

A fluorescence microscopy image showing numerous organoids, which are small clusters of cells. The organoids are stained with various fluorescent dyes, appearing in shades of blue, green, and red against a dark background. Some organoids show internal structures, while others are more uniform. A white line is visible in the upper right corner, possibly indicating a specific region of interest or a boundary.

The role of Organoids in precision health

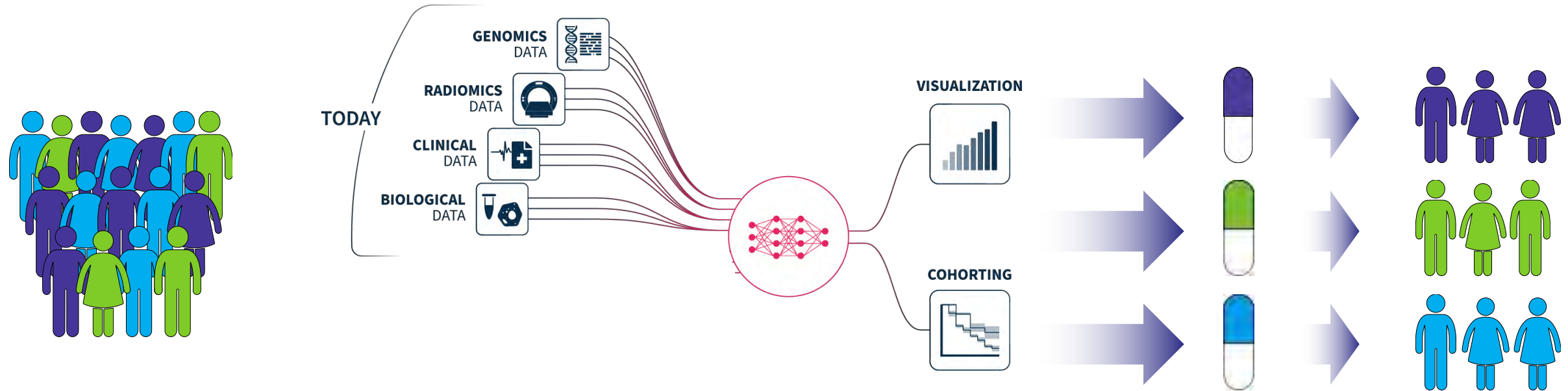
Nathalie Brandenburg, PhD, eMBA

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- A background image showing numerous organoids, which are small clusters of cells, stained with fluorescent dyes. The organoids appear as glowing blue and green spheres of varying sizes against a dark background. A white geometric shape, resembling a stylized 'L' or a corner bracket, is visible in the upper right quadrant of the image.
1. Personalized medicine today
 2. Introduction on organoids
 3. Case study: Cystic Fibrosis

A fluorescence microscopy image showing numerous cells. The cells are stained with a blue dye (likely DAPI) to highlight the nuclei. Some cells show green fluorescence, possibly indicating specific organelles or proteins. A few cells exhibit red fluorescence. A white, irregular polygonal shape is drawn in the upper right corner of the image.

Current practice in personalized medicine

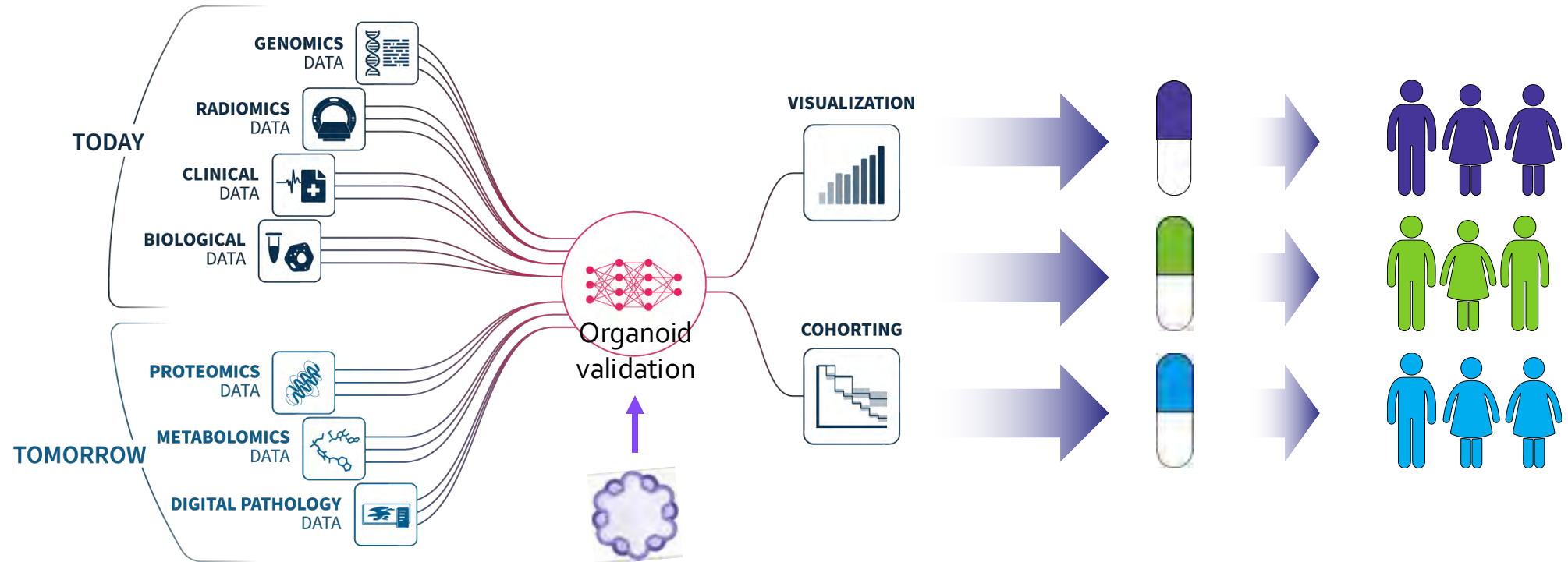
Current practice in personalized medicine



- 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

A fluorescence microscopy image showing numerous organoids, which are small, three-dimensional clusters of cells. The organoids are stained with fluorescent dyes, appearing in shades of blue, green, and red against a dark background. Some organoids show internal structures, possibly representing different cell types or developmental stages. A white line in the top right corner indicates a specific region of interest.

What are organoids ?

