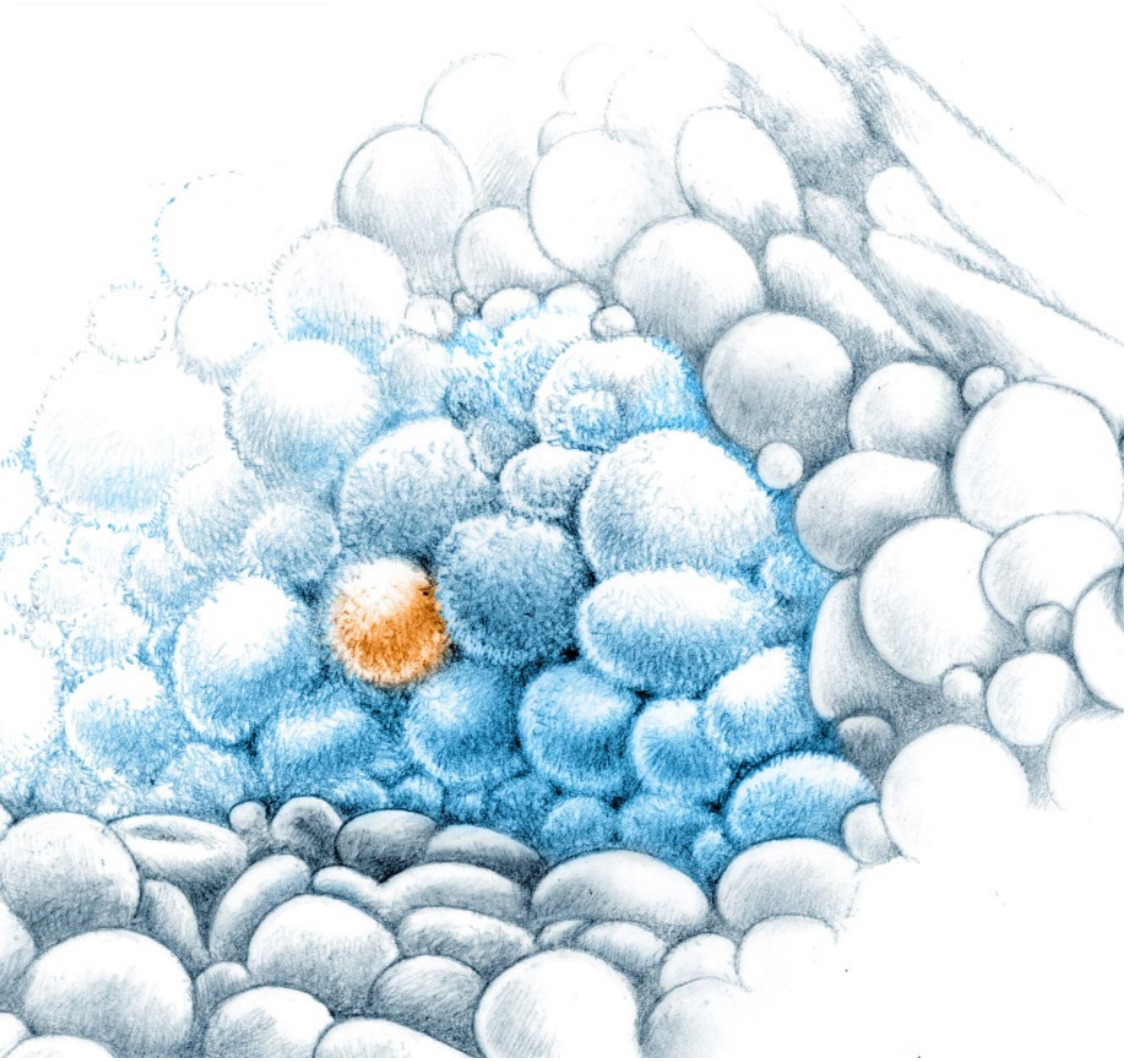
Cancéropôle Île-de-France

FÉDÉRER LA RECHERCHE ET L'INNOVATION MÉDICALE EN CANCÉROLOGIE



# Contribution of tumor organoid models to basic and translational oncology research and applications to predictive medicine


**Louis-Bastien Weiswald**

**Inserm U1086 ANTICIPE**

Interdisciplinary Research Unit for the Prevention and Treatment of Cancer

**ORGAPRED core facility**

« Tumor organoids for research and predicting response to treatment » core facility



www.canceropole-idf.fr

MODÈLES 3D POUR L'ÉTUDE DU MET

Jeudi 14 septembre 2023

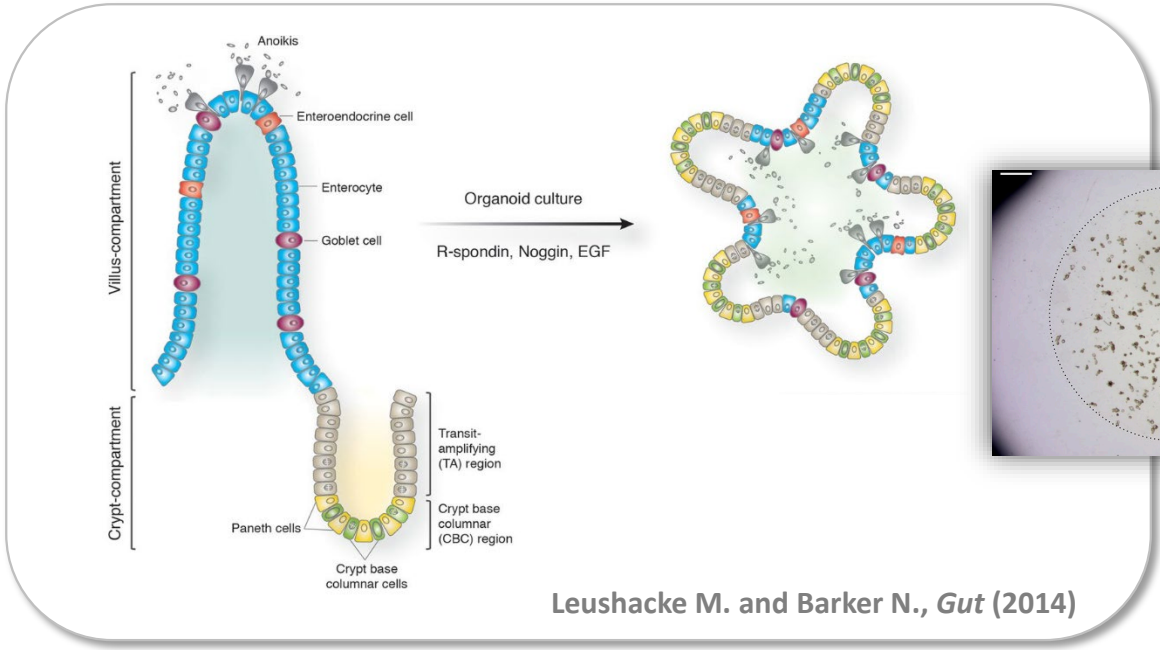
# Organoids

**3D** multicellular structures

Mimick *in vitro* **micro-anatomy of original organ**

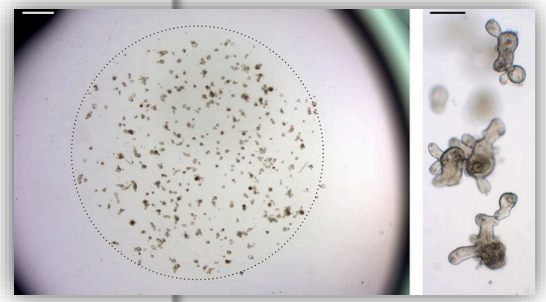
**Self-renewal** and **differentiation** capacities of stem cells

- **Self-organization** similar to that of the tissue of origin
- Organ-specific **cell types**
- Physiological **function** that are specific to that organ



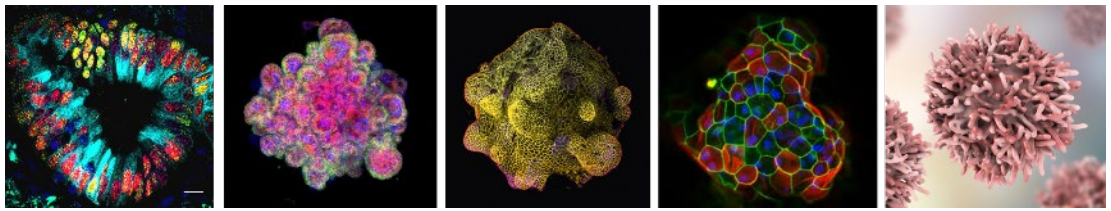

Leushacke M. and Barker N., *Gut* (2014)

**Intestine**

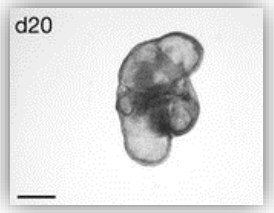


Sachs N. et al., *Development* (2017)

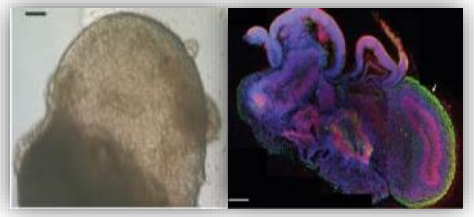
Tissue-specific culture methods and media



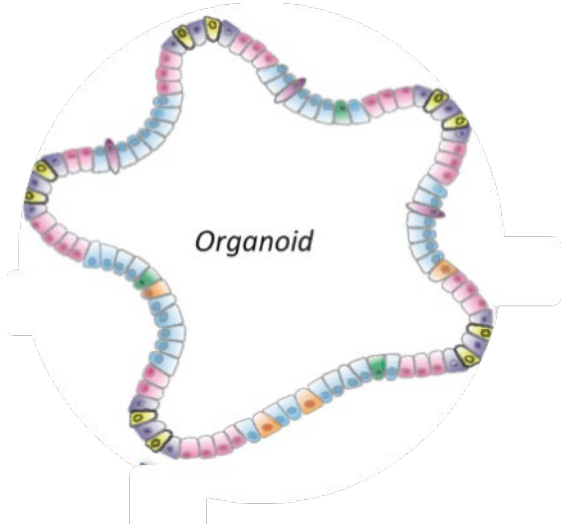
**Lung**



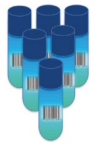

**Brain**

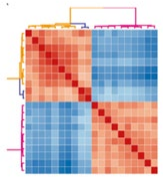


# Organoids: potential applications



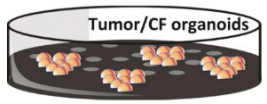

**Biobank of patient-derived organoids**
**&**
**Molecular caracterization**
*(transcriptome, proteome, epigenome, metabolome analysis)*





Dutta D. et al., *Trends Mol Med* (2017)

## Disease modeling

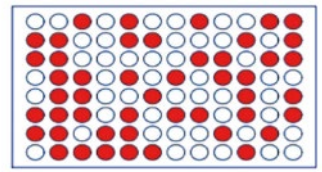



## Regenerative medicine

H. Clevers lab

## Drug design

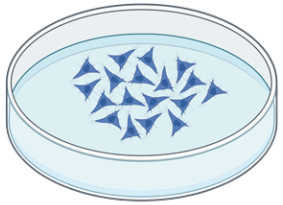
**Effectiveness** and **toxicity**
of new potential drug candidates



