What is an organoid?

an artificially grown mass of cells or tissue that resembles an organ

The ability to grow human tissues from stem cells in 3D culture has the potential to revolutionize the drug discovery process and regenerative medicine.
3D organoid models

**Organotypic**
Organoids resemble the *in vivo* situation as closely as possible.

**Multiple cell types**
Organoids consist of multiple cells and contain at least two cell types.

**Self-organization**
Organoids spontaneously assemble into ordered structures and do not require preformed patterns.

**3D organization**
Maintains cell differentiation and enables expansion of progenitor cells.

**Growth factors**
Selected on the basis of their role(s) in health and disease or their effect in 2D cultures.

**Extracellular matrix**
Provides cues for differentiation and cell orientation, but does not limit self-organization by enforcing an architecture.

**Adult organ derived**
Enhances clinical applicability and enables patient-specific study of disease and personalized medicine.

**Stem or progenitor cells**
Required for long-term expansion of organoids.
Transit-Amplifying cells (Progenitors)

Stem Cells

Differentiated cells

DIFFERENTIATION

Intestinal epithelium renewal – Intestinal Stem Cells

Yan, et al., PNAS 2012
Intestinal epithelium renewal – Intestinal Stem Cells

Fibroblasts

Differentiation

Self Renewal Proliferation

Wnt
BMP
Noggin

Yan, et al., PNAS 2012
Intestinal crypt: origin of the cancer stem cells

Normal Stem Cells  $\rightarrow$ Cancer Stem Cells

Oncogenic Hit

Tumor development $\Rightarrow$ Adenocarcinoma (cancer)

Barker et al., Nature 2009
The 3D colon organoid model

Adapted from Barker, Nature 2014
The 3D colon organoid model

Patients
(IBD, CRC,...)

Resections, biopsies

OrganoCan consortium

Adapted from Barker, Nature 2014

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The 3D colon organoid model

1) Colorectal resection / biopsie

2) Crypt extraction

3) Plating in matrigel

Specific medium (Wnt3A, Noggin, R-spondin, EGF...)

Day 1

From day Day 3 to 14
The 3D colon organoid model

1) Is a polarized structure
1) Is a polarized structure
2) Reconstitutes the epithelial cell populations
3) Reconstitutes cryptic structures
3D Colorectal Human Organoids can be...

4) Co-cultured with stromal cells (here: fibroblasts)

5) Be analyzed in terms of RNAs, proteins expressions, secretome...

6) Frozen, stored and thawed
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Healthy patients
Crohn disease
Ulcerative colitis
Colorectal Cancer

Organoid cultures: Intestinal / Colorectal, Bladder, Pancreas...

High Content Screening: Imaging, Analysis, Profiling

PerkinElmer
OrganoCan Project:
Development of a High Content Screening approach based on 3D human colon organoid to identify drug candidates against ColoRectal Cancer

Drug screening application

1) Patient:Mice tissue resections
2) Epithelium extraction
3) Plating in 96 well plate for screening
4) Plating in 96 well plate for screening
5) Plate scanning and imaging
6) Application to patient treatment protocol

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Pancreas
Colon
Bladder
Prostate

Data Mining High Content Profiler
Image analysis High Content Screening
THANKS TO...

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CONTRE LE CANCER

LA LIQUE

l’Europe s’engage en France

FEDER