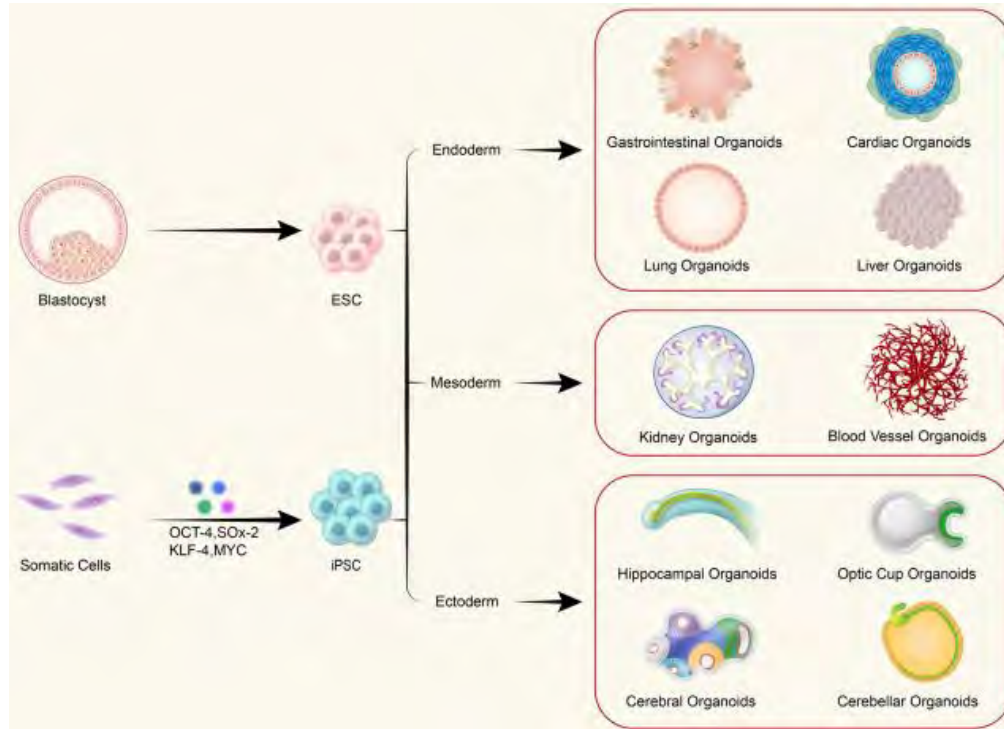
Organoids are personalized mini-organs in a dish

- 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

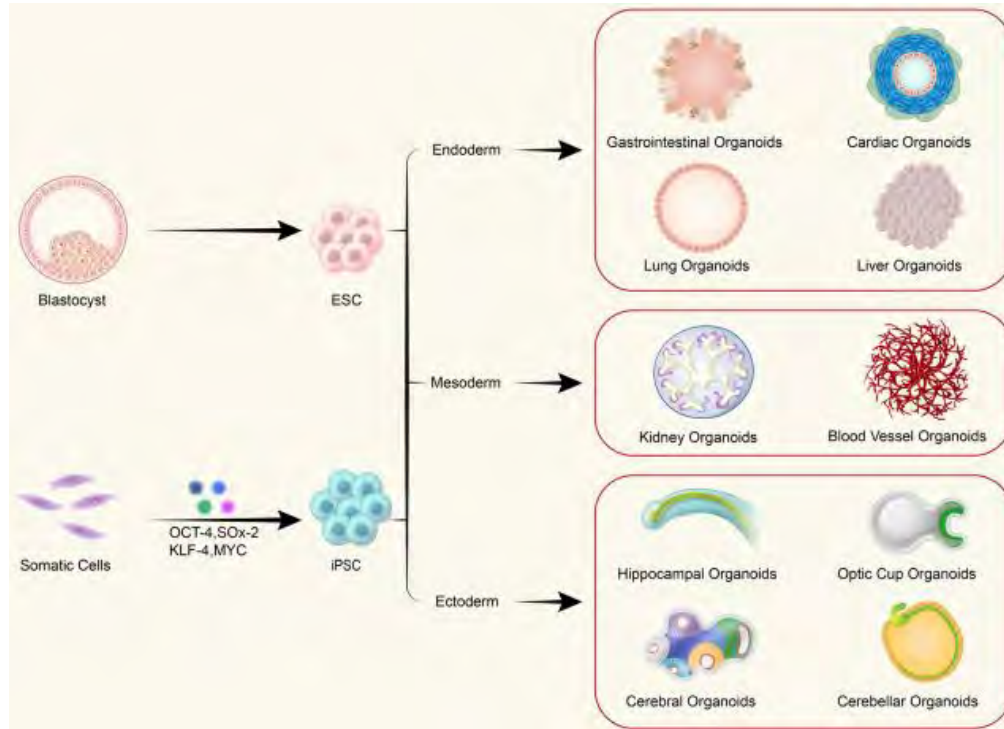
Pluripotent stem cells derived organoids



- 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

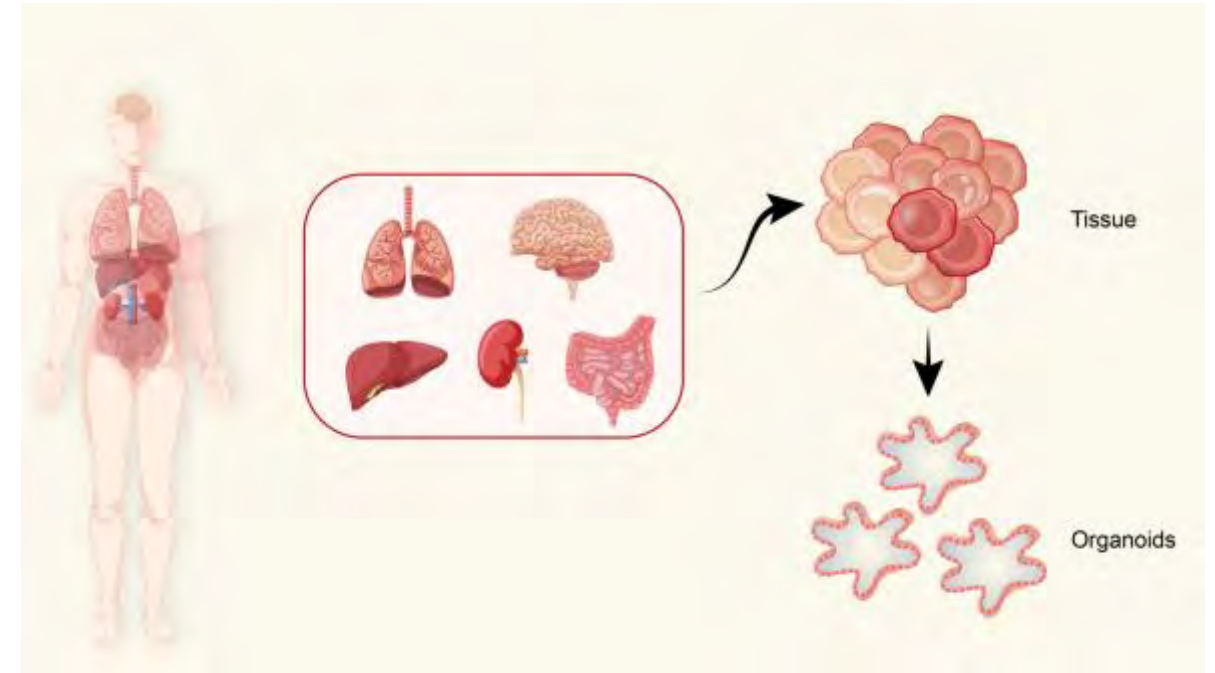
Organoids can be generated from various cell sources

