# HUB ORGANOIDS

A patient in the lab

## HUB Cystic Fibrosis Organoid Model Predicting a Patient`s Response

Cystic fibrosis (CF) is a genetic disease that is caused by mutations of the gene encoding for Cystic Fibrosis Transmembrane conductance Regulator (CFTR) protein. Mutations in the CFTR gene lead to impaired or loss of protein function over time resulting in severe damage to 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

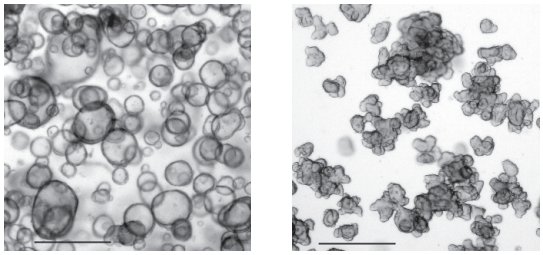
Preclinical models for studying CF and developing treatments have been notoriously difficult to establish. This has particularly been the case with models of primary cells used to mimic the *in vivo* biology and patient-specific characteristics. In addition, the large amount of mutations that have been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

### HUB Organoid Solution

- adult stem cell-derived HUB Organoids are rapidly and directly generated from patients.
- unlimited expansion of each patient-derived HUB Organoid model.
- HUB Organoids can be used in all conventional and state of the art *in vitro* assays (e.g. Forskolin-Induced Swelling (FIS) assay), providing data – correlating with a patient's clinical response.

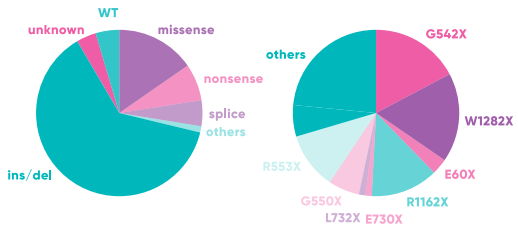
### Why HUB Organoids for CF Drug Development?

**A**



**Healthy organoids** **CF patients**

**B**




**Colon CF organoids ~500** **Organoids with nonsense mutations ~100**

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**

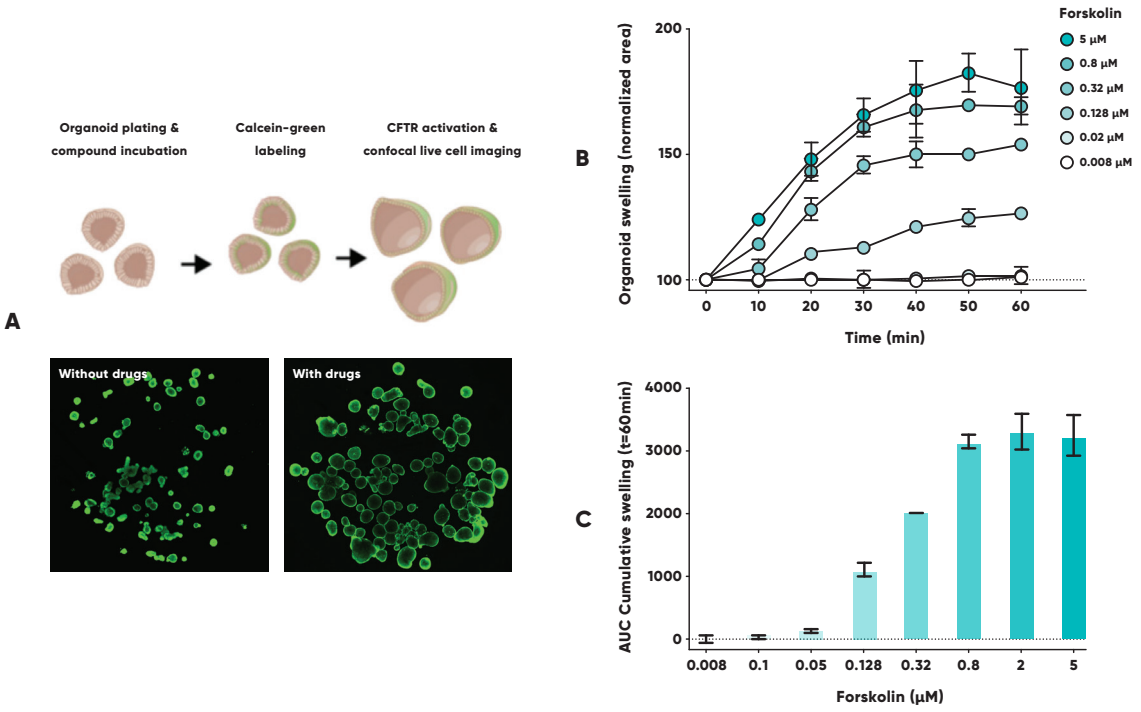



Fig 2: (A) Schematic overview of FIS assay in absence (left) and presence (right) of drug; representative pictures are shown. (B) Organoid swelling over time at different forskolin concentrations (C) and area under curve (AUC) of those swelling curves. Here shown for F508del/F508del organoids treated with compound x/y.

## Services for CF Offered by HUB

- CF organoid biobank collection (>500 mutations)
- drug efficacy testing
- immunohistochemistry, immunofluorescence
- gene editing
- gene therapy assays
- preclinical clinical trials, patient stratification
- companion diagnostic
- biomarker development
- *in vitro* assay readouts, e.g. FIS assay
- on request
  - assay development – custom assays
  - gene expression analysis (DNA and RNAseq)
  - novel organoid biobanks – establishment of organoid biobanks with specific CFTR mutations

# Hubrecht Organoid Technology

Yalelaan 62
3584 CM Utrecht
The Netherlands
+31 (0)88 1236300
marketing@huborganoids.nl
huborganoids.nl