matched cells from the nose (nasal epithelial cells) and genetic data called the CFIT Program. We are studying these systems and providing access to other CF researchers so that they may use these tools for developing personalized medicine in CF.

Why is this important?

Current CF modulator therapies such as ORKAMBI benefit some patients with the F508del mutation but not others, and we do not understand all the reasons why. In addition to understanding the variation of responses with the more common mutations, we recognize that some mutations do not yet have any modulator therapy. Resources are needed to study

responses of individual patient in the lab so that as new drugs are developed we can predict which drug will be most effective in each individual patient: true personalized medicine. Information that helps predict patient-specific clinical effectives will help produce resources that support the development of new drugs both for the F508del mutation but also for many rare mutations where there are currently no drugs available.

What did you do?

So far, we've collected tissues from 57 people with CF. While the majority of people have two copies of F508del, others have two copies of rare CF-causing mutations. We collected nasal cells (similar to airway cells) and blood from which we are generating cells with unlimited growth potential (pluripotent cells) that can be turned into different tissues including: lung, pancreas and intestine. We are using these cells to optimize drug testing in the laboratory. We started analysis of the genetic background for each patient using advanced gene sequencing methods so that the basis for patient-specific drug responses can be defined.

What did you find?

We found considerable variability in the responses to ORKAMBI® in laboratory based studies of nasal cells obtained from patients with two copies of the F508del mutation. We also found that there is large variability in gene expression in the tissues obtained from each of these individuals. These findings support future efforts to determine how the laboratory based studies relate to improvement in lung health for each individual, understand the genetic basis for variable cell-based drug responses and to find better drugs for those who are not responsive to ORKAMBI®.

What does this mean and reasons for caution?

It is our goal that this resource will: 1) enable drug discovery for people with F508del-CFTR and rare CF-causing mutations and 2) create genetic and cell-based tools that predict drug response for each individual, thereby ensuring that the best therapy is delivered to each patient. However, we do not yet know if the laboratory models based on stem cells and patient epithelial cells will reflect the complexity of entire CF-affected organs or of the CF patient as a whole and this remains to be determined.

What's next?

We will complete recruitment to the CFIT Program and facilitate the distribution of cell lines to other CF researchers. We will develop tools for communicating the outcomes of research enabled by this resource to other researchers, patients and policy makers.

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