Pluripotent stem cells derived organoids



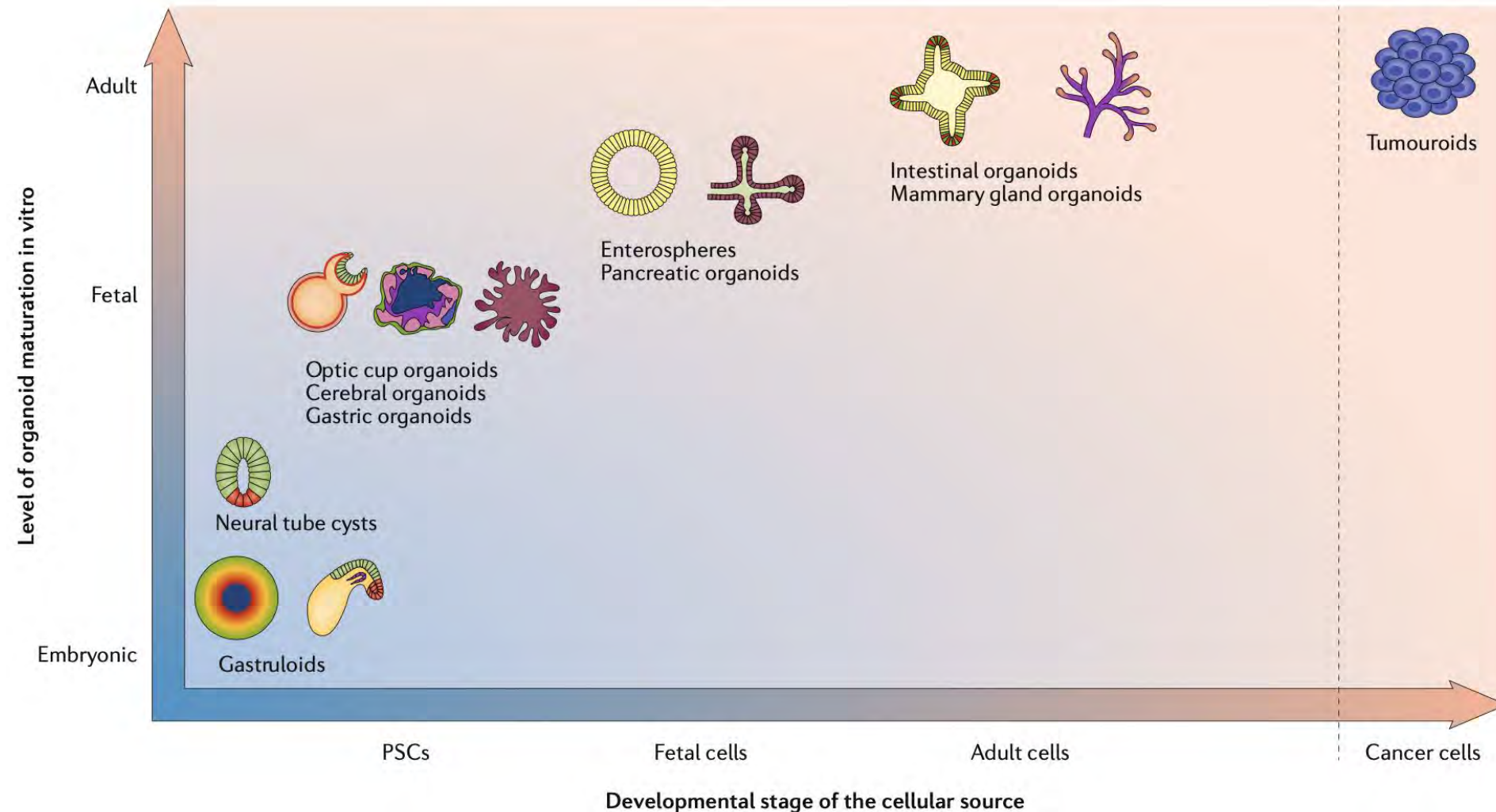
- Need maturation from the most naïve state
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- Hard to mature in vitro into an adult phenotype
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Adult stem cells derived organoids (also called Patient-derived organoids, PDOs or tissue-derived organoids)



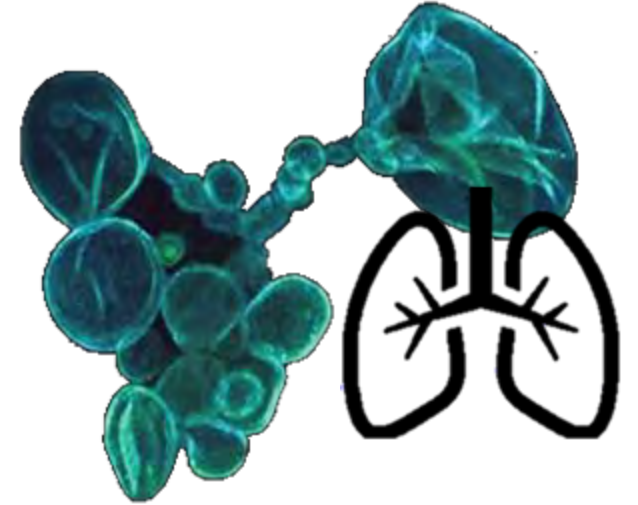
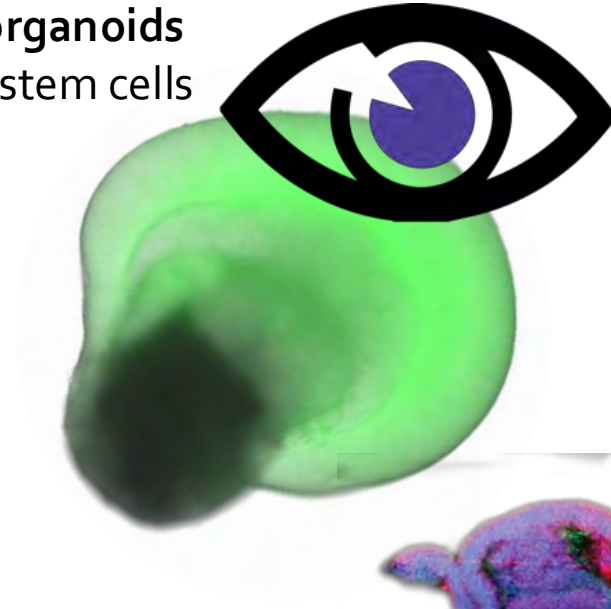
- Generated from stem cells that are already tissue-specific
- Short and simpler differentiation protocols
- More amenable to personalized medicine

