

The role of Organoids in precision health

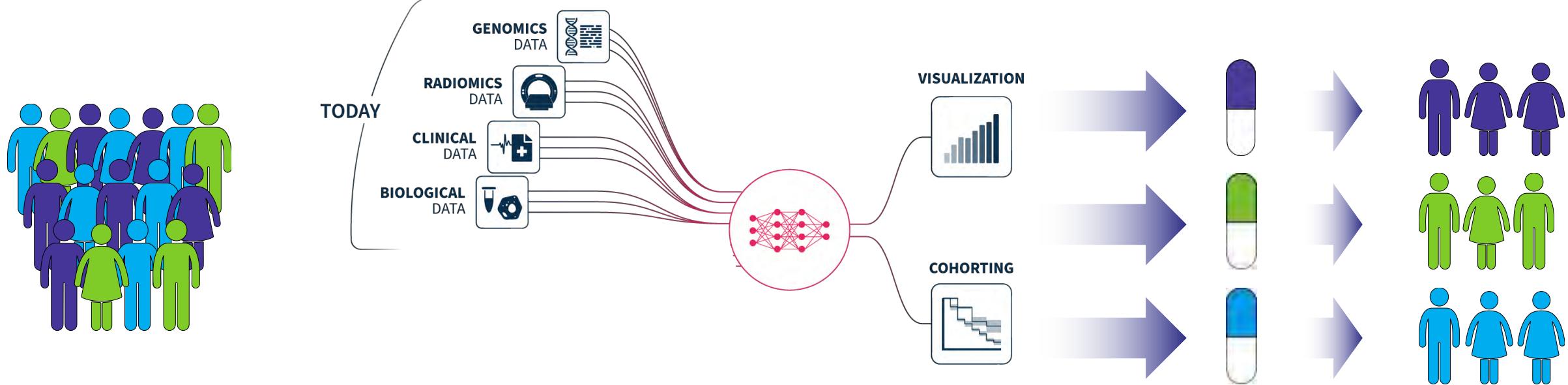
Nathalie Brandenberg, PhD, eMBA

1. Personalized medicine today
2. Introduction on organoids
3. Case study: Cystic Fibrosis



Current practice in personalized medicine

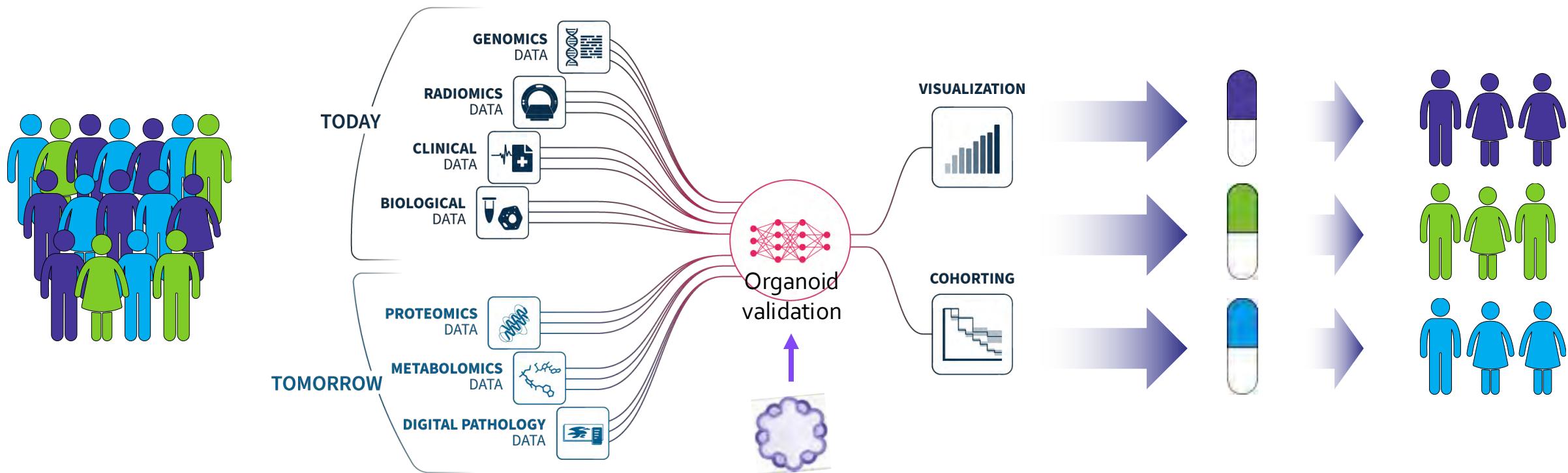
Current practice in personalized medicine



- Current approaches used in personalized medicine are genomics, radiomics, clinical and biological data.
- Multiplexing these datasets enables a certain level of personalisation.

=> However all therapeutic decisions still rely on data interpretations and assumptions

Future practice in personalized medicine – the impact of organoids



- Additional datasets (proteomics, metabolomics and spatial biology) will enable better therapeutic decisions.

=> Organoids are a validation tool of the therapeutic decision



What are organoids ?

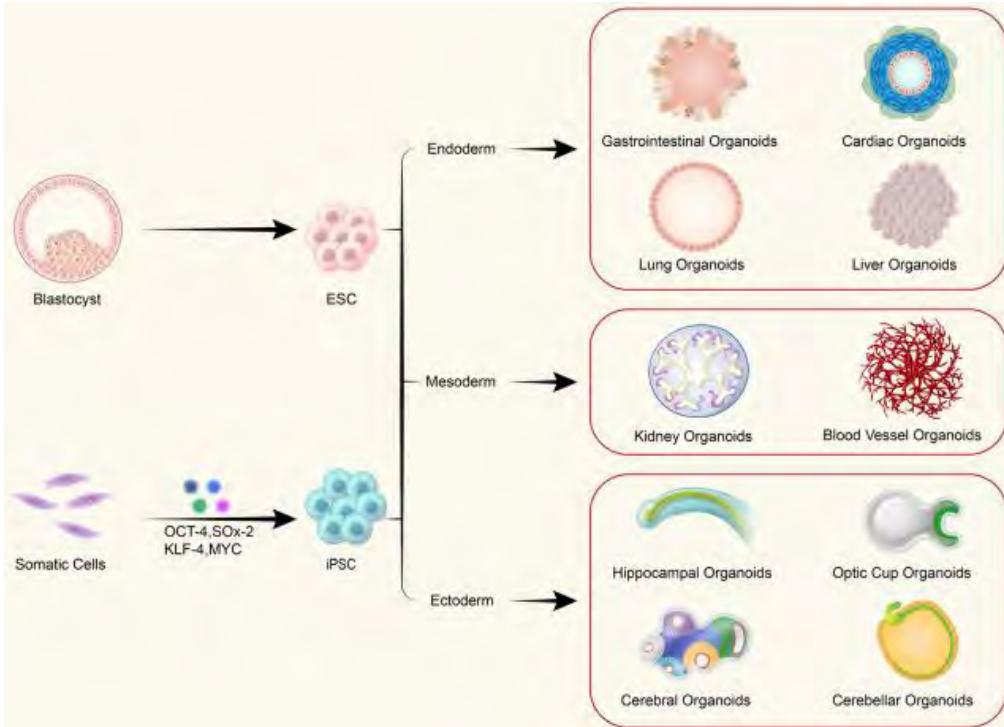
Organoids are personalized mini-organs in a dish

- Organoids are small lab-grown mini-organs from the stem cells of living patients.
- They have the entire genetic code of the patient.
- They replicate but do not mutate. And they can be stored frozen for use on demand.