Drug testing

## Personalized medicine

# History of tumor cell models



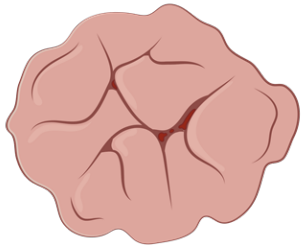
Establishment of the **first cell line** (HeLa) derived from a cervical cancer sample

**1951**



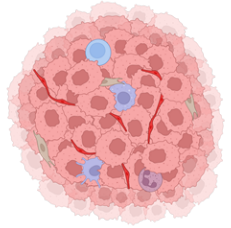
Culture of the transformed cell line V79 derived from lung fibroblasts of Chinese hamster as **spheroids**

**1970**



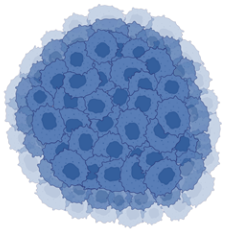
Culture of **tumor explants** sliced from different human tumors

**1986**



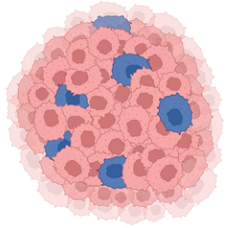
Establishment of **organotypic spheroids** from human gliomas

**1990**



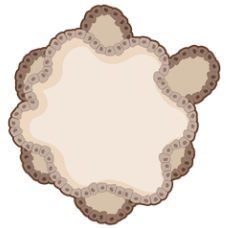
Establishment of **tumorospheres** from human breast and brain tumors

**2003**



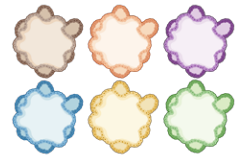
Establishment of **tissue-derived tumor spheres** of human colorectal cancer

**2009**



Establishment of **tumor organoids** from human colon tumors

**2011**

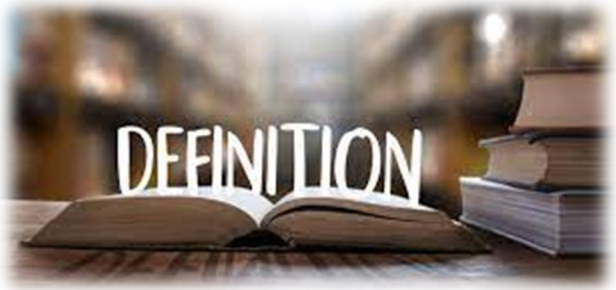


Establishment of the first panel of **tumor organoids** from human prostate tumor samples

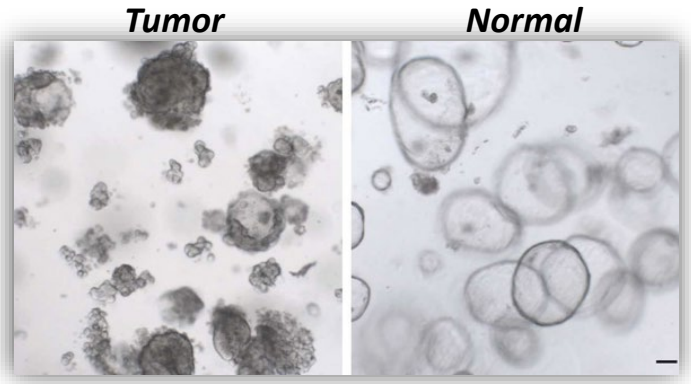
**2014**

Adapted from Thorel. et al., *Médecine/Sciences* (2022)

# Tumor organoids




**Gastric organoids**




Bartfeld et al., *Gastroenterology* (2015)

*Definition of normal organoids inapplicable for tumor organoids?*

- **Tumor organoids** ***(Mark Rubin, Englander Institute for Precision Medicine, New York)***
  - Tumor cells derived from tumor specimen / biopsies / cytopunction / malignant effusions of patients
  - Proliferate most of the time as spheres
  - Culture for at least 5 passages
  - Cryopreservation

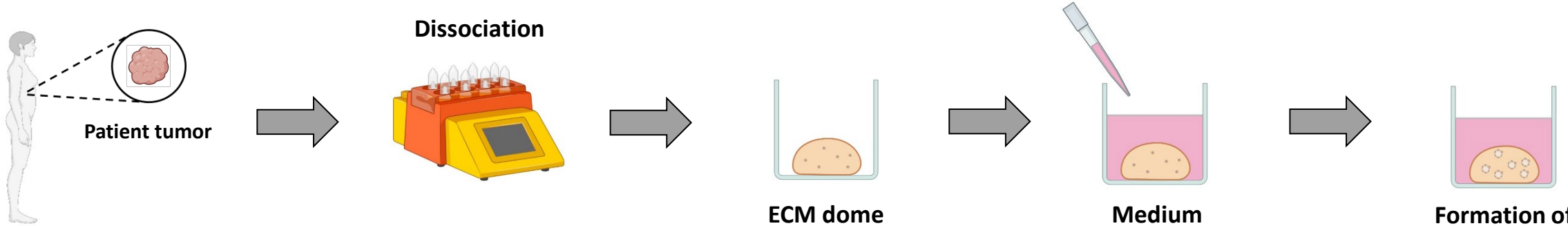
→ **= Tumoroids**

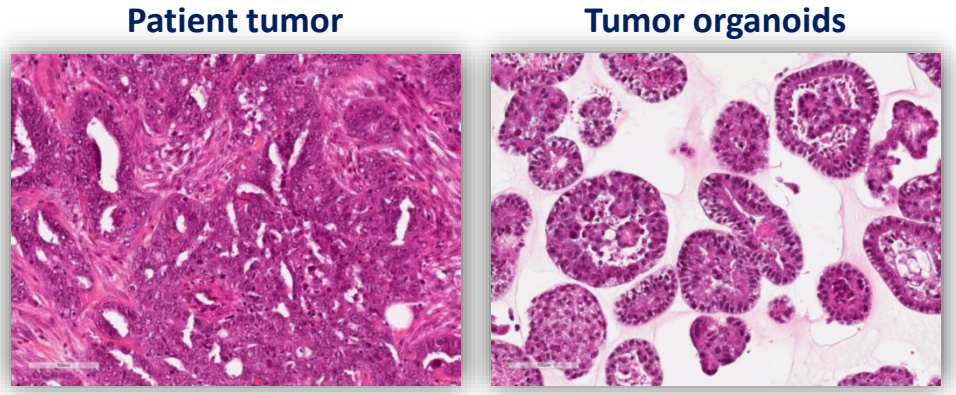
# Overview of the tumor organoid panels

| System | Cancer type | Success rate | References |
|---|---|---|---|
| **Digestive** | Pancreatic cancer | **62%** (52/83) | Drihuis E. et al., *PNAS* 2019 |
| | | **75%** (103/138) | Tiriac H. et al., *Cancer Discov* 2018 |
| | | **85%** (17/20) | Huang L. et al., *Nat Med* 2015 |
| | | | Boj SF. et al., *Cell* 2015 |
| | Colorectal cancer | **100%** | Fujii M. et al., *Cell Stem Cell* 2016 |
| | | **~ 90%** (22/27) | van de Wetering M. et al., *Cell* 2015 |
| | Hepatocellular carcinoma | **26%** (10/38) | Nuciforo S. et al., *Cell Rep* 2018 |
| | | 100% | Broutier L. et al., *Nat Med* 2017 |
| | Gastric carcinoma | **50%** | Yan HHN. et al., *Cell Stem Cell* 2018 |
| | | **71%** (10/14) | Gao M. et al., *Ann Surg Oncol* 2018 |
| | Metastatic gastrointestinal carcinoma | **70%** (> 100) | Vlachogiannis G. et al., *Science* 2018 |
| | | **76%** (13/17) | Buzzelli JN. et al., *Stem Cell Res* 2018 |
| | Esophageal carcinoma | **31%** (10/32) | Li X. et al., *Nat Comm* 2018 |
| | Appendiceal carcinoma | **75%** (9/12) | Votanopoulos KI. et al., *Ann Surg Oncol* 2019 |
| **Respiratory** | Lung carcinoma | **88%** (14/16) | Sachs N. et al., *Embo j* 2019 |
| | Non-small cell lung cancer | **71.43%** (10/14) | Li YF. et al., *Neoplasma* 2020 |
| | (Primary & Metastatic) | **100%** (3/3) | Zhang Z. et al., *Plos One* 2018 |
| | | **28%** (5/18) | Sachs N. et al., *Embo j* 2019 |
| | Mesothelioma | **100%** (2/2) | Mazzocchi AR. et al., *Sci Rep* 2018 |
| **Urinary** | Prostate cancer | **16%** (4/25) | Puca L. et al., *Cell* 2018 |
| | (Primary & Metastatic) | **18%** (6/32) | Gao D. et al., *Cell* 2014 |
| | Bladder carcinoma | **70%** (12/17) | Lee SH. et al., *Cell* 2018 |
| | Renal cell carcinoma | **74%** (25/35) | Bolck HA. et al., *Eur Urol Focus* 2021 |
| **Reproductive** | Breast carcinoma | **~ 80%** (> 155) | Sachs N. et al., *Cell* 2018 |
| | Endometrial carcinoma | **100%** (15/15) | Turco MY. et al., *Nat Cell Bio* 2017 |
| | Ovarian cancer | **65%** (n = 32) | Kopper O. et al., *Nat Med* 2019 |
| **Nervous** | Glioblastoma | **91.4%** (total) | Jacob F. et al., *Cell* 2020 |
| | | **66.7%** (IDH1 mutant) | |
| | | **75%** (recurrent) | |

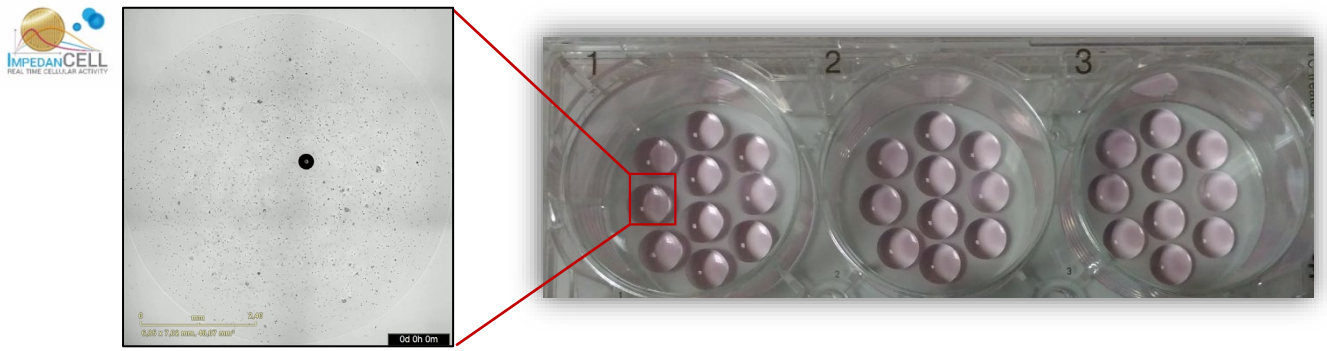
Adapted from Foo MA. et al., *Biomarker Res* (2022)