The starting cell type determines organoid maturation levels in vitro

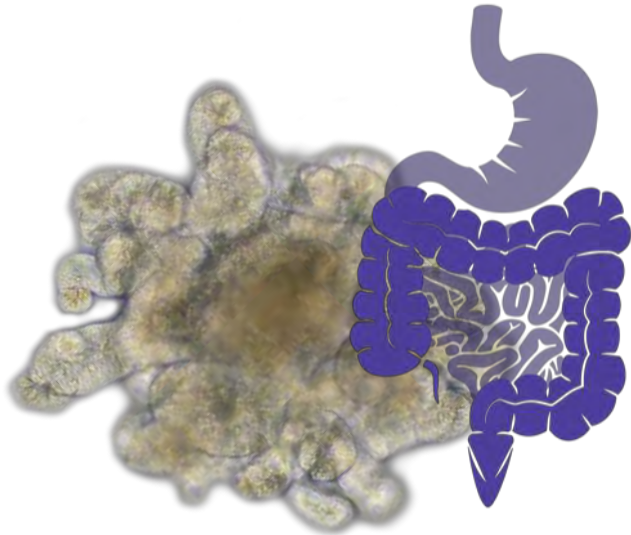


Organoids, a few examples

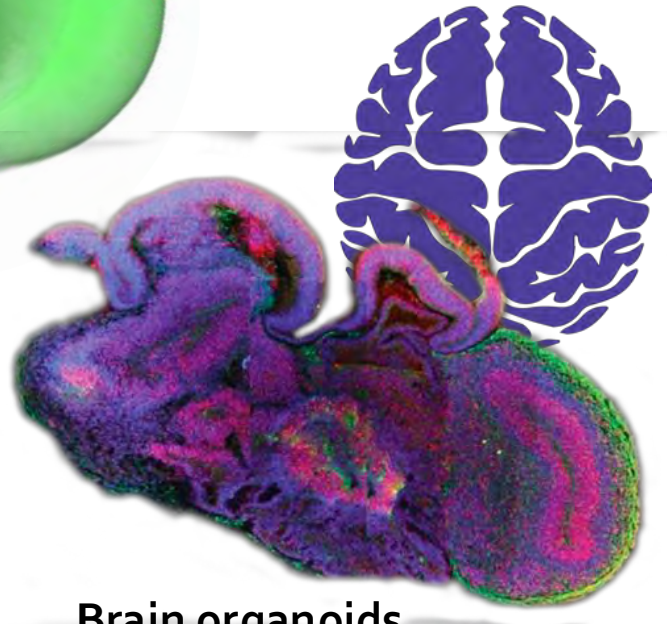
Retinal organoids
from pluripotent stem cells



Lung organoids
from adult stem cells



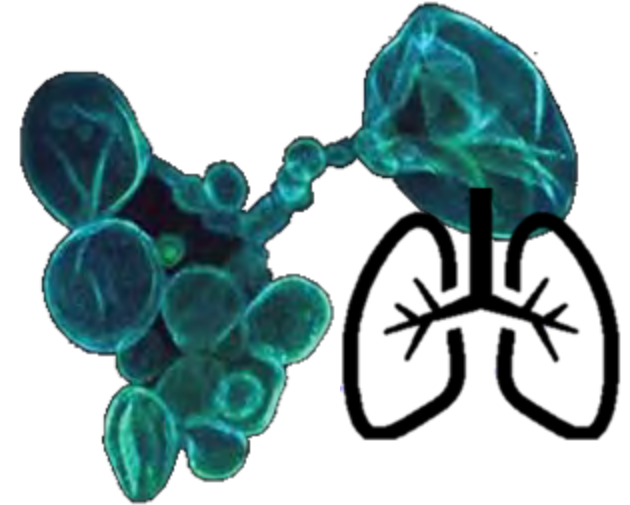
Intestinal organoids
from adult stem cells



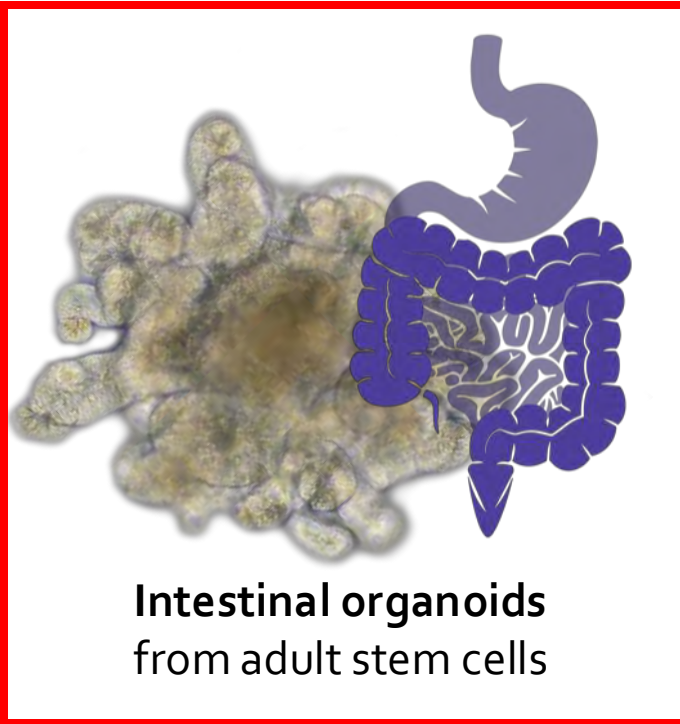
Brain organoids
from pluripotent stem cells

Organoids, a few examples

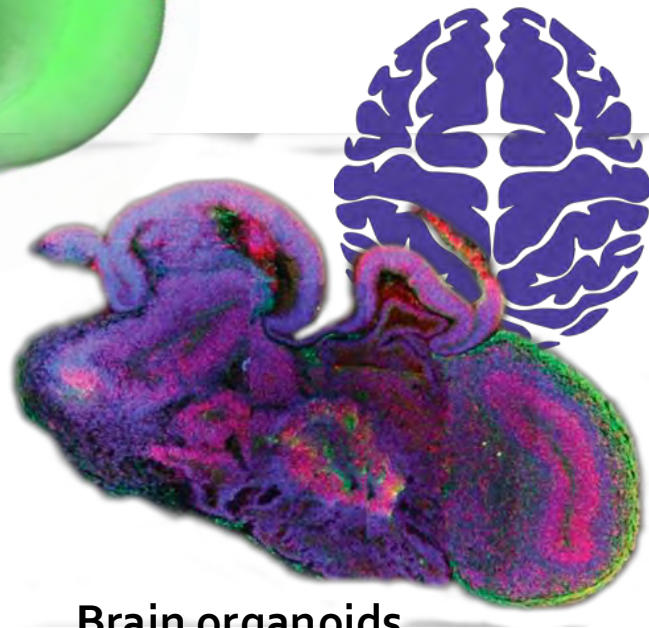
Retinal organoids
from pluripotent stem cells