Organoids can be generated from various cell sources

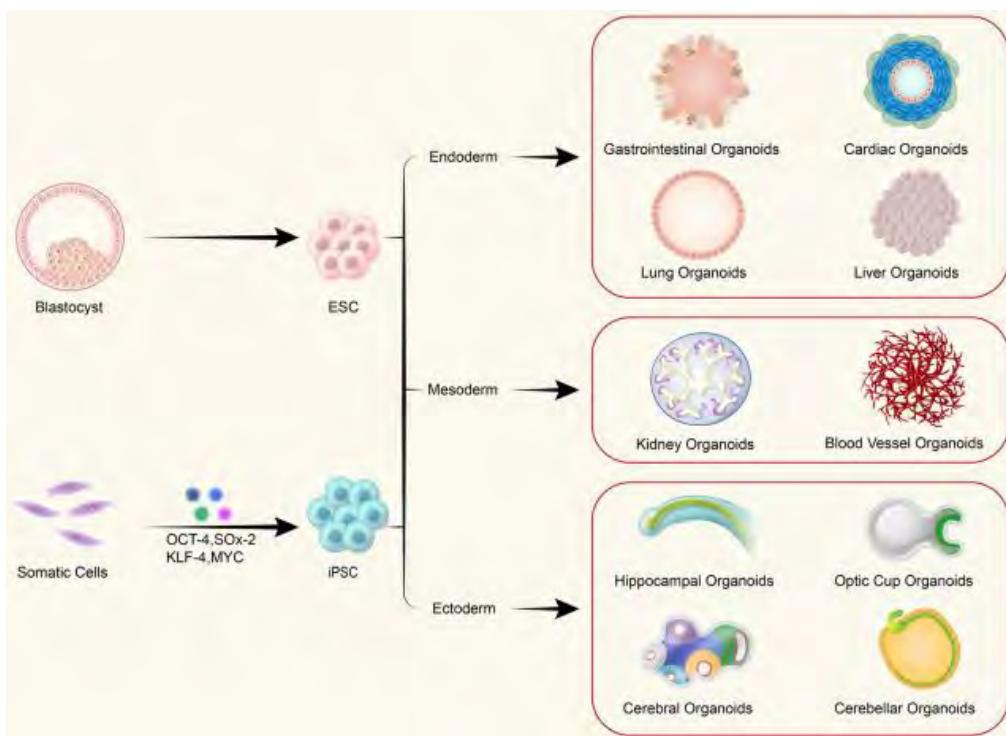
Pluripotent stem cells derived organoids



- Need maturation from the most naïve state
- Usually long and complex differentiation protocols
- Hard to mature in vitro into an adult phenotype
- More difficult to use in personalized medicine

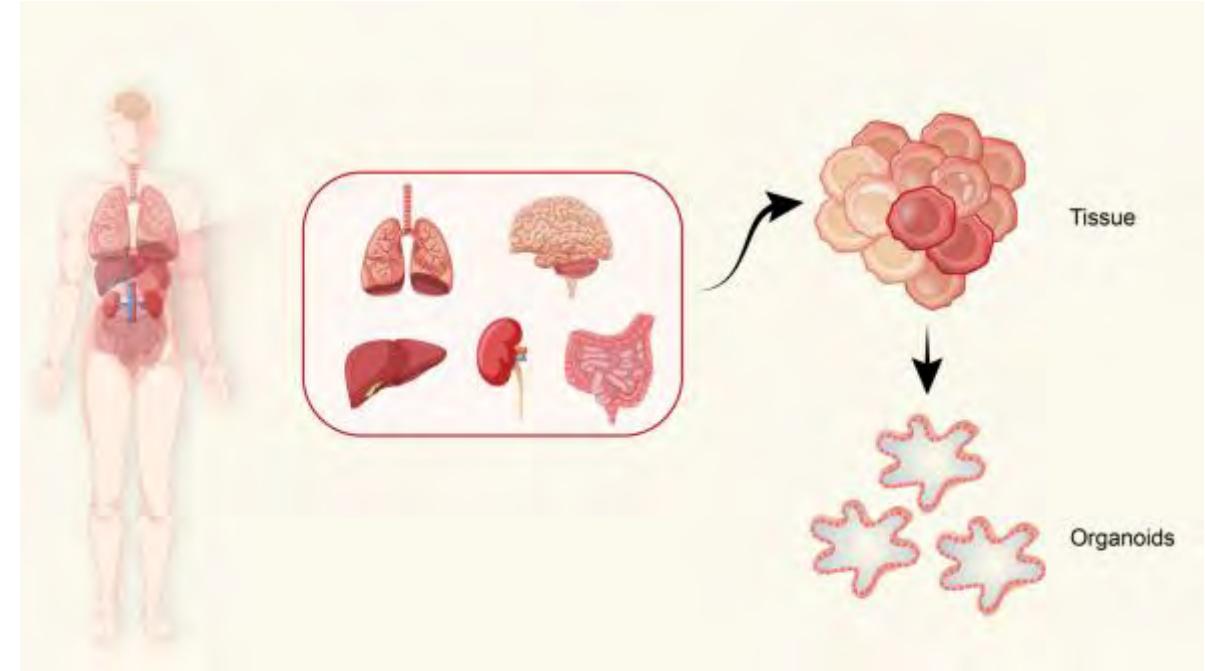
Organoids can be generated from various cell sources

Pluripotent stem cells derived organoids



Adult stem cells derived organoids

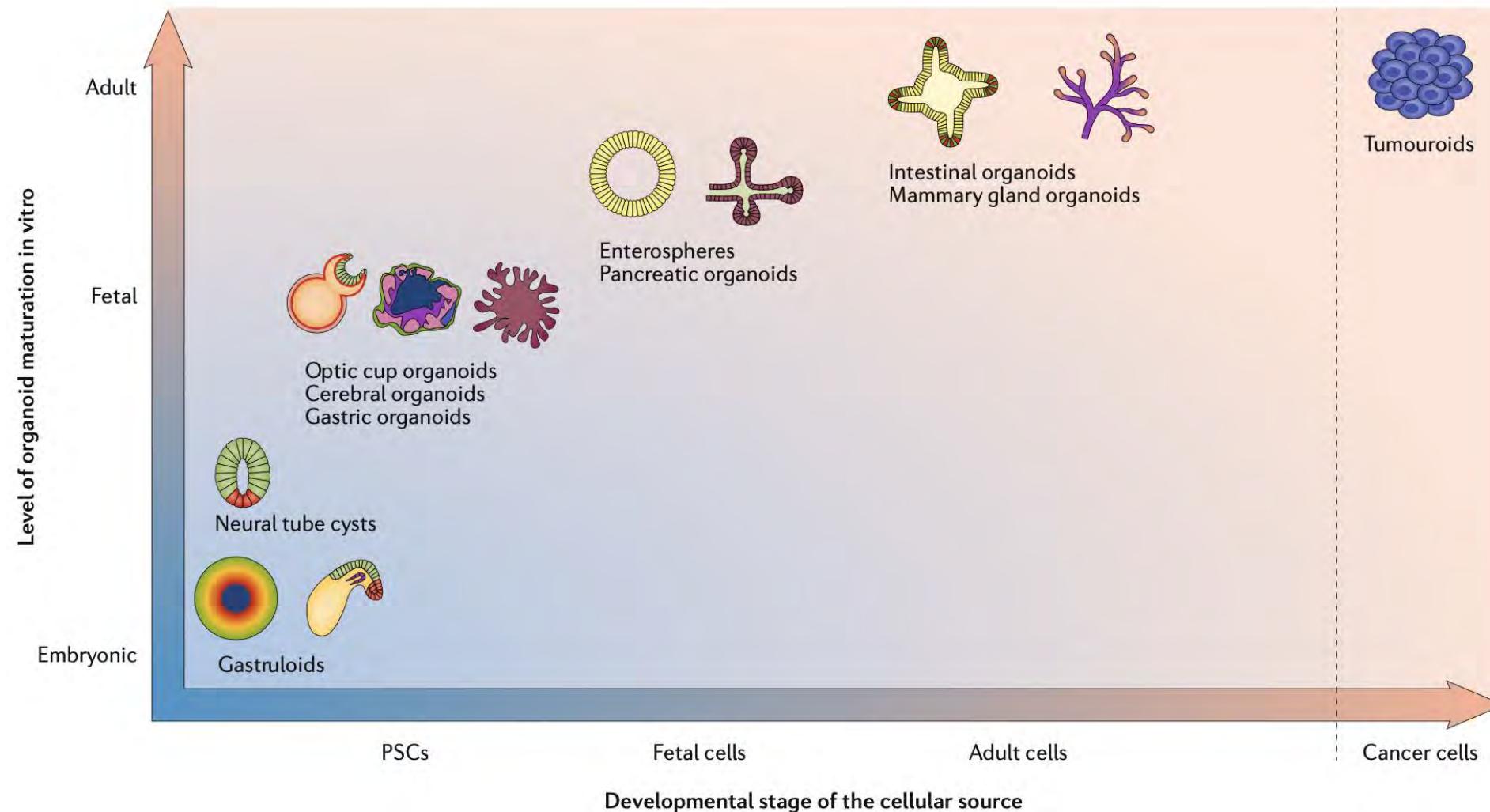
(also called Patient-derived organoids, PDOs or tissue-derived organoids)