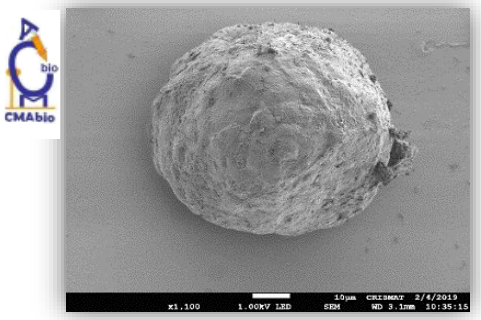
# Protocol for derivation of tumor organoids




Collaboration Pathology service
(Comprehensive Cancer Centre F. Baclesse)




## Tumor organoid medium

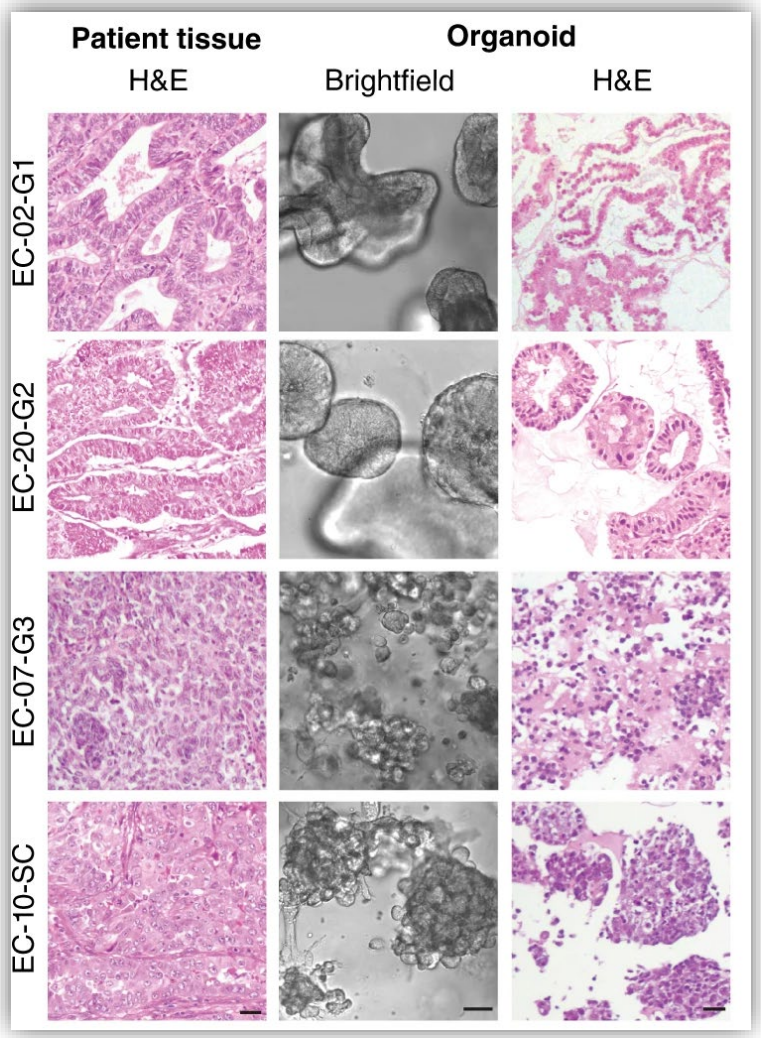
- R-spondin et Wnt3a
- Noggin
- Growth factors (EGF, FGF-2…)
- Inhibitors (ROCK, p38, TGF-β pathway)
- Antioxydants

**+ inhibitors / growth factors specific of the tumor type**

# Tumor organoids *vs* tumors of origin

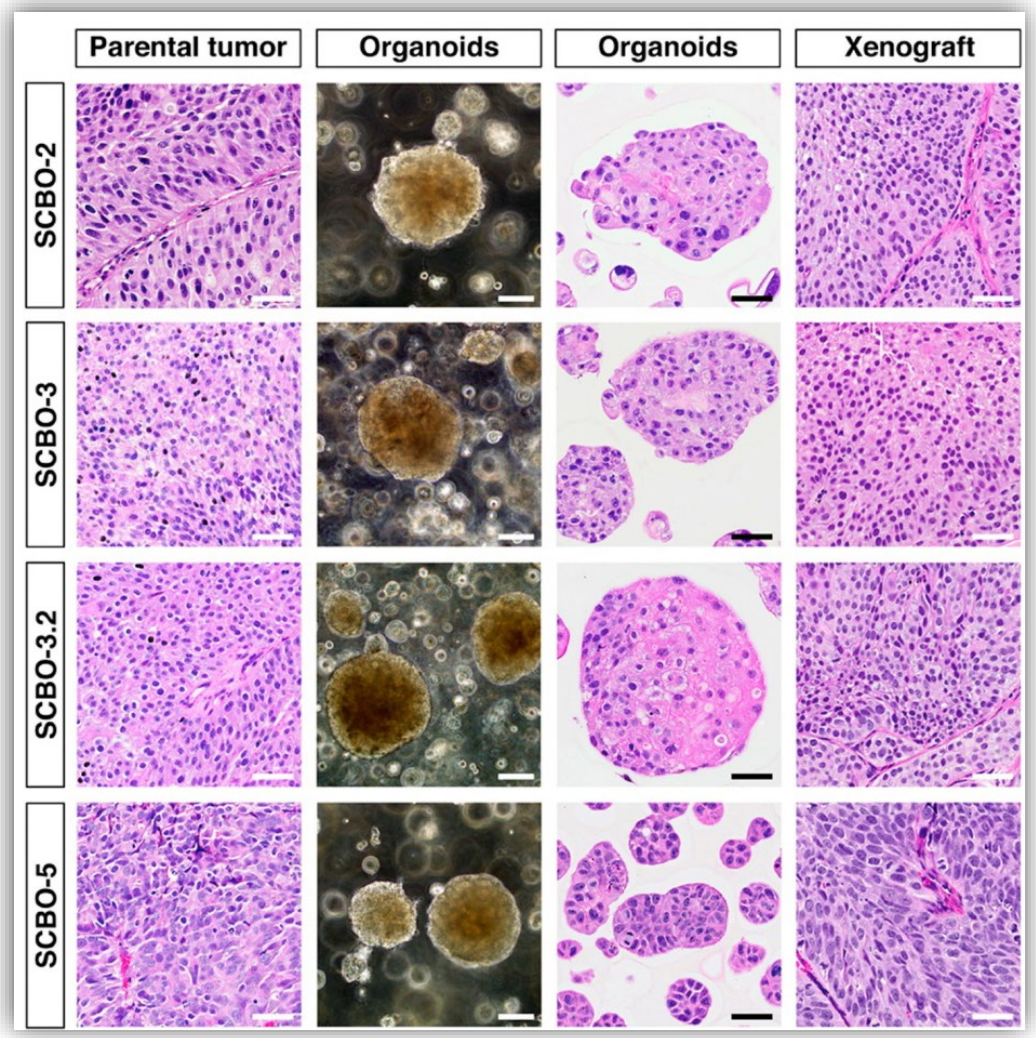
➢ **Histology**

## Endometrial cancer organoids




Berg, HF. et al., *Comm Med* (2021)

## Bladder cancer organoids

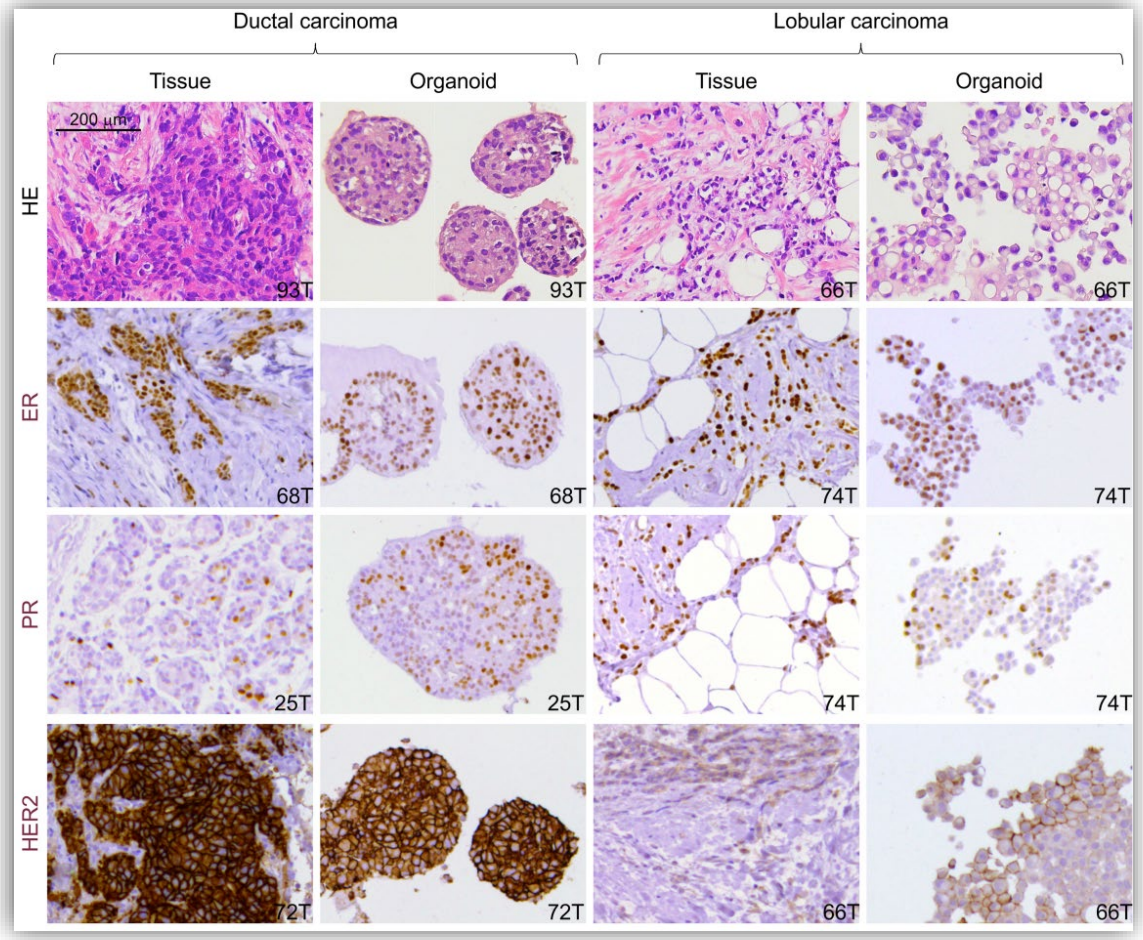



Lee, SH. et al., *Cell* (2018)