Lung organoids
from adult stem cells

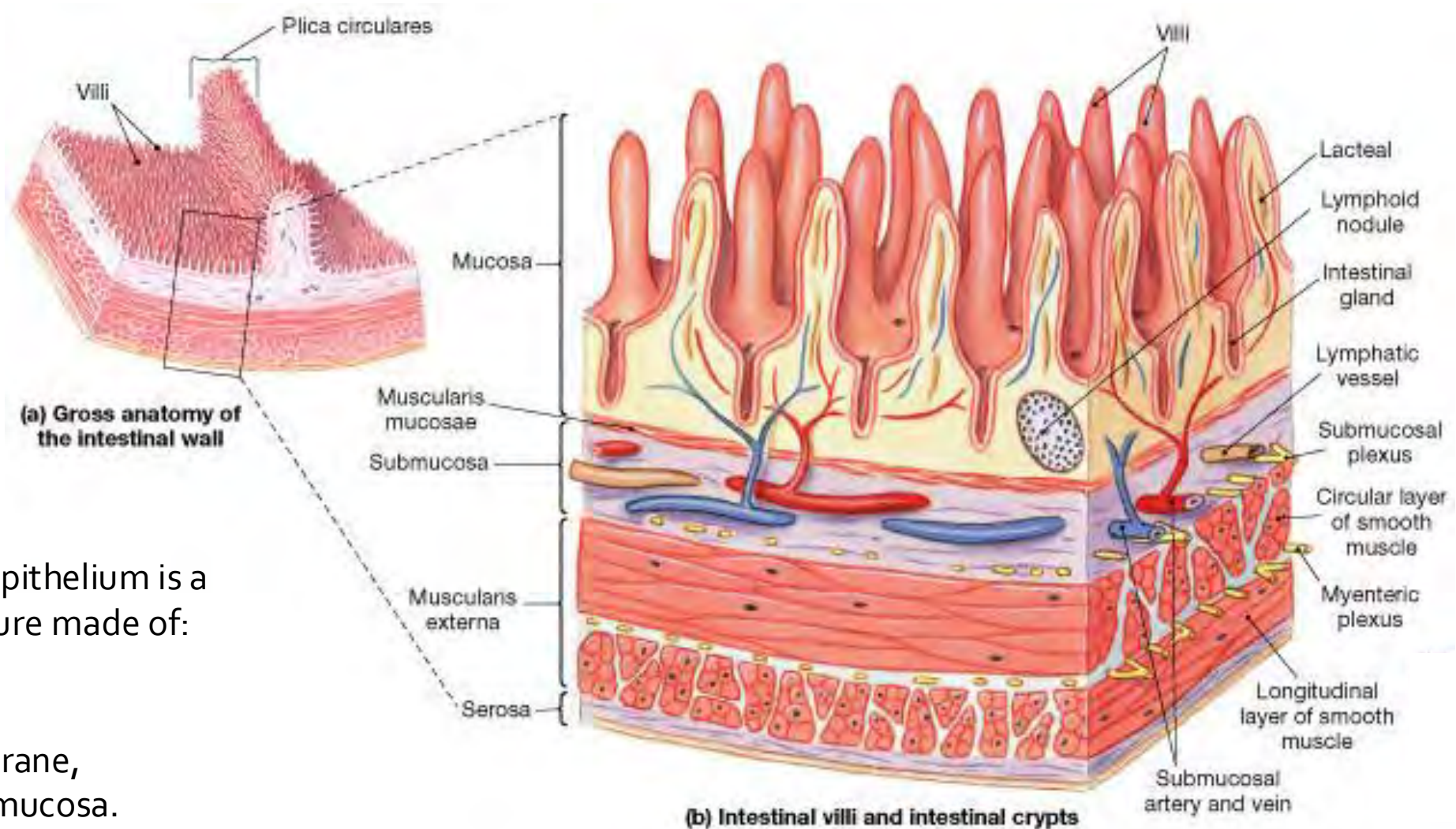


Intestinal organoids
from adult stem cells



Brain organoids
from pluripotent stem cells

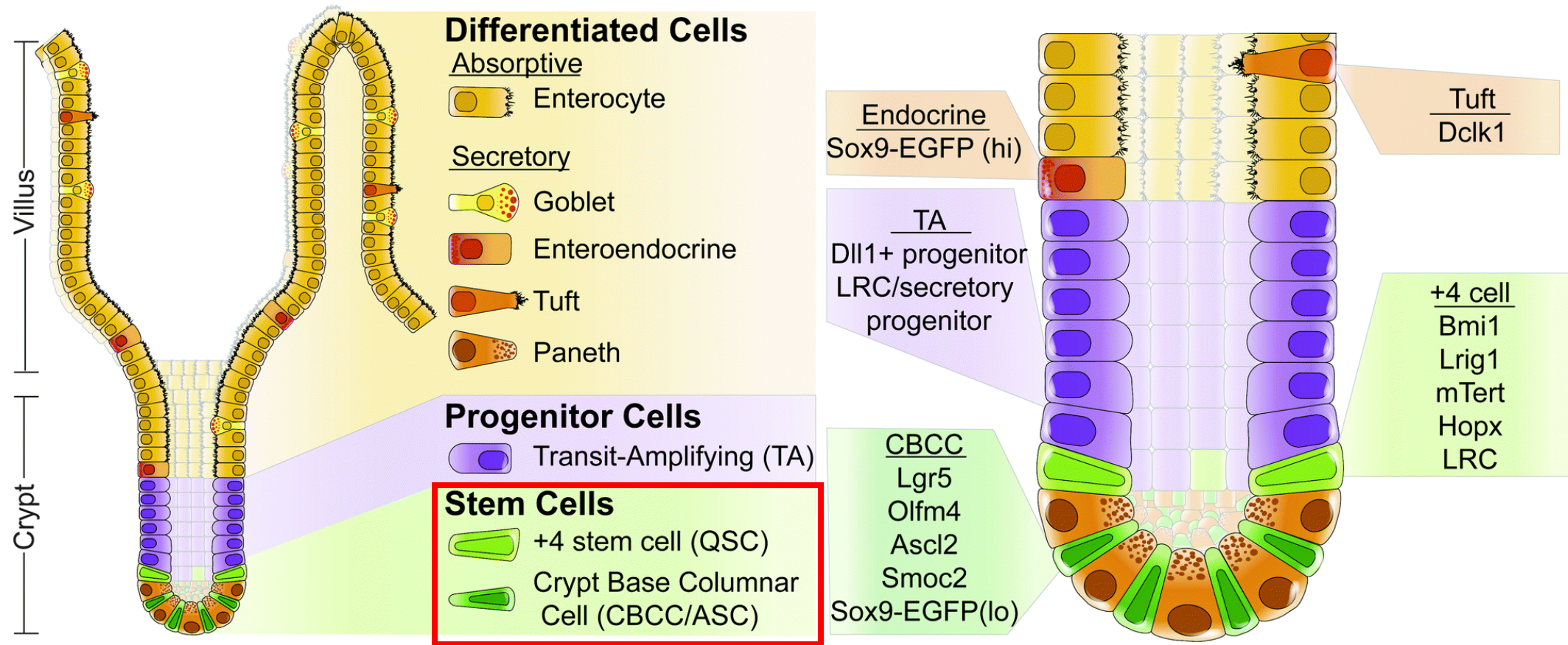
The example of the intestine



The intestinal epithelium is a complex structure made of:

