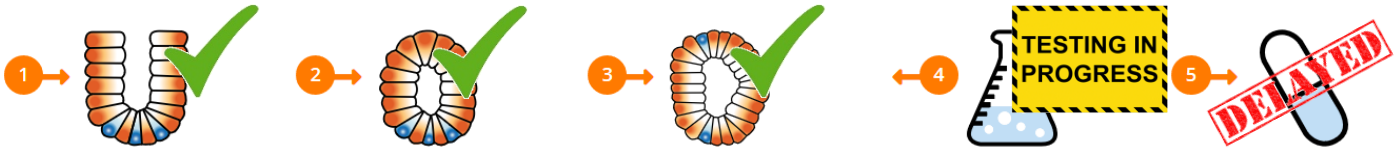
Newsletter HIT-CF Europe

April 2021

The HIT-CF Europe project aims to provide new treatment options to people with cystic fibrosis (CF) and ultra-rare genetic profiles. The project will evaluate the efficacy and safety of drug candidates provided by Eloxx Pharmaceuticals and Proteostasis Therapeutics, Inc. (PTI) in patients selected through preliminary tests in the laboratory on their mini-intestines – also called organoids.



We take some tissue from the intestine | **This tissue is cultured in the lab** | **The result is an organoid** | **On this organoid we test medicines** | **And we bring the correct medicines to the patients**

Primary screen of Eloxx compound on organoids finished!

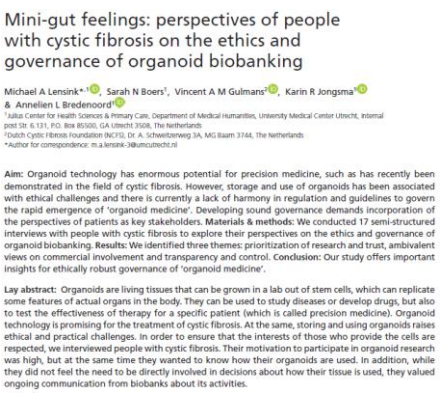
We are very happy to announce that our collaborators in the labs finalised the primary screening of the organoids with the Eloxx compound. Even at this early stage, it is clear that there are people with CF caused by rare stop mutations who respond to the Eloxx drug, which is great news. These results will now be validated through a secondary screen after which 26 people will be selected to participate in a clinical trial with the Eloxx drug. We anticipate to start this trial by the beginning of 2022.

CHOICES delayed until the end of this year

As we communicated in earlier newsletters, the merger of PTI with Yumanity Therapeutics is causing severe delays in the kick-off of CHOICES, the clinical trial in which PTI compounds will be given to 52 people with CF based on their organoid response. The HIT-CF team is currently looking into the best way to get the PTI drugs to the selected patients, but it is certain that this will not be before the end of this year. The HIT-CF team remains fully committed to carry out CHOICES and make HIT-CF a success for patients with rare mutations.

Briefing package to obtain EMA Qualification Opinion of organoid model ready

One of the major goals of HIT-CF is to have the organoid assay accepted as a valid measurement to support off-label use of approved CF drugs, so that people with CF caused by rare mutations can also benefit from innovative drugs based on their organoid response. An important step in the path towards that wide acceptance, is obtaining the European Medicine's Agency (EMA) Qualification Opinion (QO) that the assay is a functional biomarker for CFTR function. The QO is a scientific advice and 'quality mark' that supports the validity of the organoid assay in predicting the efficacy of drugs in CF. The HIT-CF team has worked hard to prepare the concept briefing package accompanying our request and it will soon be submitted. We expect a decision by the EMA in the beginning of 2022.



Mini-gut feelings: perspectives of people with cystic fibrosis on the ethics and governance of organoid biobanking

Michael A Lensink*[1], Sarah N Boers[1], Vincent A M Gulmans[2], Karin R Jongsma[1] & Annelien L Bredenoord[1]

[1]Julius Center for Health Sciences & Primary Care, Department of Medical Humanities, University Medical Center Utrecht, Internal post Str. 6.131, P.O. Box 85500, GA Utrecht 3508, The Netherlands
[2]Dutch Cystic Fibrosis Foundation (NCFS), Dr. A. Schweitzerweg 3A, MG Baarn 3744, The Netherlands
*Author for correspondence: m.a.lensink-3@umcutrecht.nl

Aim: Organoid technology has enormous potential for precision medicine, such as has recently been demonstrated in the field of cystic fibrosis. However, storage and use of organoids has been associated with ethical challenges and there is currently a lack of harmony in regulation and guidelines to govern the rapid emergence of 'organoid medicine'. Developing sound governance demands incorporation of the perspectives of patients as key stakeholders. **Materials & methods:** We conducted 17 semi-structured interviews with people with cystic fibrosis to explore their perspectives on the ethics and governance of organoid biobanking. **Results:** We identified three themes: prioritization of research and trust, ambivalent views on commercial involvement and transparency and control. **Conclusion:** Our study offers important insights for ethically robust governance of 'organoid medicine'.

Lay abstract: Organoids are living tissues that can be grown in a lab out of stem cells, which can replicate some features of actual organs in the body. They can be used to study diseases or develop drugs, but also to test the effectiveness of therapy for a specific patient (which is called precision medicine). Organoid technology is promising for the treatment of cystic fibrosis. At the same, storing and using organoids raises ethical and practical challenges. In order to ensure that the interests of those who provide the cells are respected, we interviewed people with cystic fibrosis. Their motivation to participate in organoid research was high, but at the same time they wanted to know how their organoids are used. In addition, while they did not feel the need to be directly involved in decisions about how their tissue is used, they valued ongoing communication from biobanks about its activities.

Interview study on the perspectives of people with CF on organoid biobanking published

As mentioned in the previous newsletter, another goal of HIT-CF is to install a permanent biobank containing the organoids that were cultured for the project. To learn more about how people with CF feel about their tissue being stored and used for research and drug development by different parties, how they perceive ownership and what their wishes are concerning feedback, our ethics collaborator Mike Lensink performed 17 semi-structured interviews with people with CF. His findings will be used to inform the ethical framework and governance of the HIT-CF biobank. You can read the full article by clicking on the image on the left.

To learn more about the HIT-CF project, visit www.hitcf.org or send an e-mail to HITCF@umcutrecht.nl

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