# Tumor organoids *vs* tumors of origin

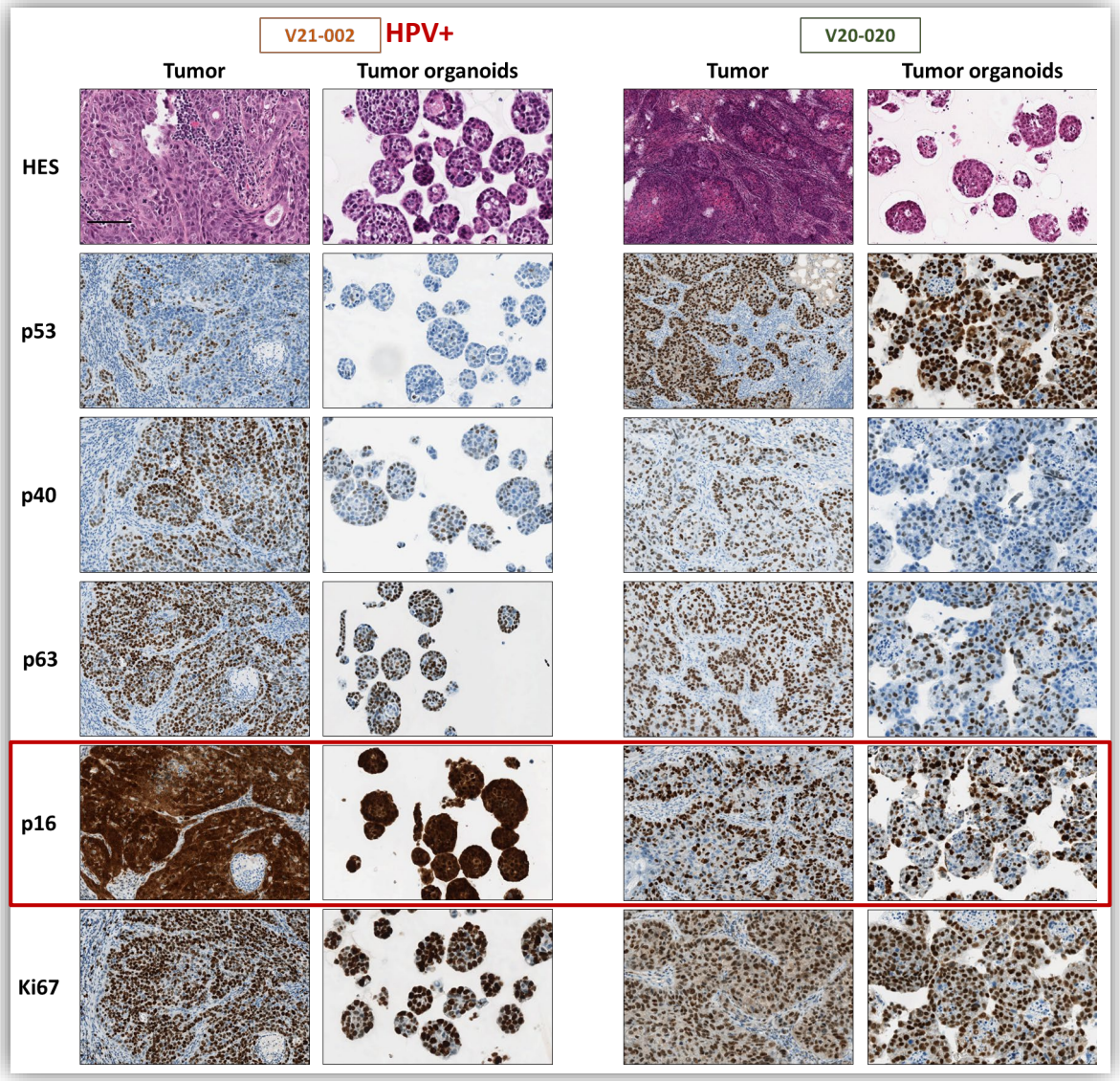
## ➢ Tumor markers

### Breast cancer organoids




Sachs N. et al., *Cell* (2018)

### Head and neck cancer organoids

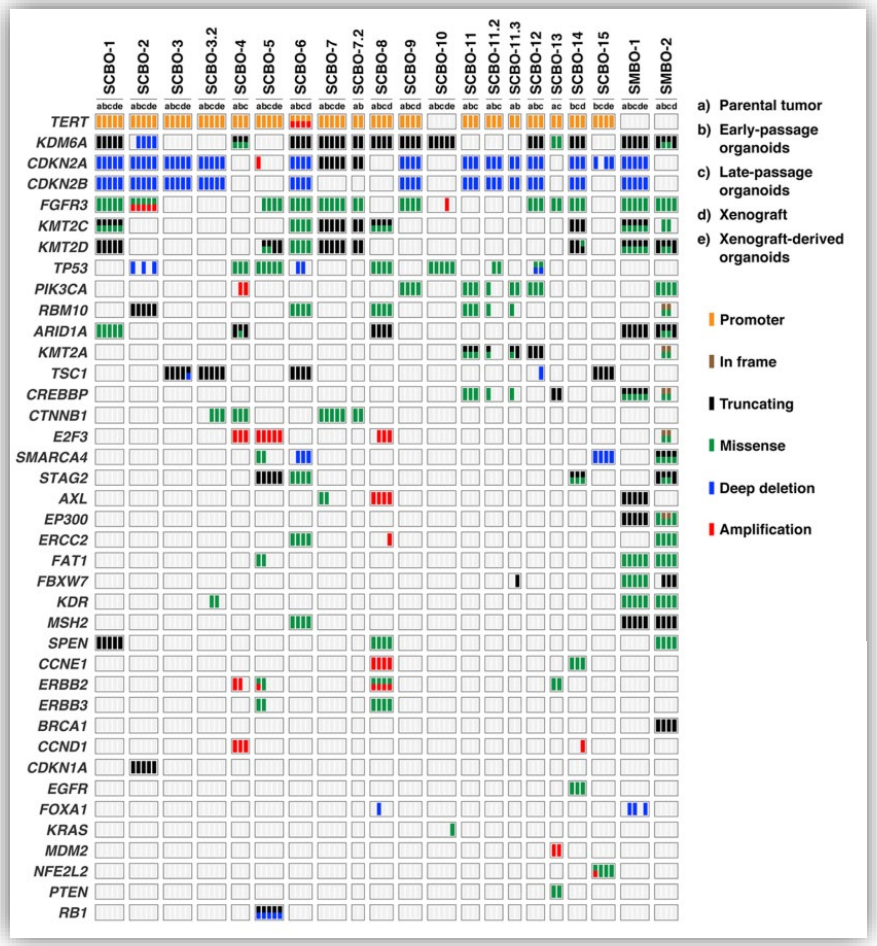



Perréard M. et al., *in preparation*

# Tumor organoids *vs* tumors of origin

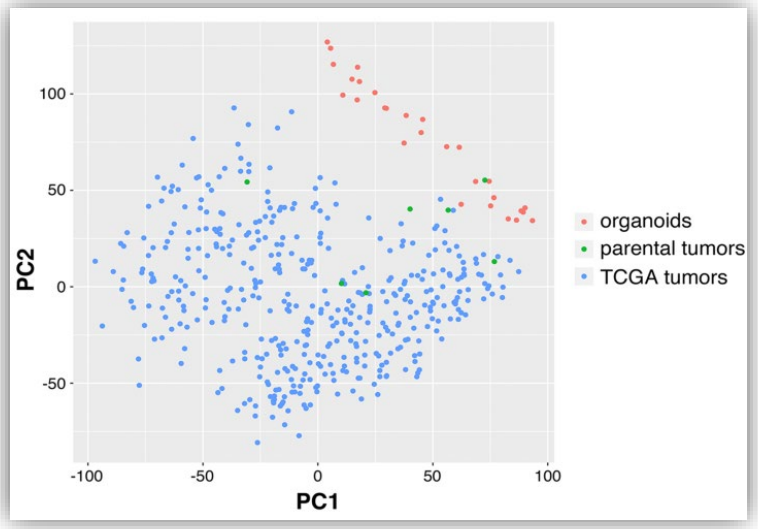
## ➢ Molecular characterization

### Mutations (bladder cancer)



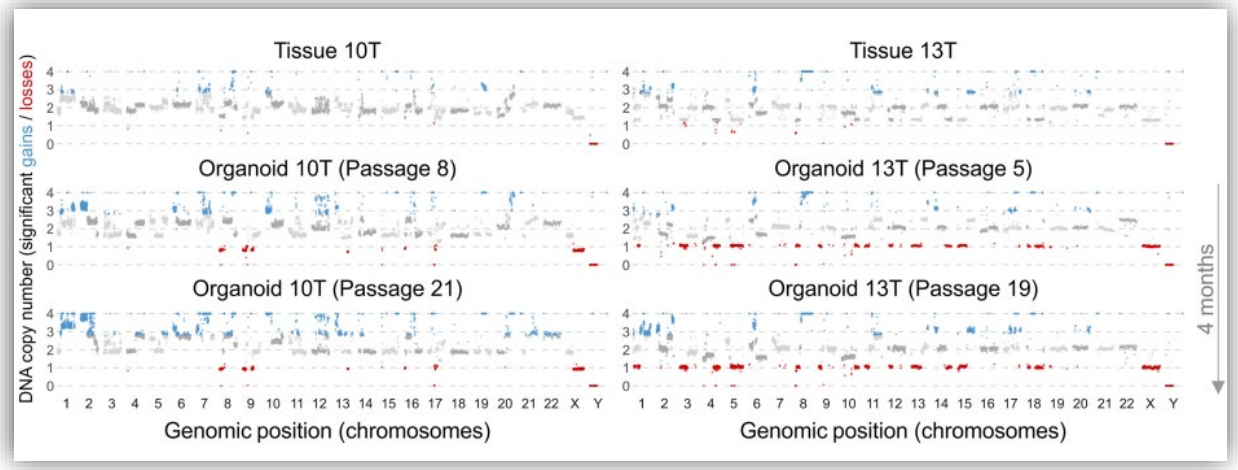

Lee, SH. et al., *Cell* (2018)

### Transcriptomic analysis (bladder cancer)




Lee, SH. et al., *Cell* (2018)

### Copy number variations (breast cancer)




Sachs N. et al., *Cell* (2018)

# Key applications of tumor organoids

- **Basic research**
- **Development of new therapeutic strategies** (need for a panel of tumor organoids)
- **Pharmacological screening** (need for high-throughput approaches)
- **Identification of predictive molecular signatures** (molecular characterization required)
- **Predictive functional assays in clinical management:**

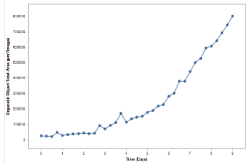
**Precision oncology**


Adapted from Thorel. et al., *Médecine/Sciences* (2022)

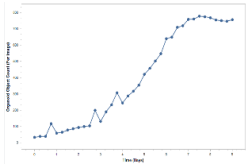
# Tumor organoids: evaluation of response to treatments