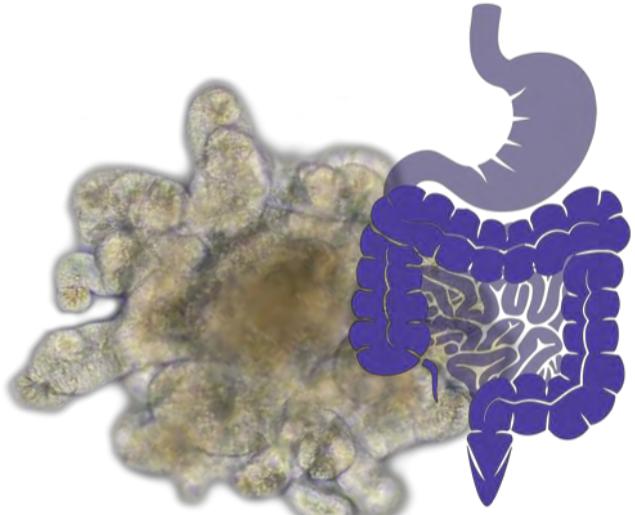
- Need maturation from the most naïve state
- Usually long and complex differentiation protocols
- Hard to mature in vitro into an adult phenotype
- More difficult to use in personalized medicine

- Generated from stem cells that are already tissue-specific
- Short and simpler differentiation protocols
- More amenable to personalized medicine

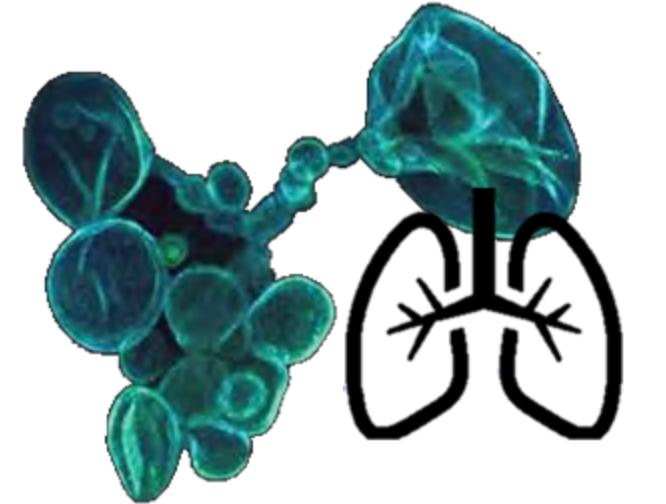
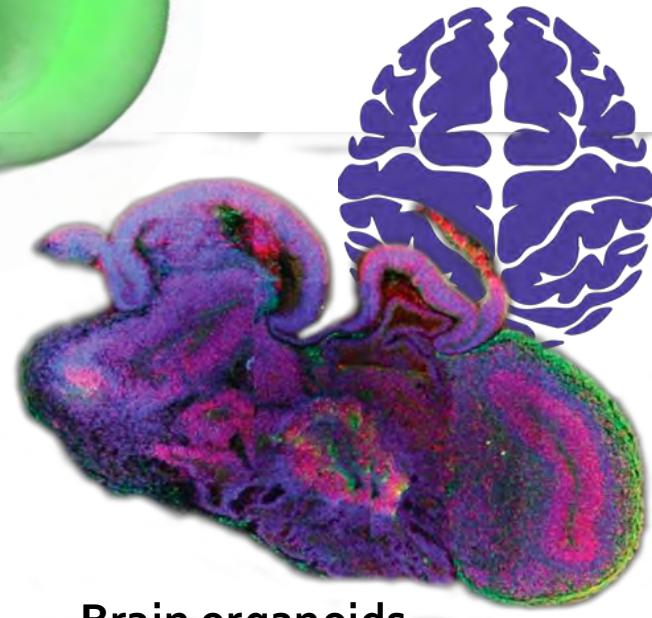
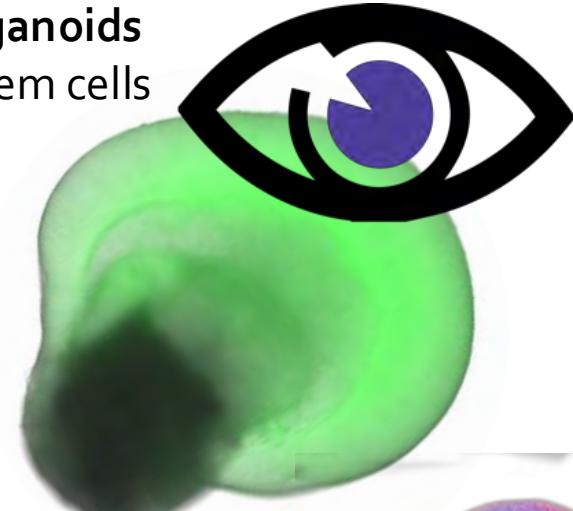
The starting cell type determines organoid maturation levels in vitro