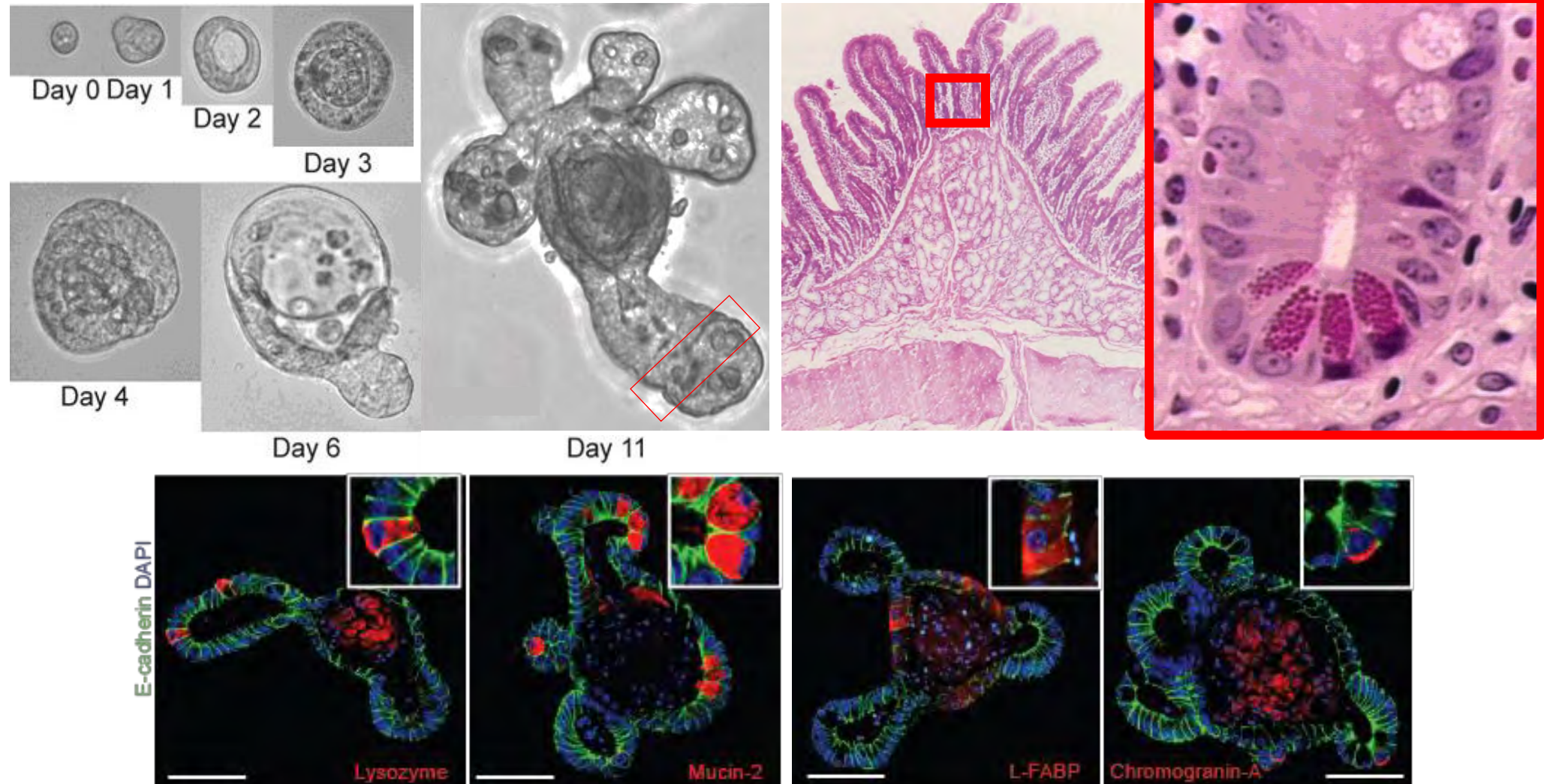
- Villi,
- Crypts,
- Basal membrane,
- Underlying mucosa.

The cellular & molecular composition of the intestinal crypt



The example of the intestine, in the mouse

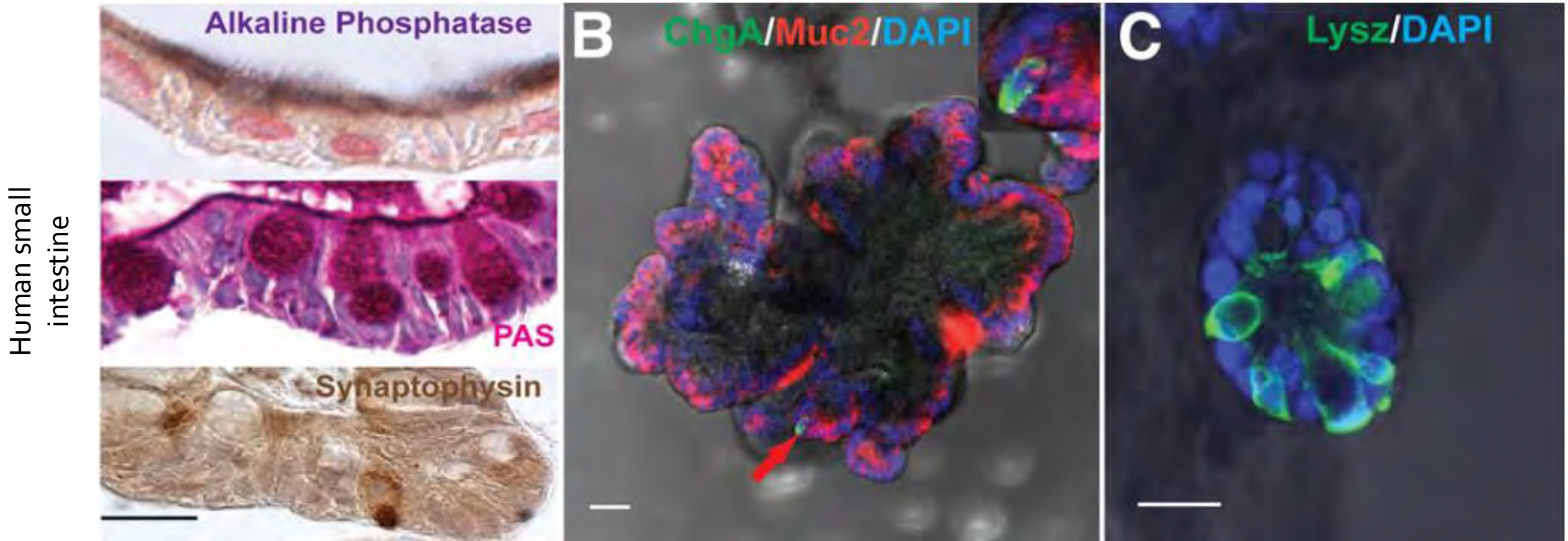
Mouse small intestine



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 Master Course EPFL - BIO491