**Real-time live-cell imaging**
*(ImpedanCELL core facility, E. Brotin & C Denoyelle)*

**Organoid number**

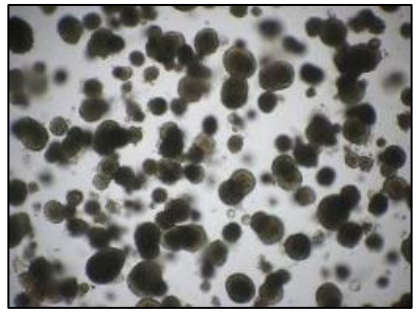


**Organoid total area**

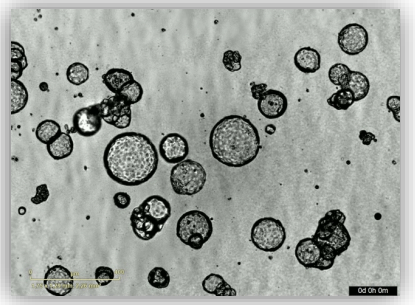


**Tumor organoids**

Treatments

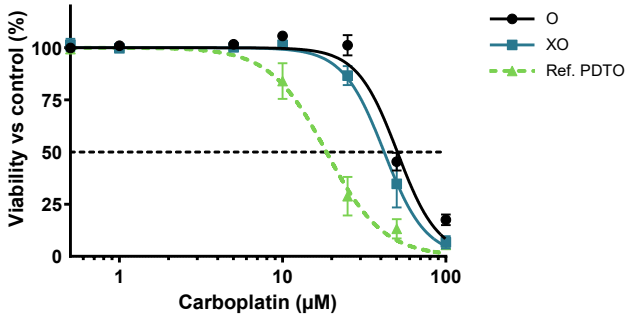


**Morphology**



Hadj Bachir et al., *Biol Cell* (2022)

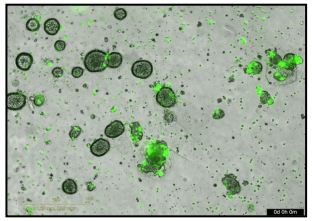
**Cell viability assay**
CellTiter-Glo 3D (Promega)



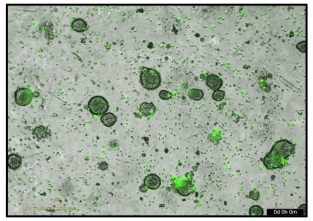

Thorel L. et al., *J Exp Clin Cancer Res* (in press)

**Real-time live-cell imaging**
*(ImpedanCELL core facility, E. Brotin & C Denoyelle)*

Control

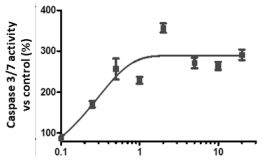


Mcl-1 inhibitor

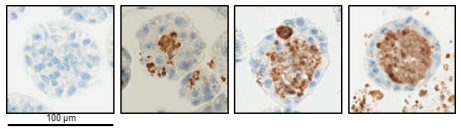


**Celltox™ Green Cytotoxicity Assay**

**Caspase activity**
Caspase 3/7-Glo (Promega)

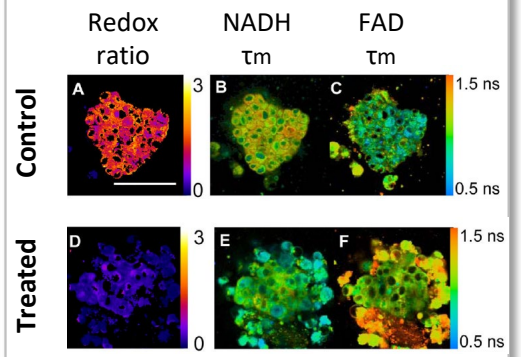



**Immunohistochemistry**



**Cleaved caspase-3 antibody**

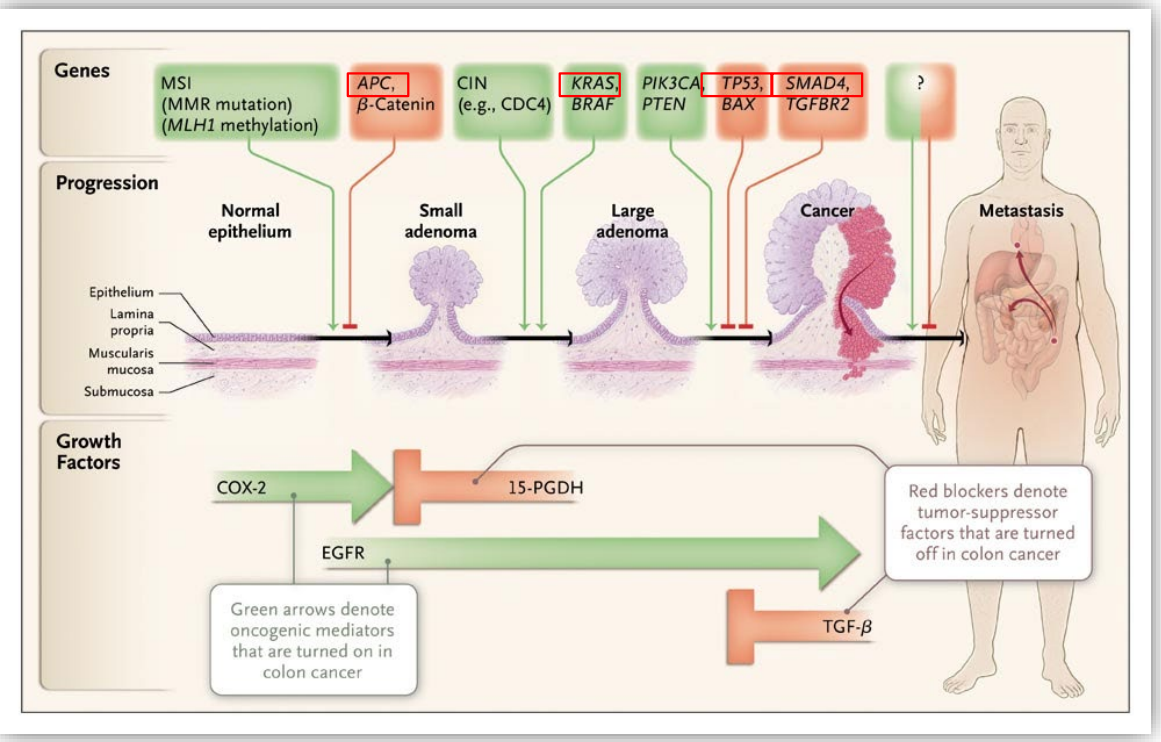
**Metabolism imaging**




Walsh AJ. et al., *Cancer Res* (2015)

# Basic research: tumorigenesis

## Adenoma-carcinoma sequence in colorectal cancer



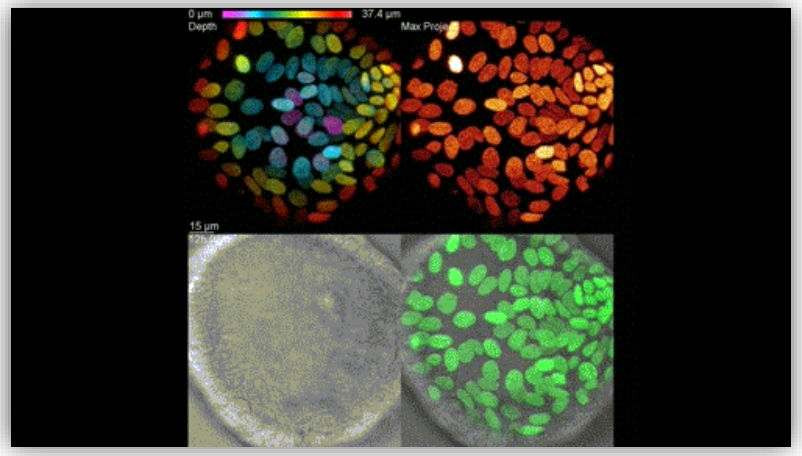

Markowitz SD. et al., *NEJM* (2009)

**Introduction of sequential cancer mutations in normal human intestinal organoids using CRISPR/Cas9 technology**

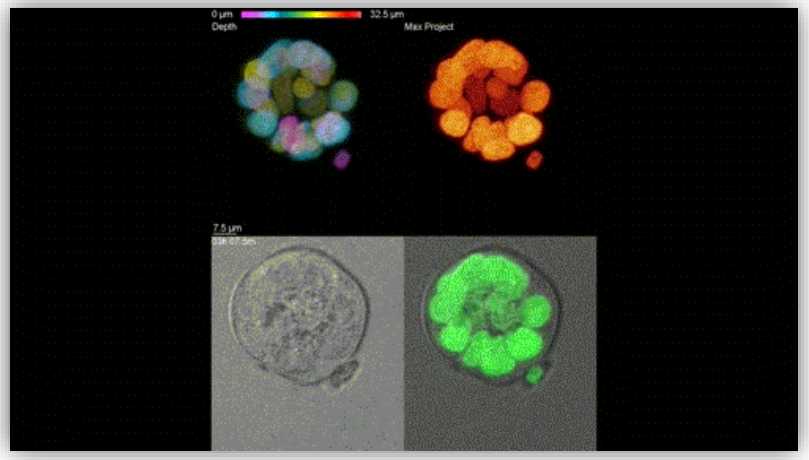
Drost J. et al., *Nature* (2015)

## Evaluation of chromosomic instability (CIN) in the different mutant organoids

### Wild-type organoids

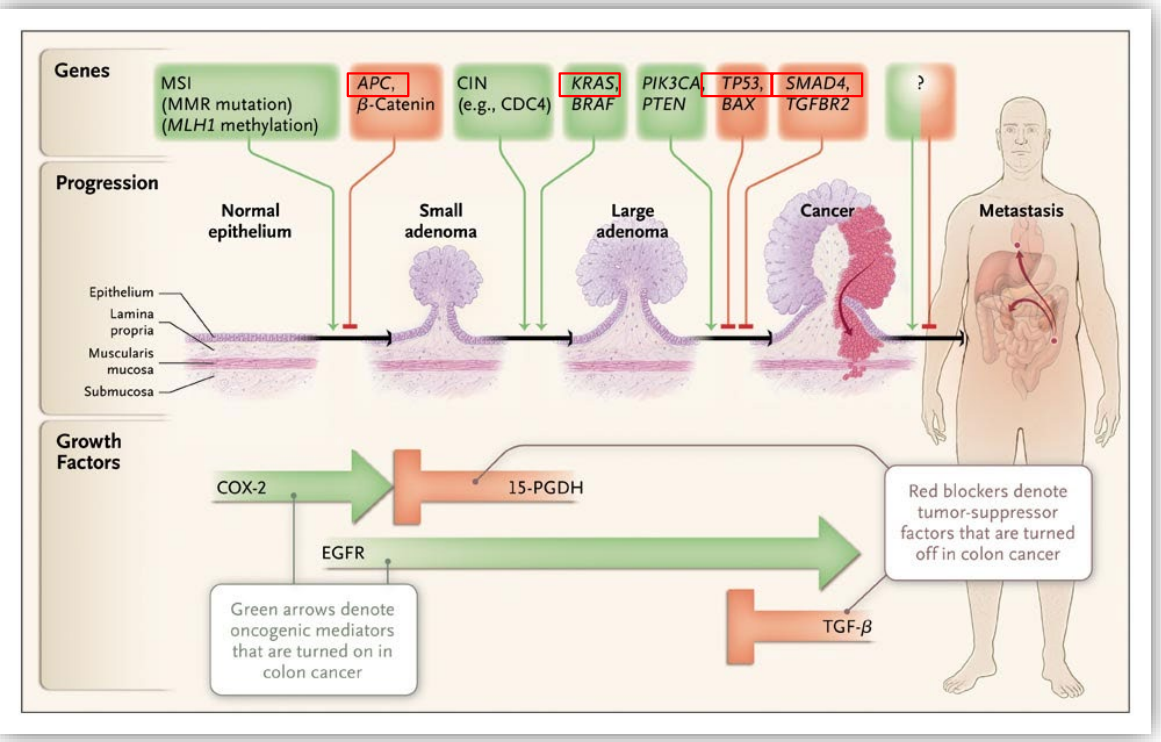


### APC$^{KO}$/P53$^{KO}$ organoids



# Basic research: tumorigenesis

## Adenoma-carcinoma sequence in colorectal cancer



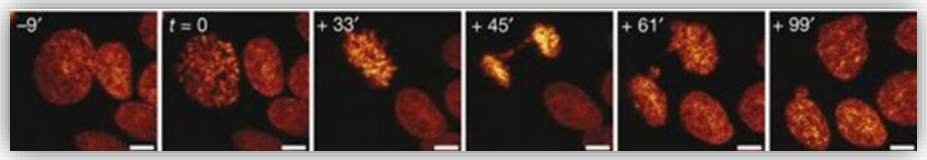

Markowitz SD. et al., *NEJM* (2009)