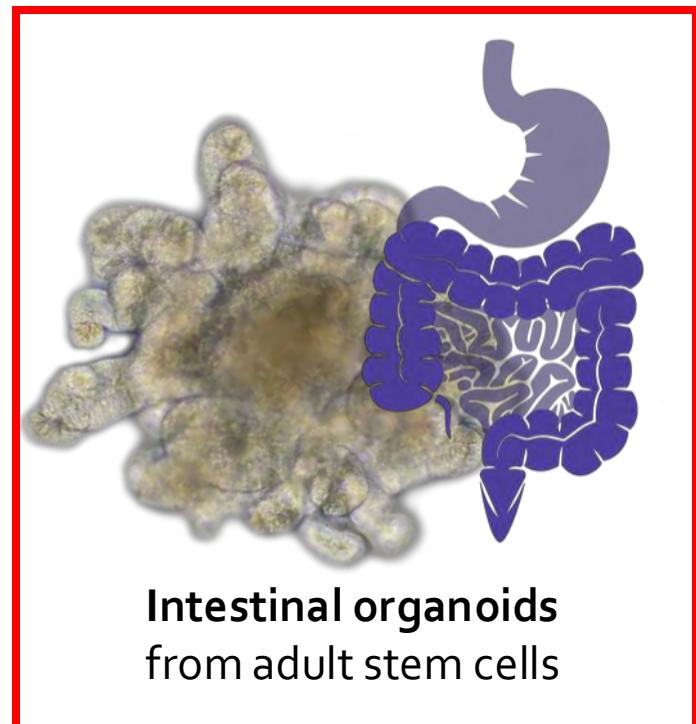
Organoids, a few examples



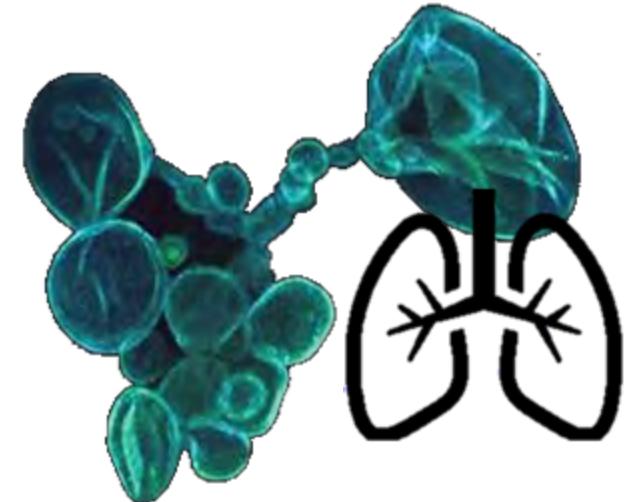
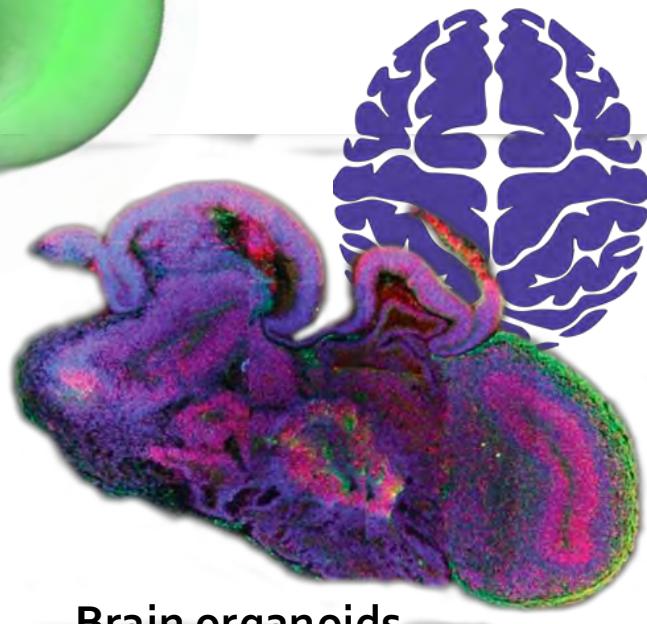
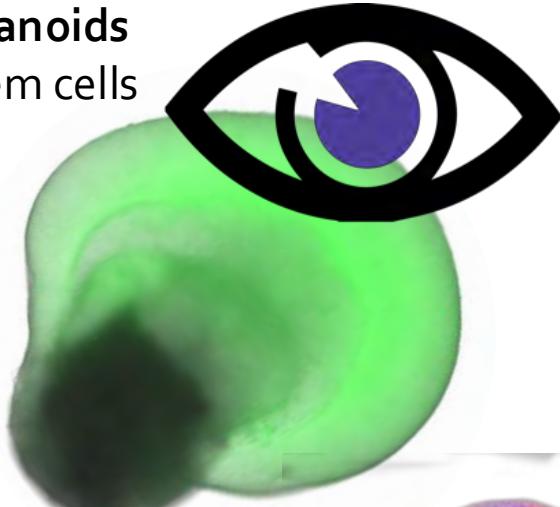
Retinal organoids
from pluripotent stem cells



