HUB ORGANOIDS

A patient in the lab

Next Generation Cystic Fibrosis Model for Drug Development

Cystic fibrosis (CF) is a genetic disease that is caused by mutations of the gene encoding for the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Mutations in the CFTR gen lead to impaired protein function, causing severe damage to the lungs, digestive system and other organs in the body. A major problem in treating CF is the diversity of the genetic defect. Over 2000 different mutations have been identified in CF patients: just 12 of these are represented in 50% of the CF population, with more than 1900 mutations distributed amongst the other 50%.

The Challenge

Preclinical models for studying CF and developing treatments have been notoriously difficult to establish. This has particularly been the case with models of primary cells used to mimic the *in vivo* biology and patient-specific characteristics. In addition, the large amount of mutations that have been identified defy the development of genetically engineered model systems.

HUB Organoids' Solution

- adult stem cell-derived HUB Organoid models, rapidly and directly generated from patients (living organoid biobanks).
- unlimited expansion of each patient-derived HUB Organoid model.
- *in vitro* assay readouts directly correlating with patients` clinical response, e.g. Forskolin-induced swelling (FIS) assay.

Why Use HUB Organoids for CF Drug Development?

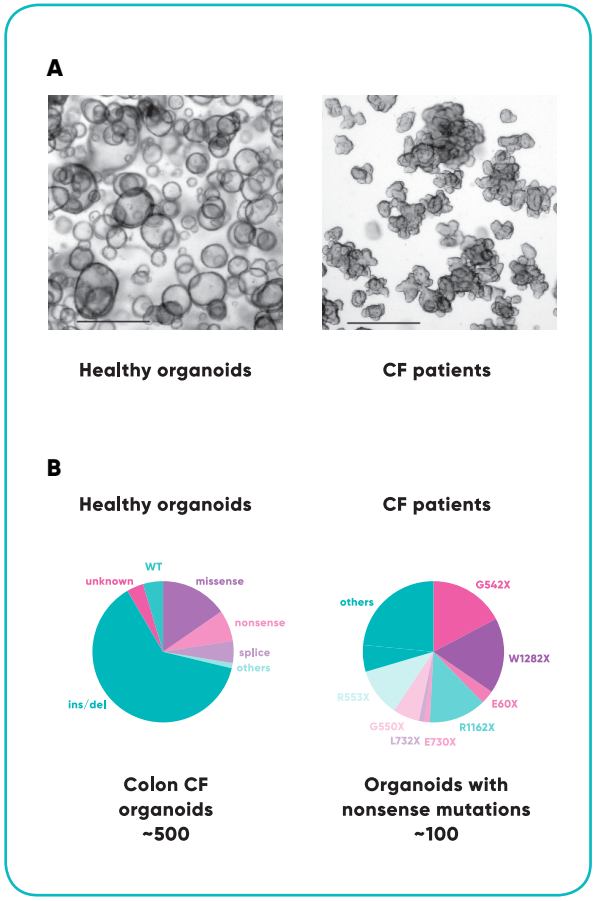

Fig 1: A) Representative images of organoids from healthy (left) and CF patients (right). B) The most common CF genotypes are captured in the living organoid biobank (left). Overview of CFTR nonsense mutations present in the living organoid biobank (right).

FIS assay to test the effectiveness of (novel) compounds on the CF population or on specific mutations

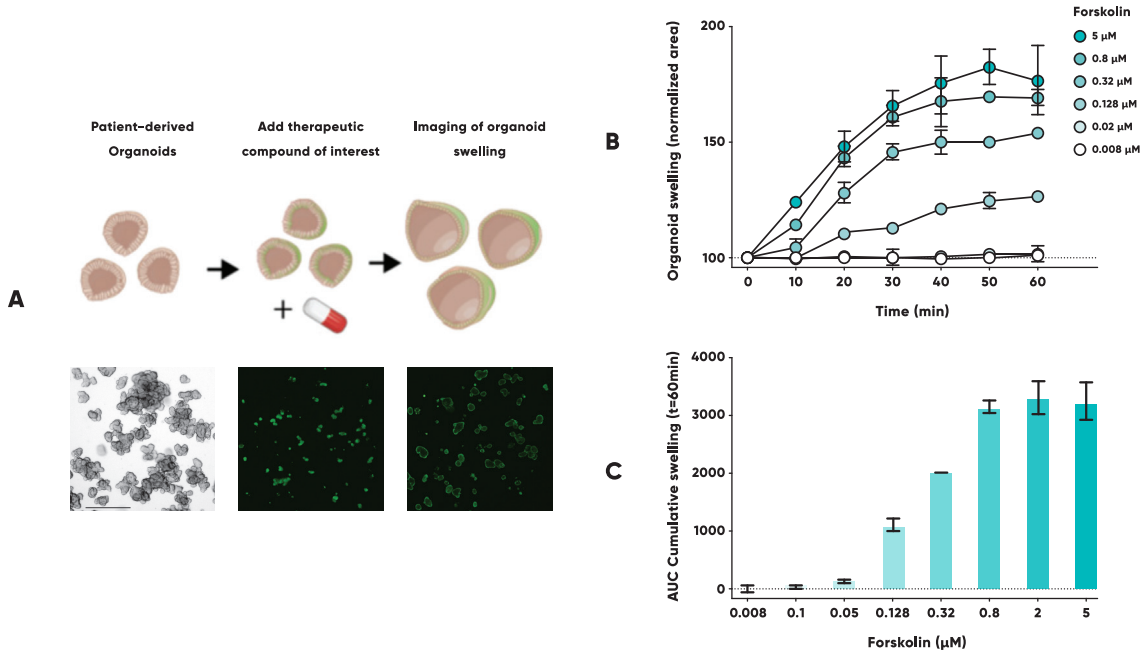

Fig 2: A Schematic overview of FIS assay workflow. Organoid swelling over time at different forskolin concentrations (B) and area under curve (AUC) of those swelling curves (C). Here shown for F508del/F508del organoids treated with compound x/y.

Services for CF Offered by HUB

- organoid cultures from our living organoid biobanks representing CFTR mutations, both common and rare
- gene editing and gene therapy
- immunohistochemistry, immunofluorescence
- imaging
- drug efficacy and safety testing/screening
- preclinical clinical trials, patient stratification
- companion diagnostic
- *in vitro* assay readouts, e.g. FIS assay
- on request:
  - assay development – custom assays upon customer request
  - gene expression analysis (DNA and RNAseq)
  - novel organoid biobanks – establishment of organoid biobanks with specific CFTR mutations

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