**Introduction of sequential cancer mutations in normal human intestinal organoids using CRISPR/Cas9 technology**

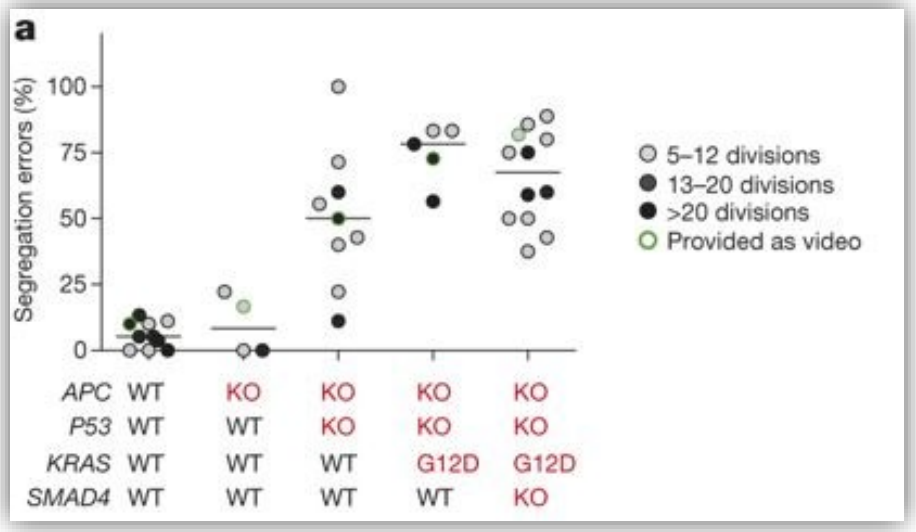
Drost J. et al., *Nature* (2015)

## Evaluation of chromosomic instability (CIN) in the different mutant organoids

### Example of mitotic error



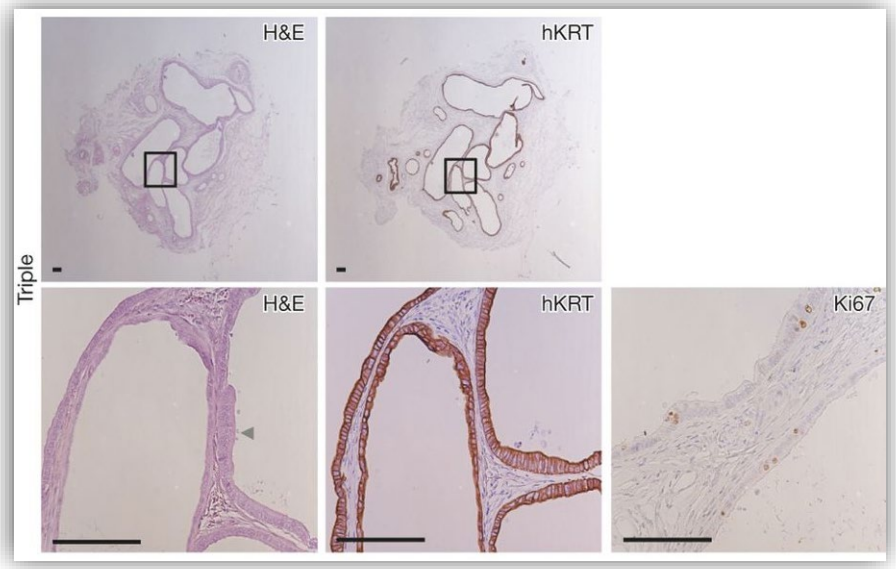

⇨ **Anaphase bridge**




**Loss of APC and p53 sufficient to induce CIN**

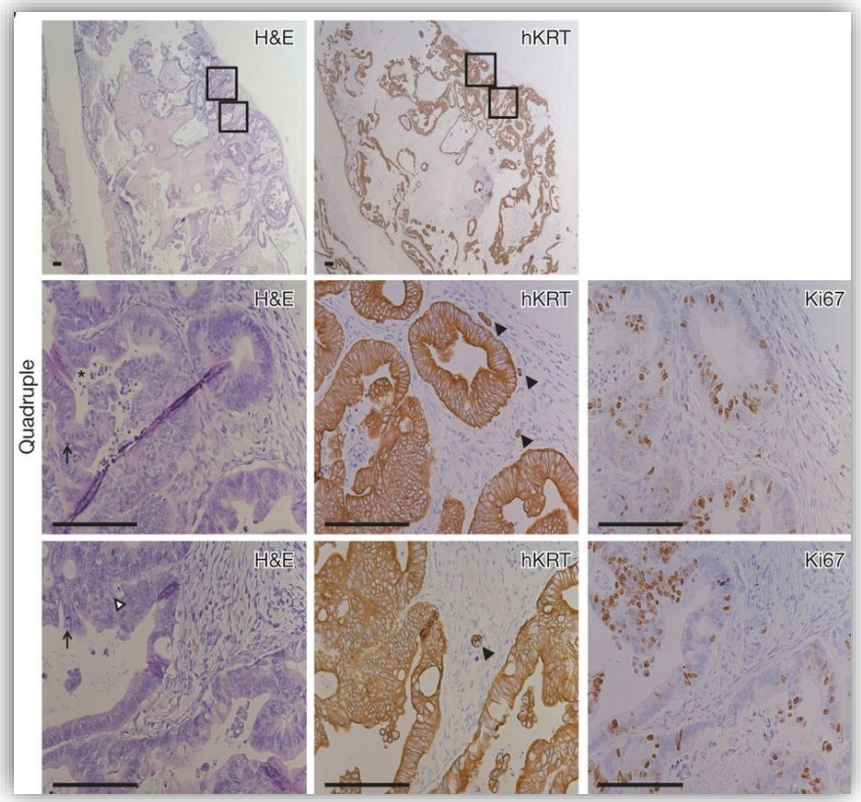
# Basic research: tumorigenesis

## Evaluation of tumorigenicity of triple-mutants organoids $KRAS^{G12D}/APC^{KO}/P53^{KO}$




- **3/12 tumors**
- Low proliferation rate
- Adenoma-like

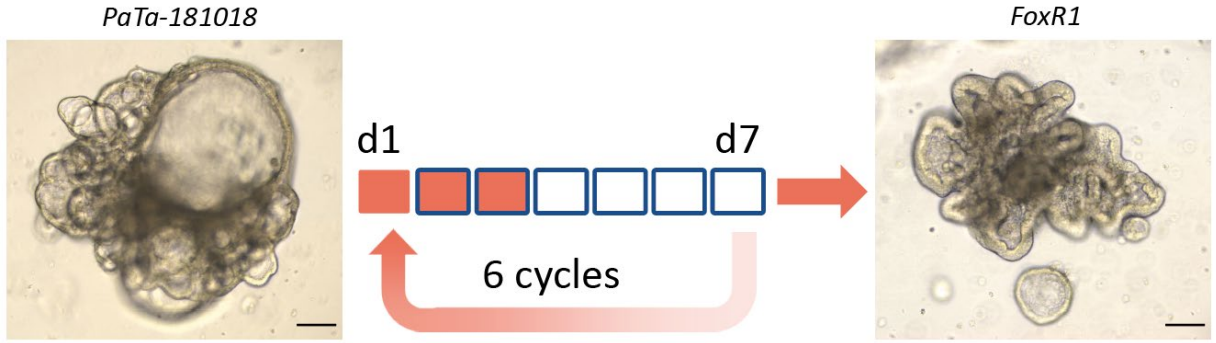
## Evaluation of tumorigenicity of quadruple-mutants organoids $KRAS^{G12D}/APC^{KO}/P53^{KO}/SMAD4^{KO}$



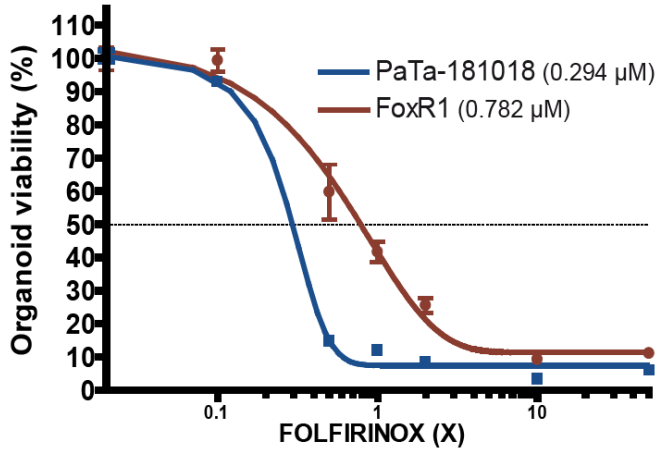

- **13/16 tumors**
- High proliferation rate
- Invasive carcinoma-like

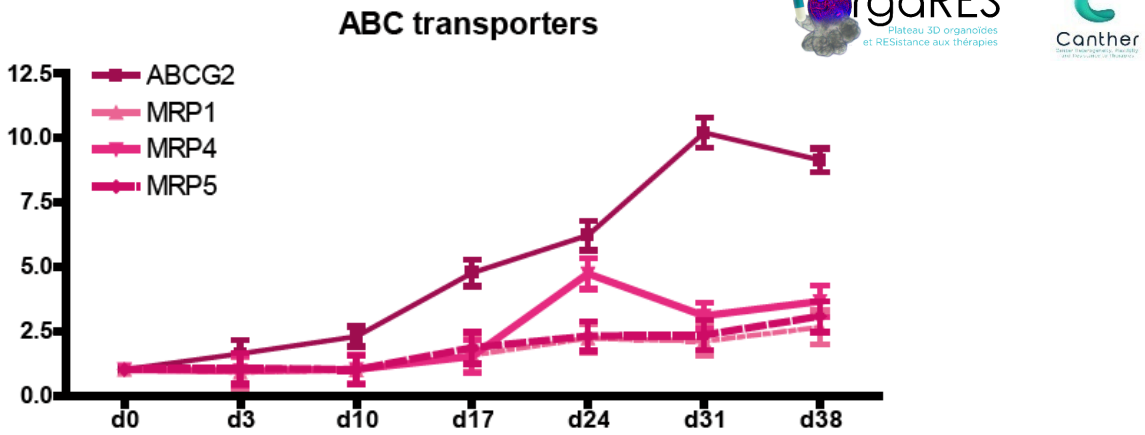
# Basic research: chemoresistance

## A new model of acquired chemoresistance to FOLFIRINOX in pancreatic cancer organoids



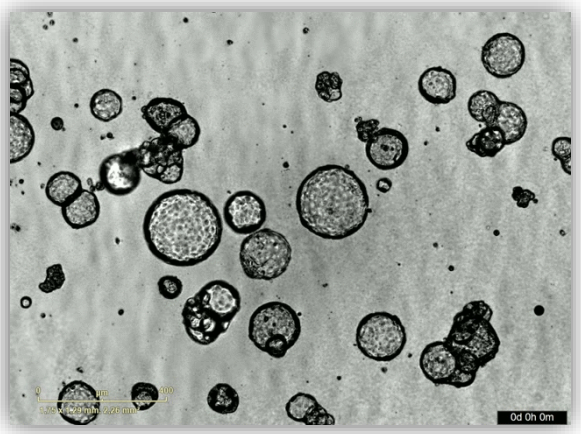

Hadj Bachir et al., *Biol Cell* (2022)