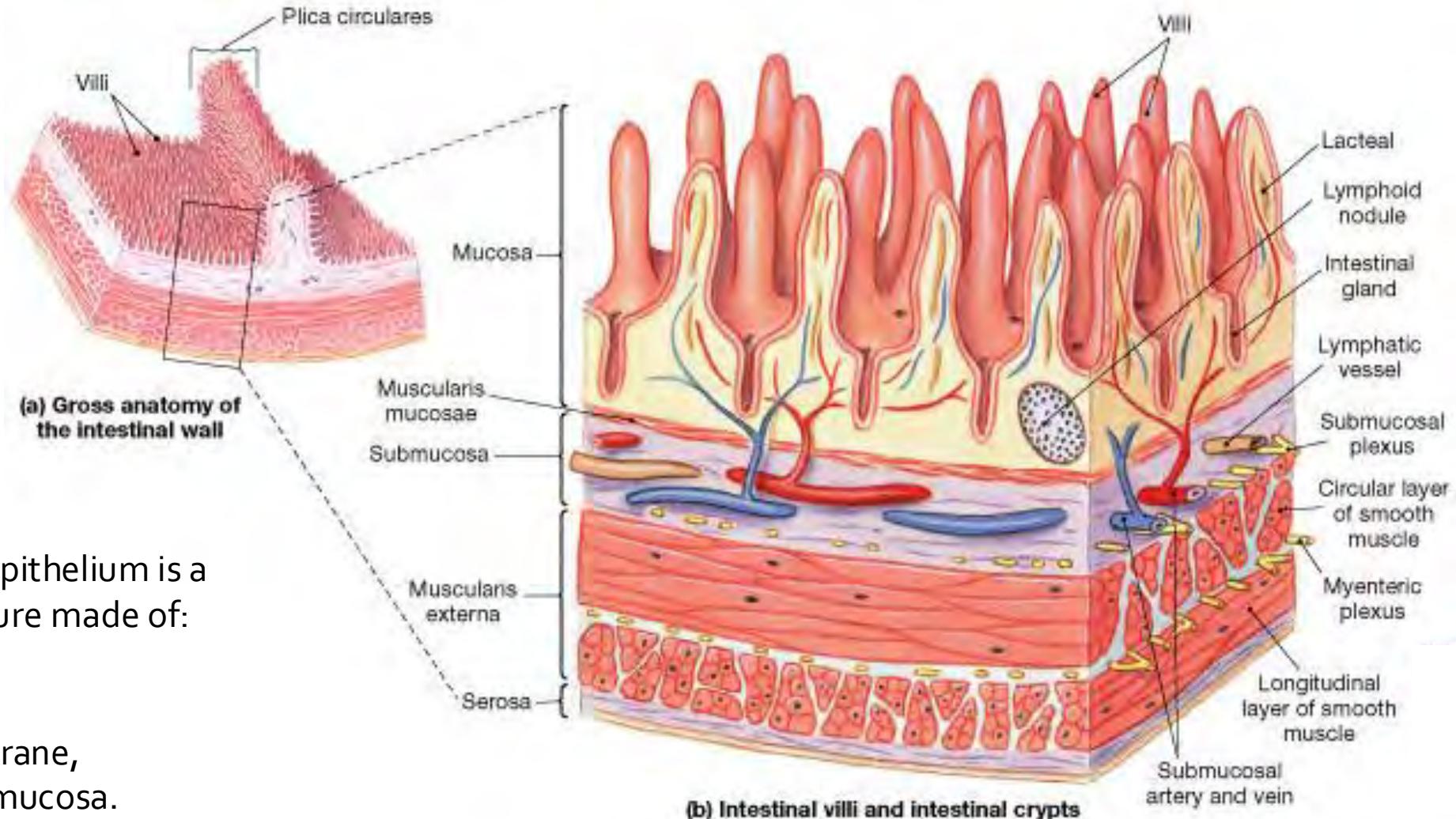
Organoids, a few examples



Retinal organoids
from pluripotent stem cells



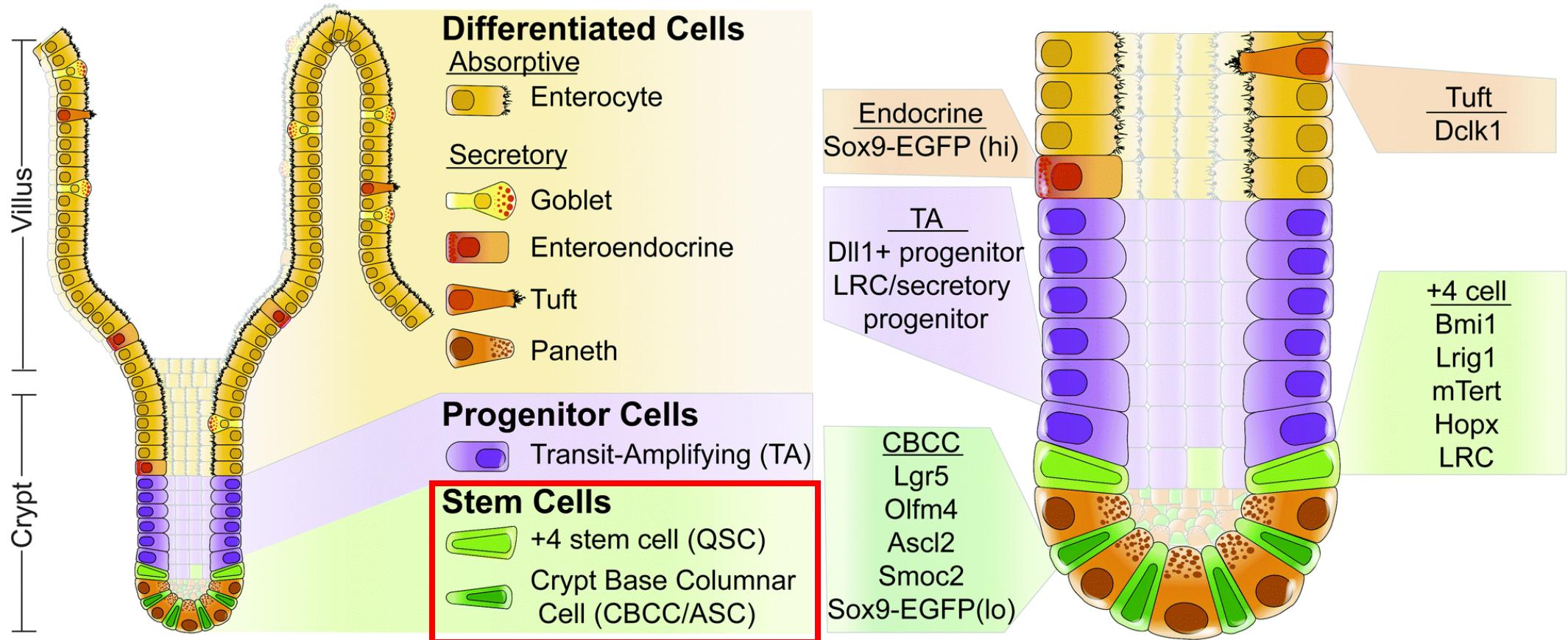
The example of the intestine



The intestinal epithelium is a complex structure made of:

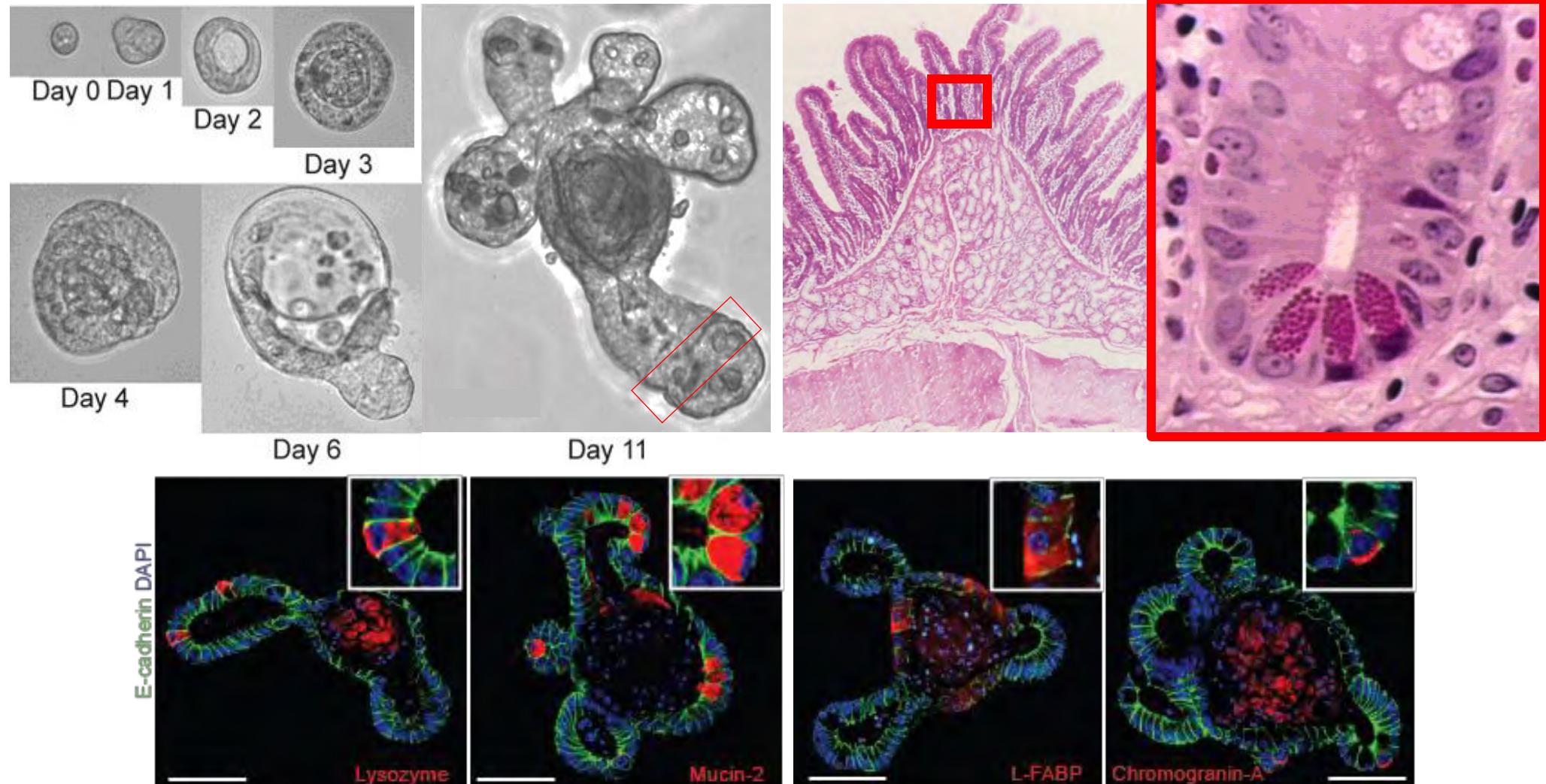
- Villis,
- Crypts,
- Basal membrane,
- Underlying mucosa.