The example of the intestine, in human



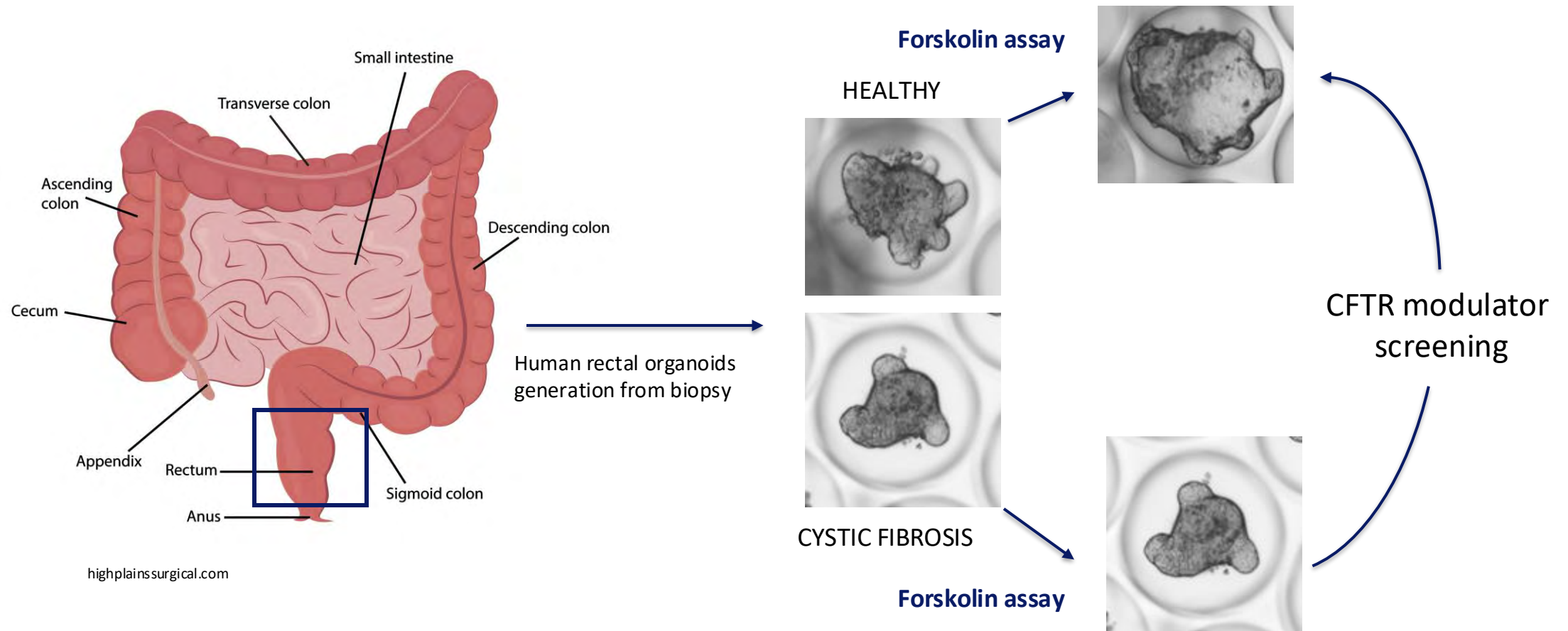
- Intestinal organoids recapitulate extraordinarily well the cellular and molecular hallmarks of the native tissue,
- Adult stem cells-derived organoids of other tissues (lung, pancreas, liver, nasal epithelium,..) resemble their organs of origin with various degrees of accuracy.

A fluorescence microscopy image showing numerous cells. The cells are stained with a blue dye (likely DAPI) to highlight the nuclei. Some cells show green fluorescence, possibly indicating specific organelles or proteins. A few cells exhibit red fluorescence. A white line is drawn in the upper right corner, possibly indicating a region of interest or a specific cell. The text "The case study of Cystic Fibrosis" is overlaid in the center of the image.

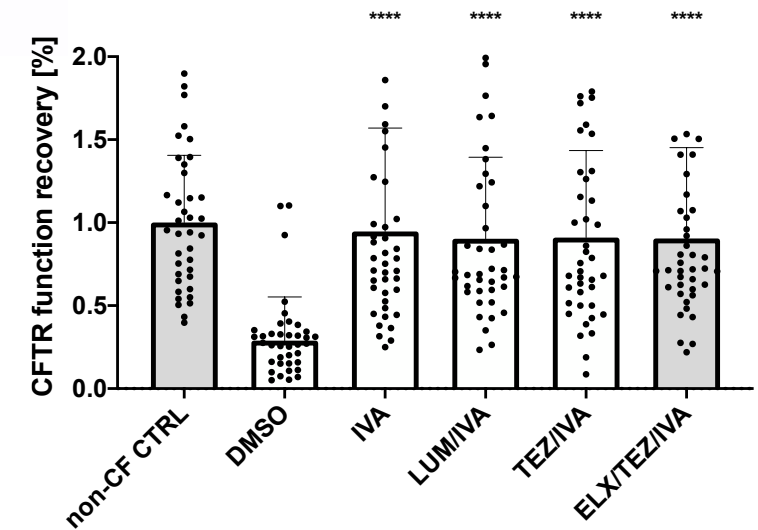
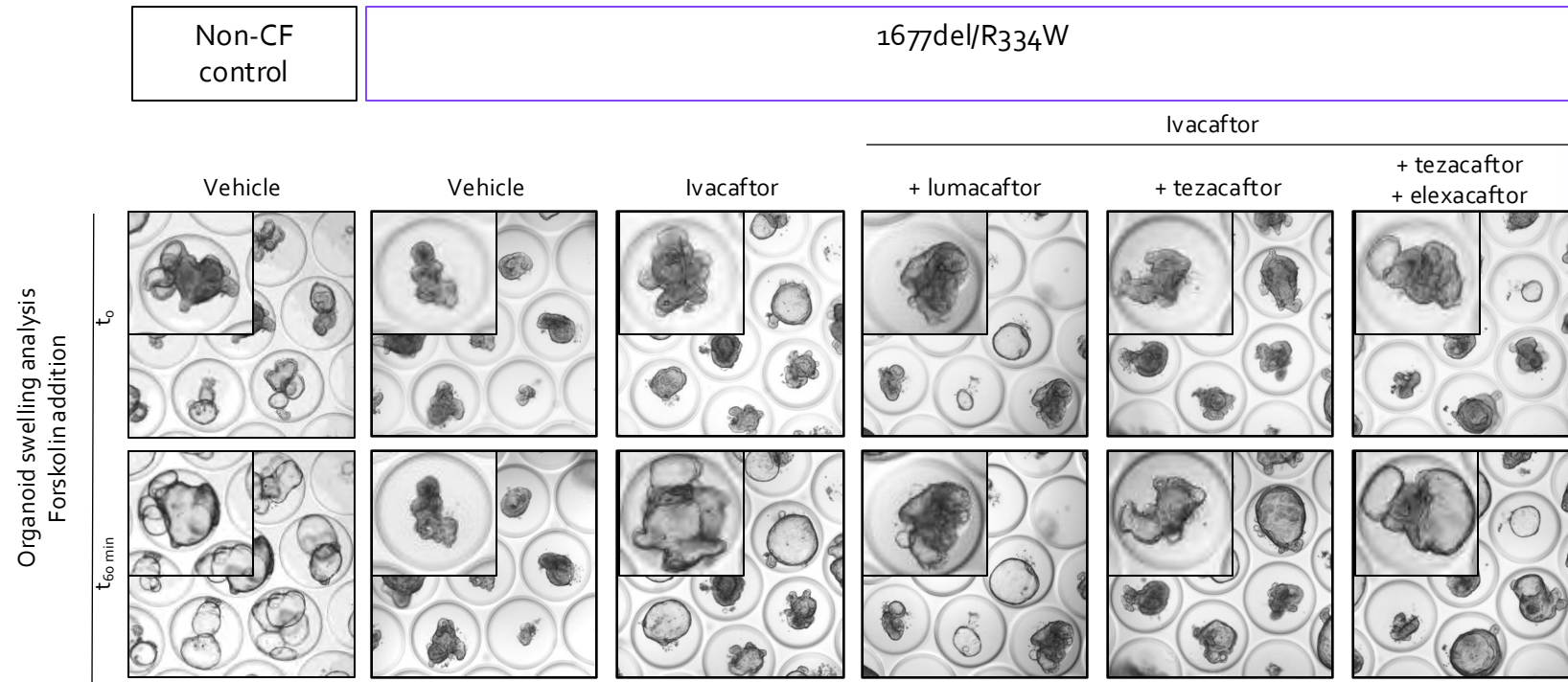
The case study of Cystic Fibrosis