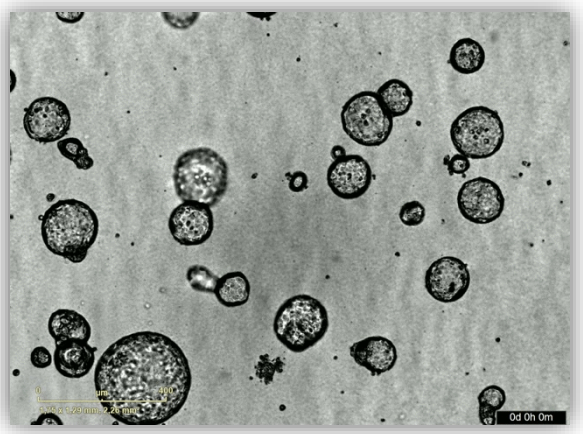




## Exposure to FOLFIRINOX

PaTa



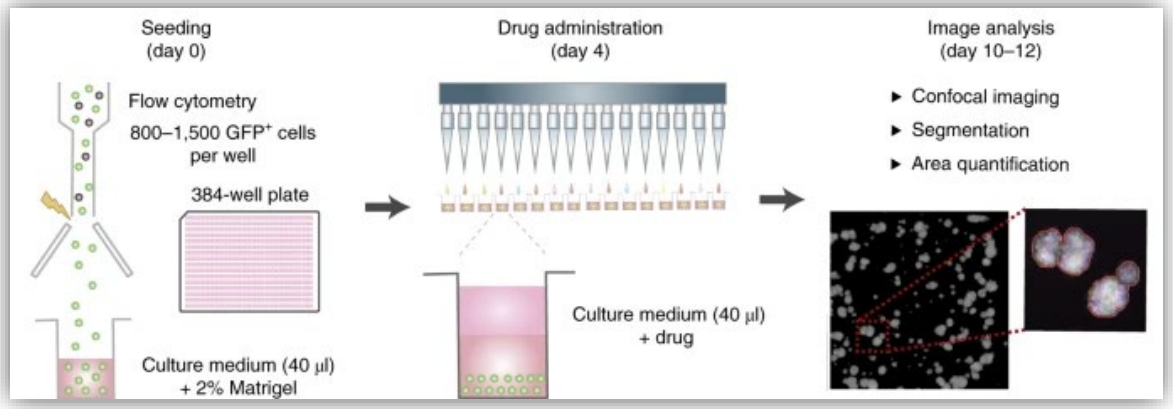
FoxR1



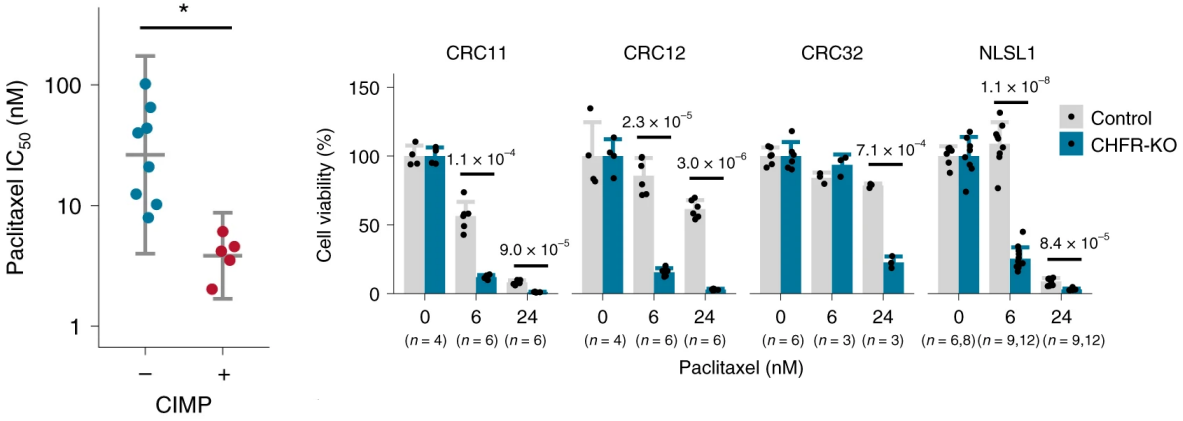
➢ **Identification of ABCG2 as biomarker of acquired chemoresistance**

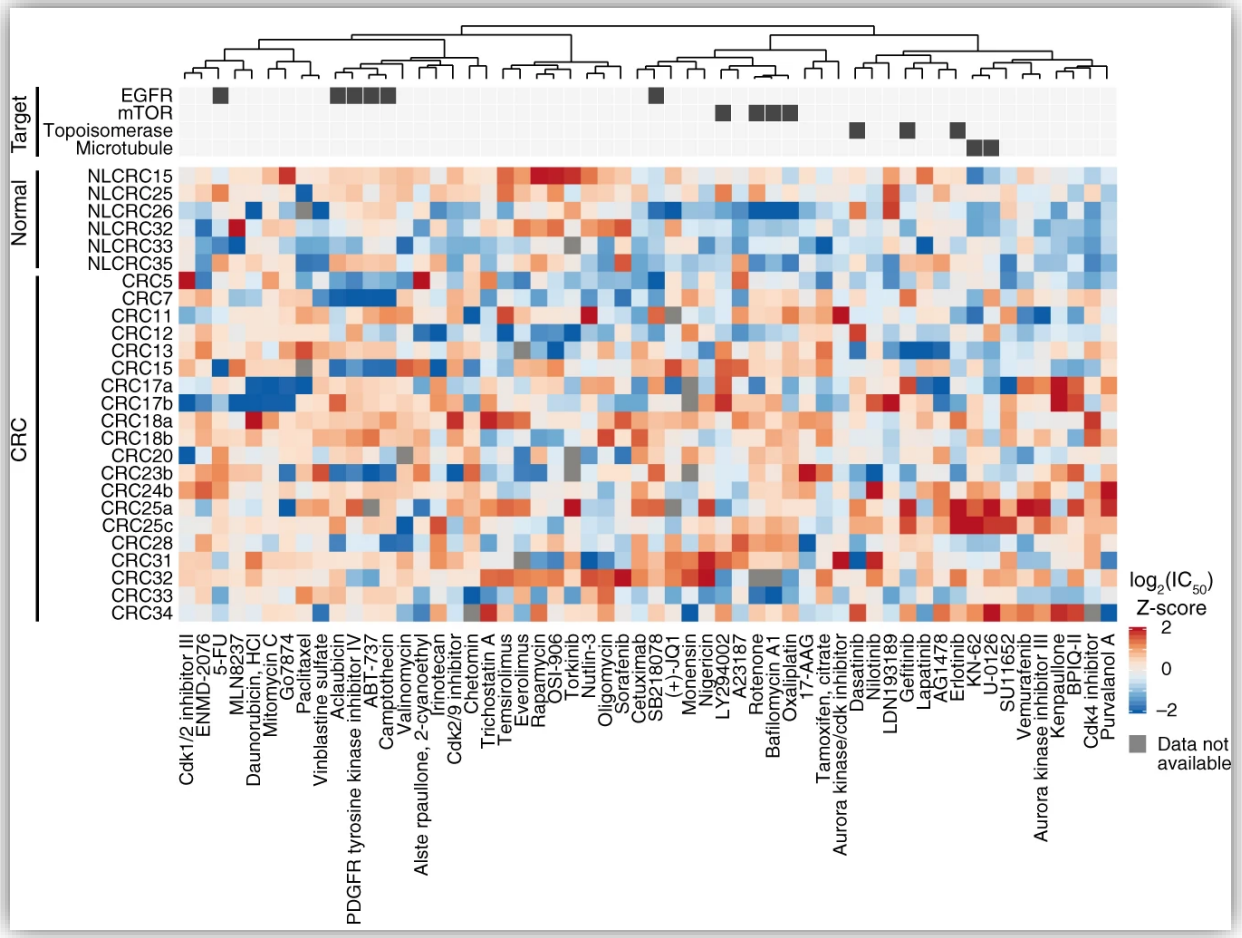
# Pharmacologic screening

## Screening of 56 compounds in 20 colorectal cancer organoid lines and 6 normal colonic lines




Toshimitsu K. et al., *Nat Chem Biol* (2022)