The cellular & molecular composition of the intestinal crypt



The example of the intestine, in the mouse

Mouse small intestine

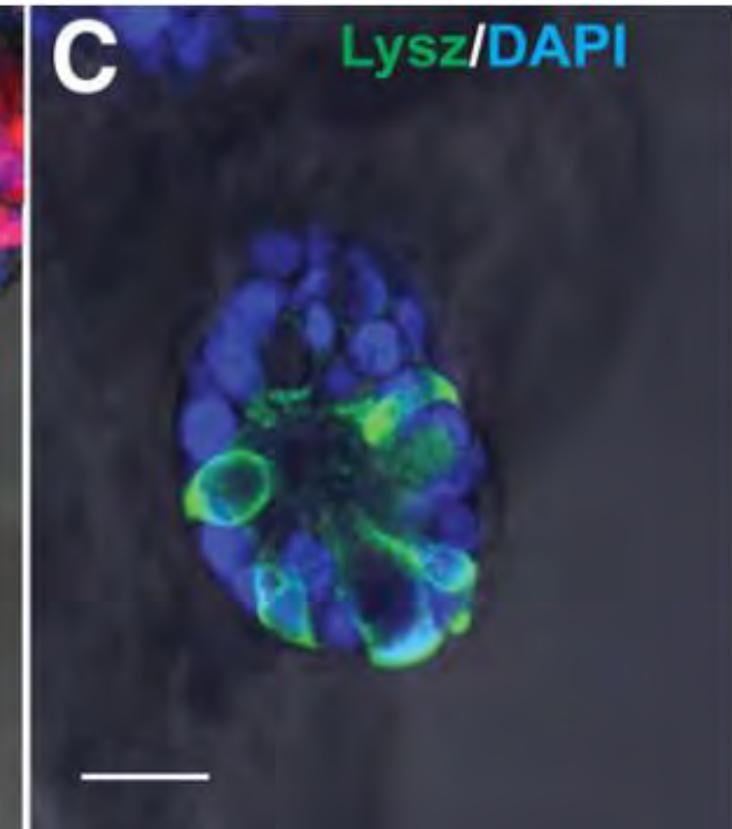
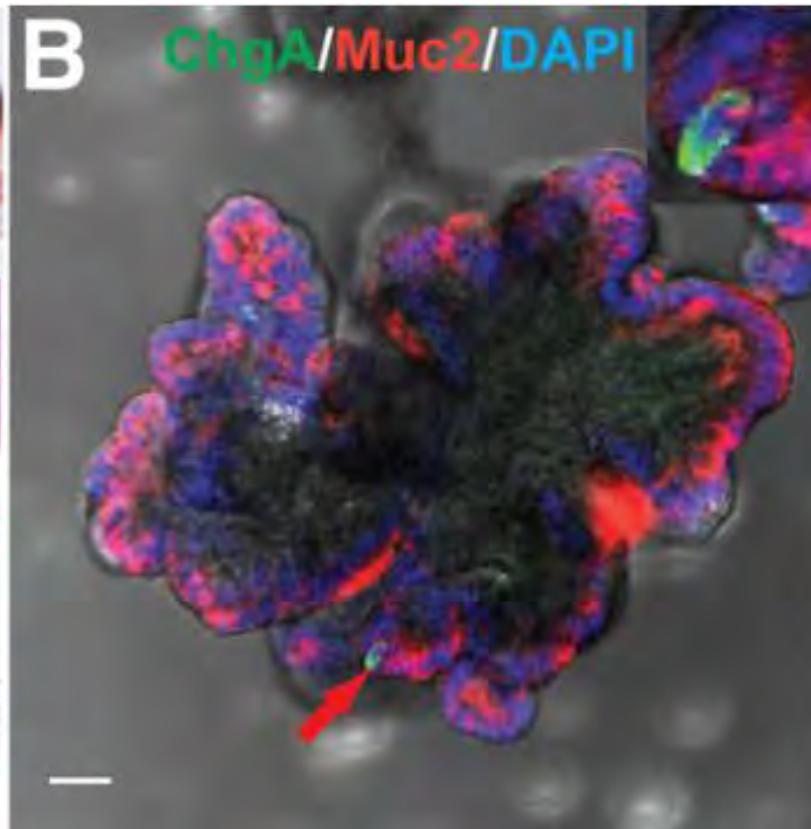
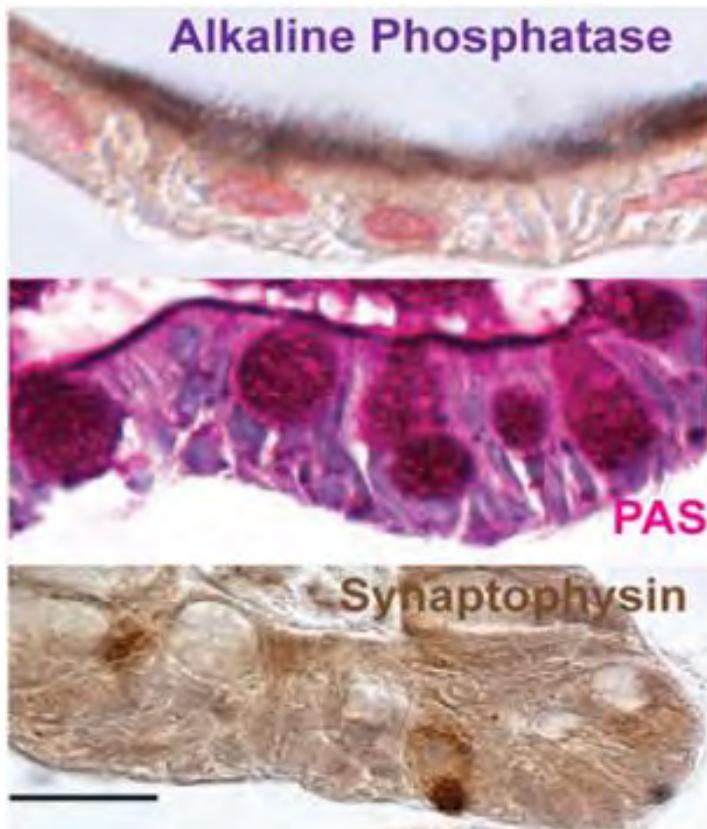


Sato T, et al. (2009) Single Lgr5 stem cells build crypt-villus structures in vitro without a mesenchymal niche. *Nature* 459(7244):262-265.

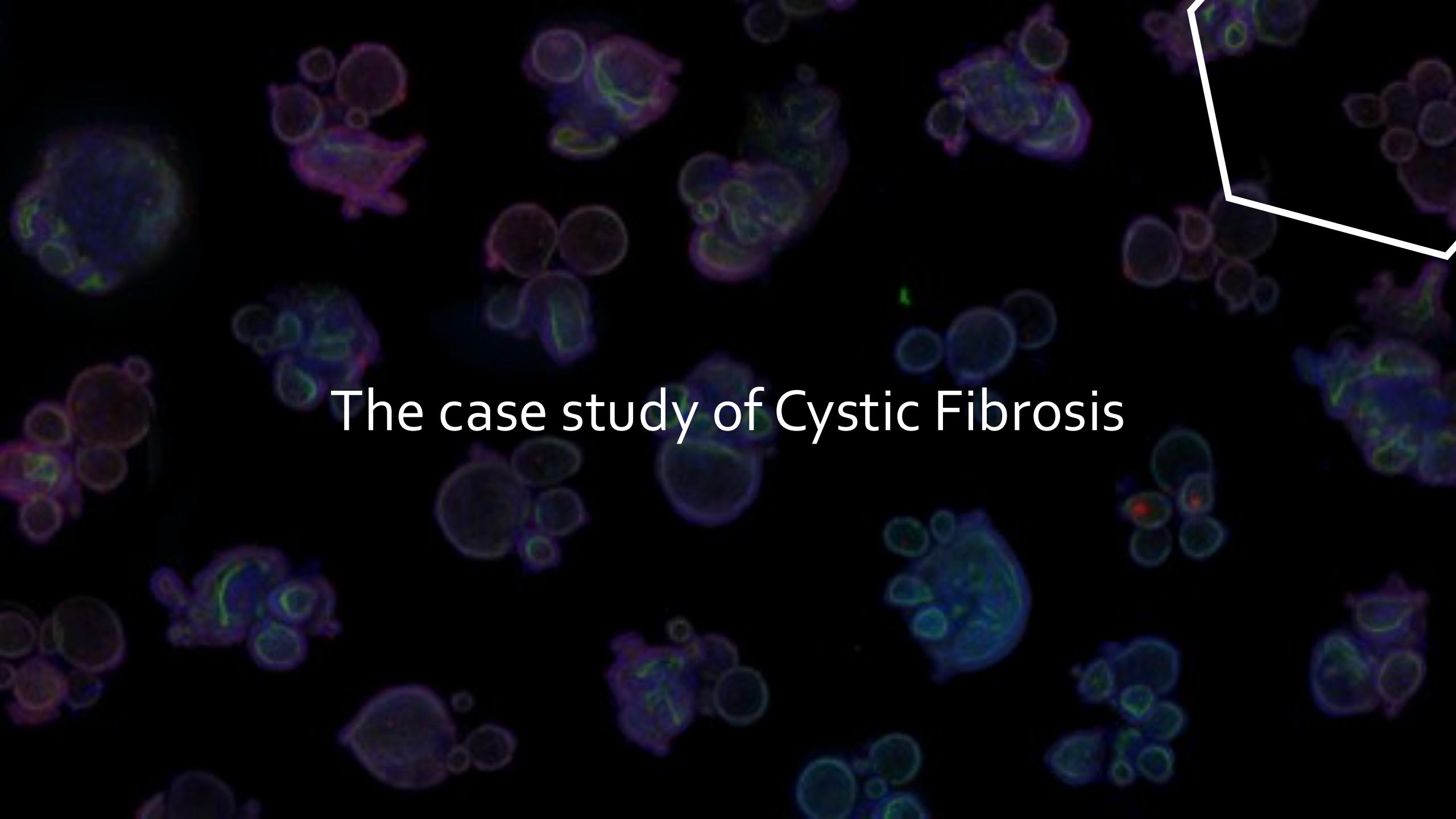
N. Gjorevski, N. Sachs, A. Manfrin, S. Giger, M. E. Bragina, P. Ordóñez-Moran, H. Clevers and M. P. Lutolf, Designer matrices for intestinal stem cell and organoid culture *Nature*, 2016
20/03/25