ORGANOIDS CAN BE DERIVED FROM CF AND HEALTHY PATIENTS

A COLLABORATIVE WORK BETWEEN CHUV AND EPFL



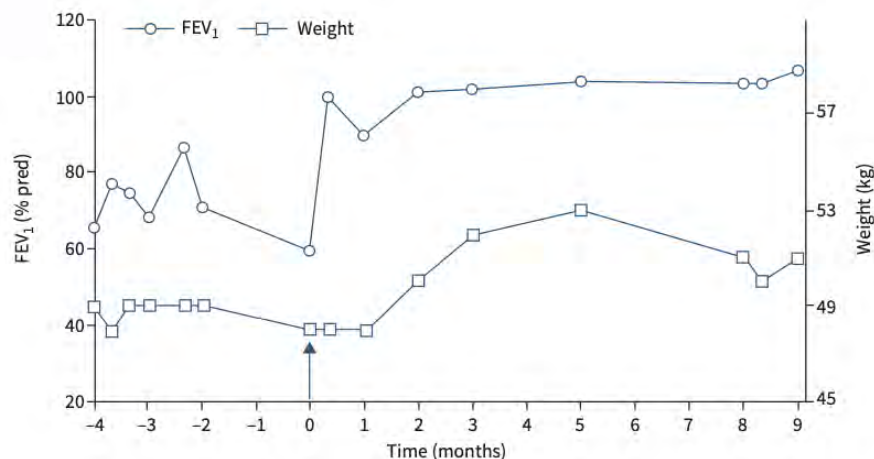
1677del/R334 MUTANT ORGANOID RESPONSE TO IVACAFTOR



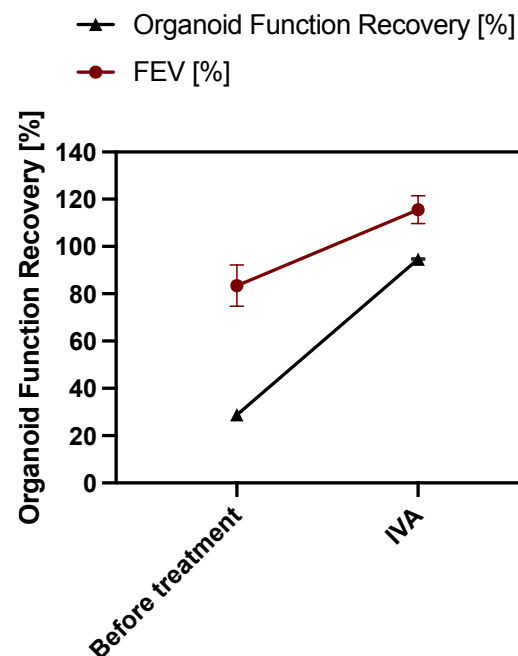
IVA = ivacaftor
LUM = lumacaftor
TEZ = tezacaftor
ELX = elxacaftor

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

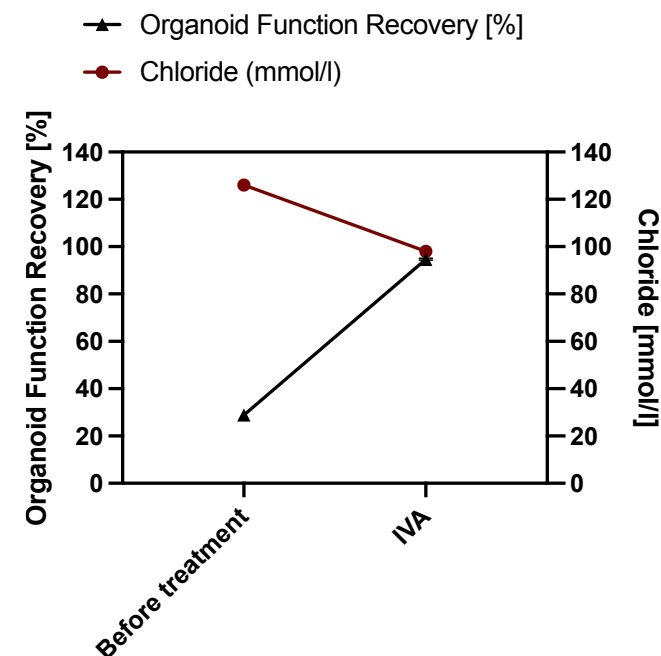
1677del/R334 PATIENT RESPONDS TO IVACAFTOR: A SUCCESS STORY



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



A fluorescence microscopy image showing numerous cells. The cells are stained with a blue dye (likely DAPI) to highlight nuclei, a green dye to highlight certain organelles or structures, and a red dye to highlight others. The cells are of various sizes and shapes, some appearing as clusters. A white line in the top right corner indicates a specific region of interest.

Questions ?