The example of the intestine, in human

Human small intestine



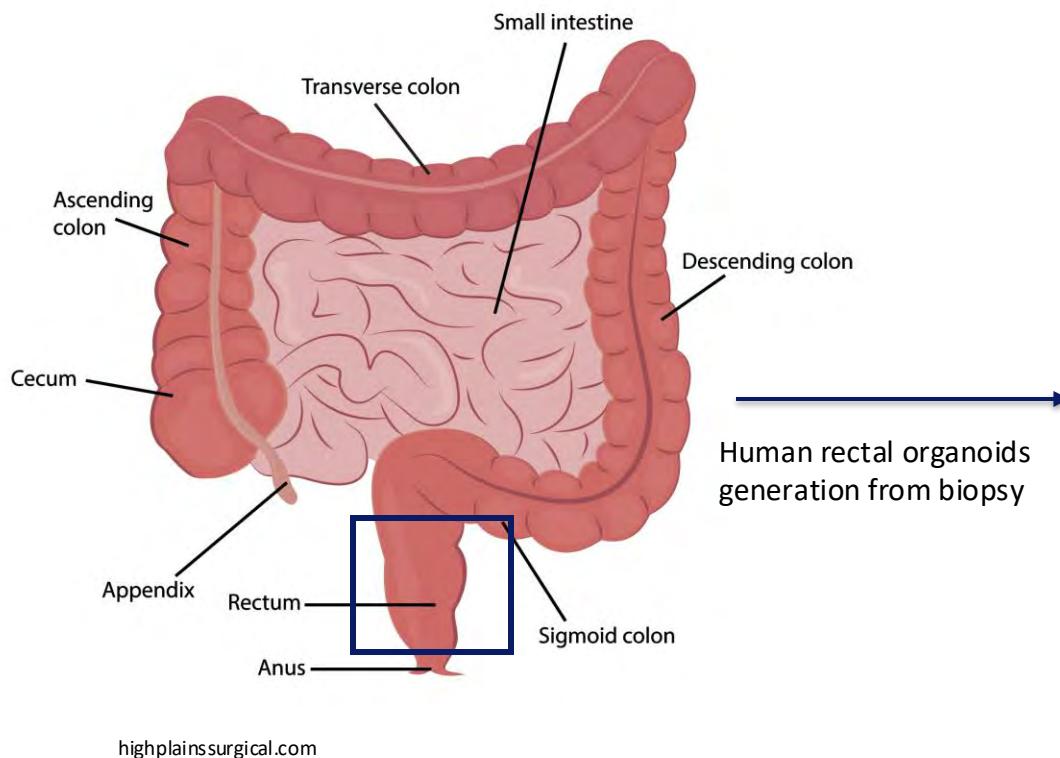
- Intestinal organoids recapitulate extraordinarily well the cellular and molecular hallmarks of the native tissue,
- Adult stem cells-derived organoids of other tissues (lung, pancreas, liver, nasal epithelium,..) resemble their organs of origin with various degrees of accuracy.



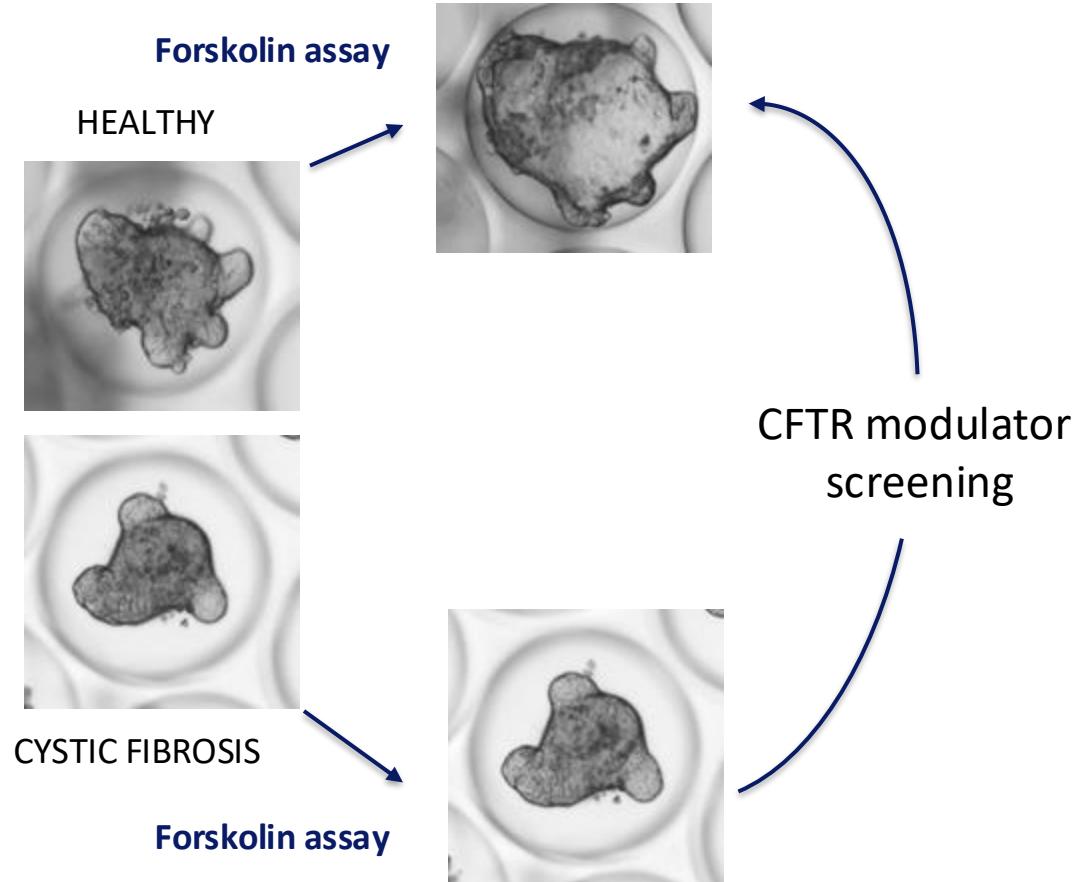
The case study of Cystic Fibrosis

ORGANOID CAN BE DERIVED FROM CF AND HEALTHY PATIENTS

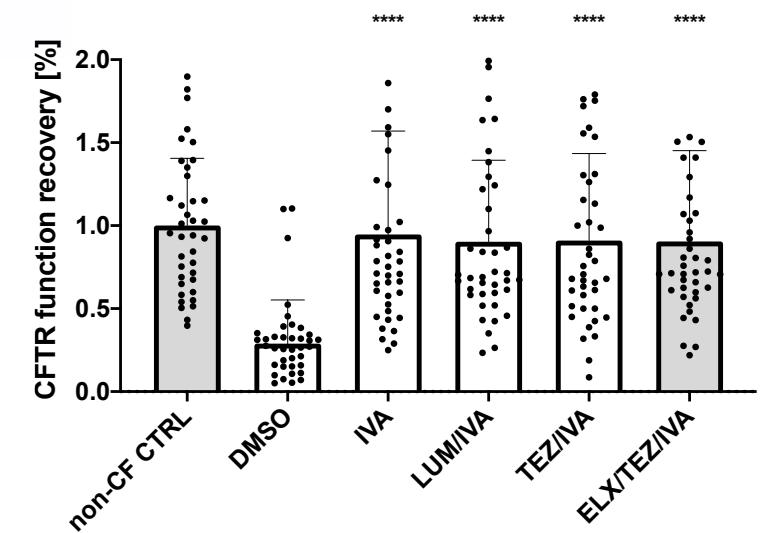
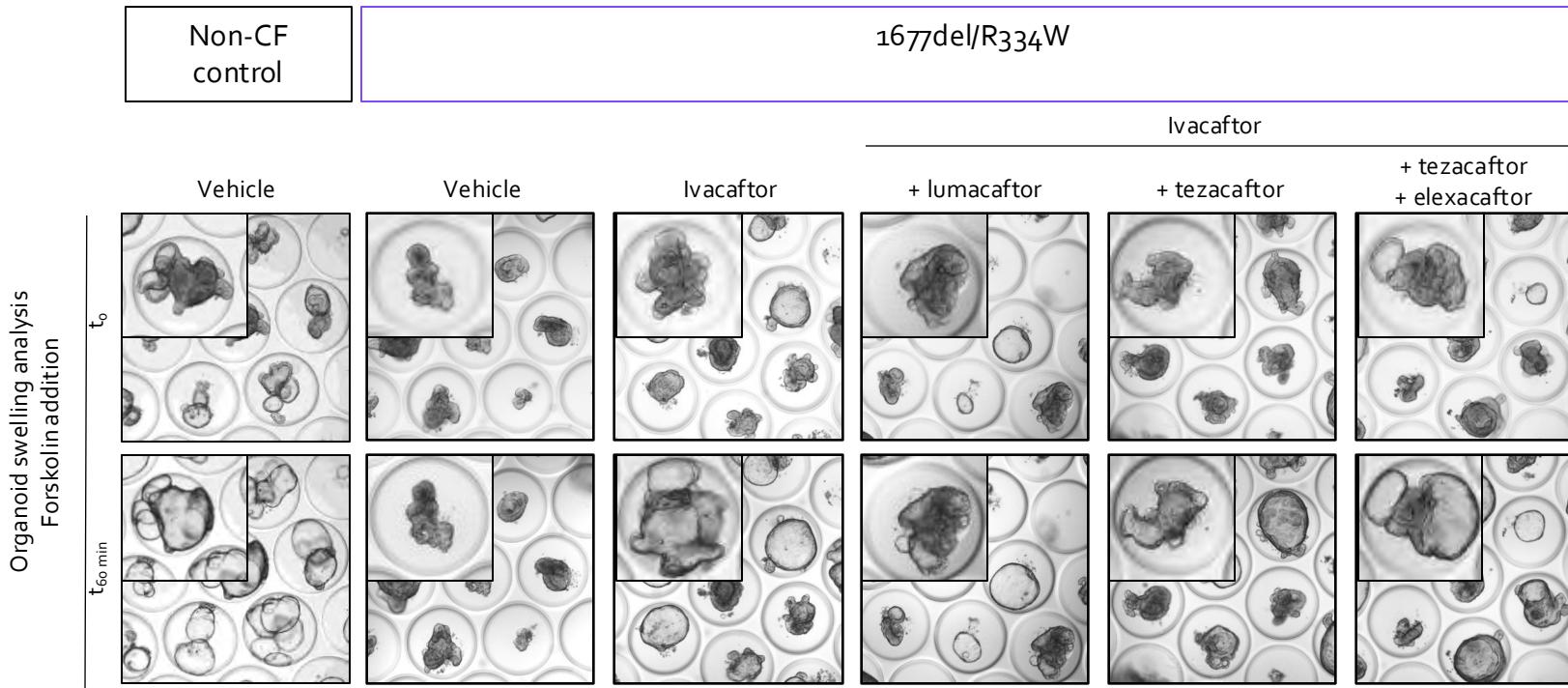
A COLLABORATIVE WORK BETWEEN CHUV AND EPFL



Human rectal organoids
generation from biopsy



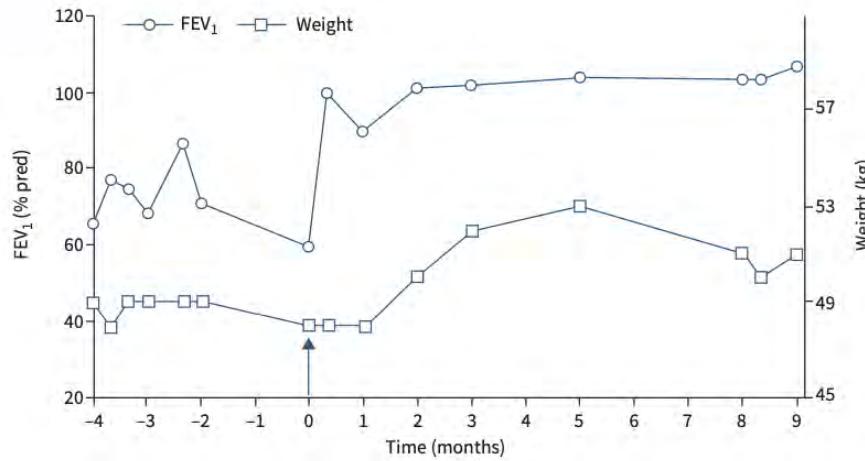
1677del/R334 MUTANT ORGANOIDS RESPOND TO IVACAFTOR



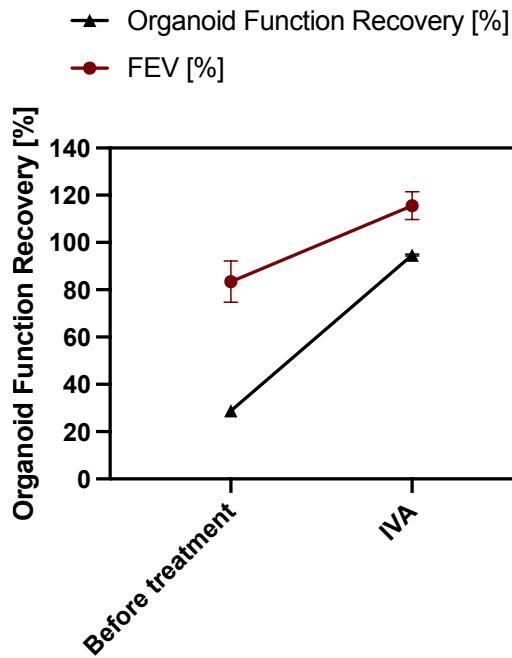
Mitropoulou *et al.* Eur Respir J. 2022 DOI: 10.1183/13993003.01341-2022

IVA = ivacaftor
LUM = lumacaftor
TEZ = tezacaftor
ELX = elexacaftor

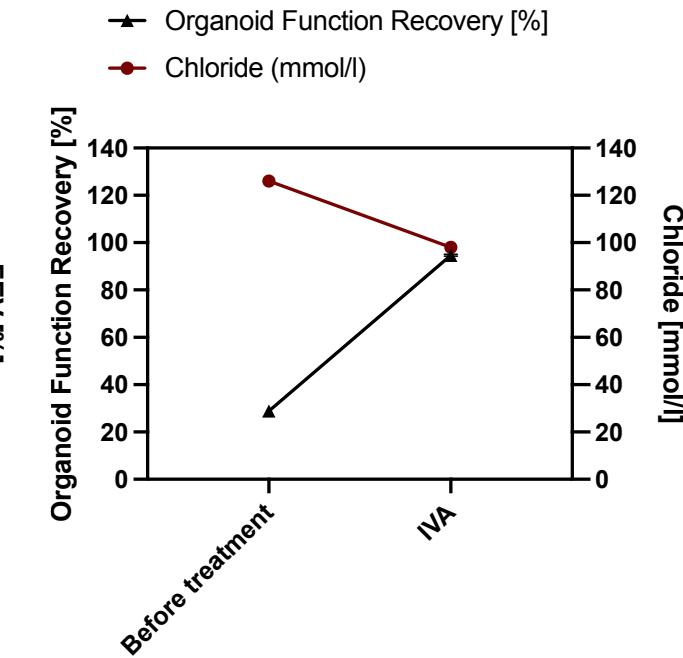
1677del/R334 PATIENT RESPONDS TO IVACAFTOR: A SUCCESS STORY



Mitropoulou et al. Eur Respir J. 2022 doi: 10.1183/13993003.01341-2022



Ceroni et al., "Predicting treatment response in cystic fibrosis using label-free imaging on patient-derived rectal organoids"
Manuscript in submission



For the first time, a Swiss health insurance accepted to reimburse a treatment based on the results of a personalised *in vitro* organoid test

Acknowledgments

COLLABORATORS



Camilla Ceroni

SUNBIOSCIENCE



Fondation
Respirer



Cystische Fibrose
Schweiz



Questions ?