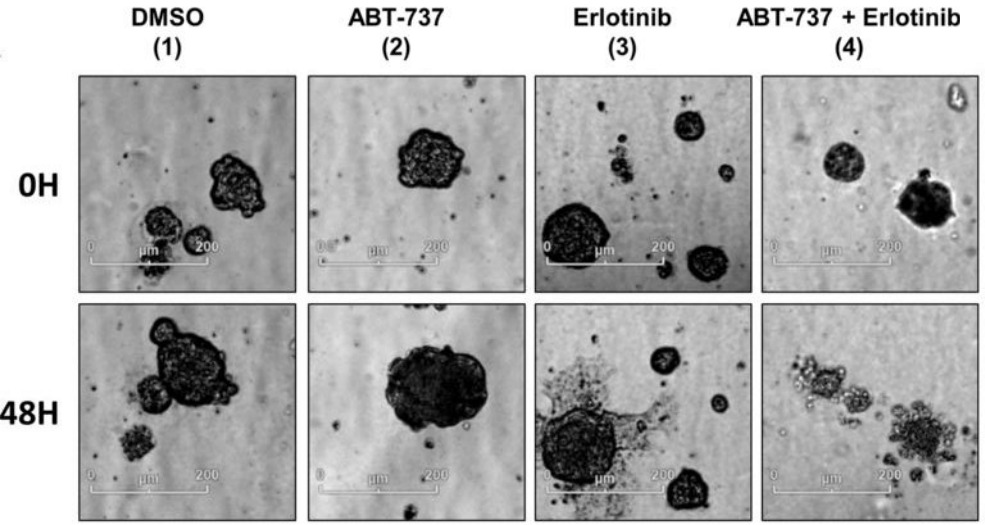


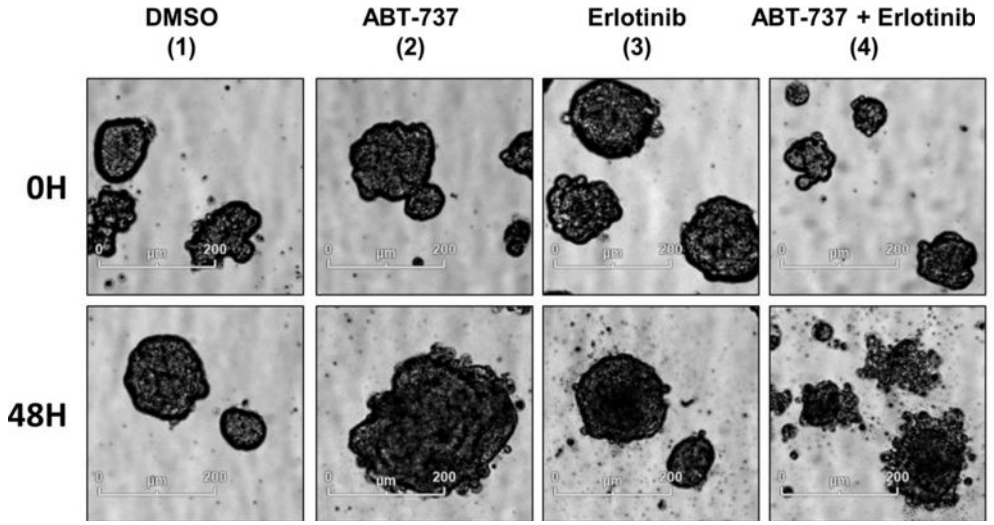



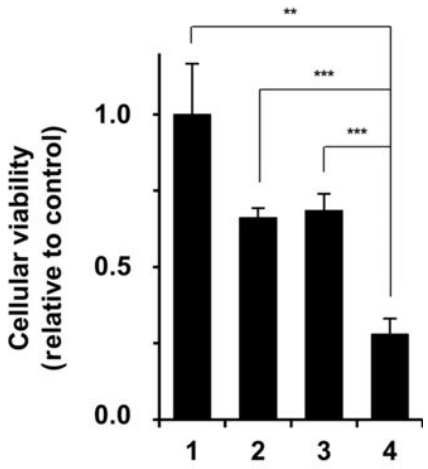

- Paclitaxel effective against CIMP+ tumor organoids
- Identification of CHFR as determinant of paclitaxel sensitivity

# Validation of new therapeutic strategies

## Identification of a « killer » miRNA targeting EGFR and Bcl-$x_L$ in ovarian cancer cell lines

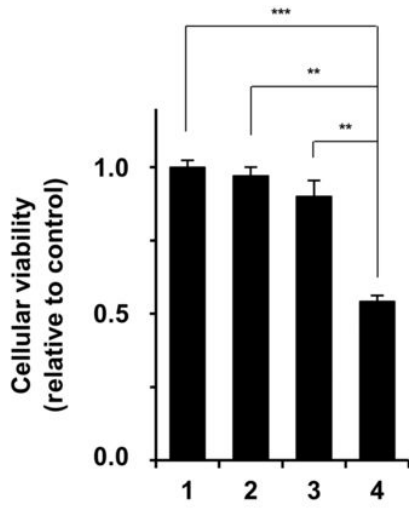



**ABT-737** : inhibitor of Bcl-$x_L$
**Erlotinib** : inhibitor of EGFR

**Validation of the association of EGFR and Bcl-$x_L$ inhibitors in ovarian cancer organoids**

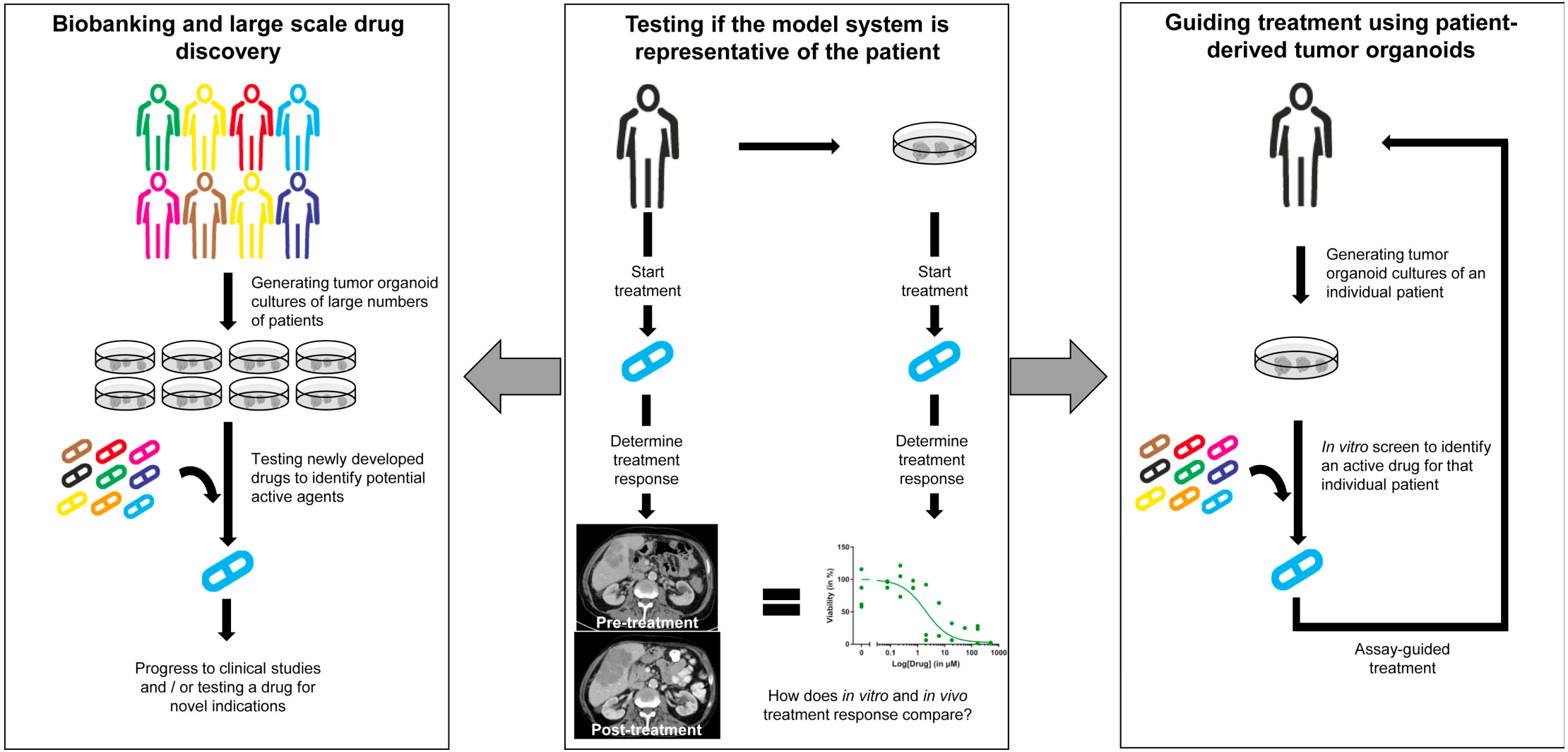


# Advantages and limits of tumor organoids

- ✓ Close to the tumor of origin
- ✓ Small tumor sample suitable for establishment
- ✓ Normal counterpart
- ✓ High success rate for most of the tumor types
- ✓ Short delay of establishment
- ✓ Genetic engineering and cryopreservation
- ✓ High-throughput screening

- × Absence of microenvironment
- × Expensive
- × Diversity of culture conditions among tumor types and laboratories
- × Potential contamination by normal cells (lung, prostate…)
- × Selection of cell subpopulations over passages
- × Maintenance in culture can be complicated
- × Use of matrigel

# Tumor organoids and precision oncology




Adapted from Weeber F. et al., *Cell Chem Biol* (2017)

# Tumor organoids: a tool for predicting response to treatments?

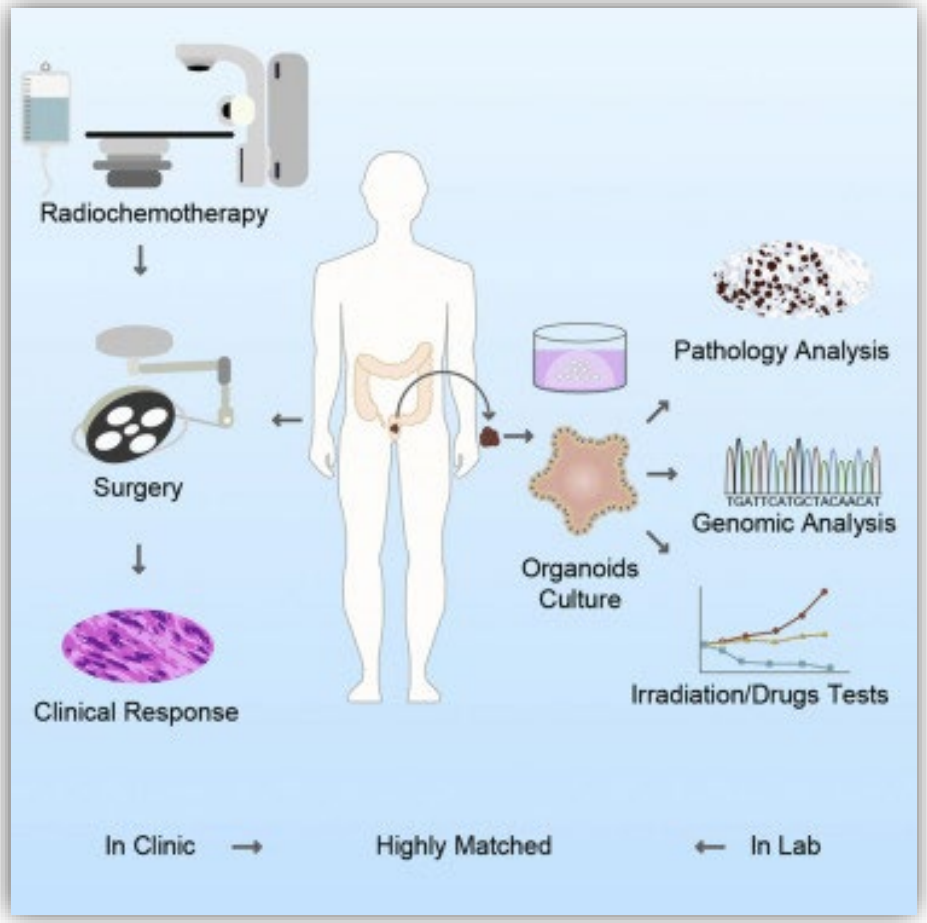
| Cancer type | Study | Establishing efficiency | Treatment | Sample size | Correlation |
|---|---|---|---|---|---|
| Breast cancer (primary) | Sachs et al., 2018 | ~80% | tamoxifen | 2 | yes |
| Colorectal cancer (metastasis) | Ooft et al., 2019 | ~63% | irinotecan | 10 | yes[b] |
| | | | FOLFIRI | 12 | yes[c] |
| | | | FOLFOX | 10 | no |
| | Ooft et al., 2021 | ~57%[a] | vistusertib, capivasertib | 6 | no |
| Colorectal peritoneal (metastasis) | Narasimhan et al., 2020 | ~68%[a] | FOLFOX | 9 | no |
| Esophageal adenocarcinoma | Li et al., 2018 | ~31% | 5-FU, epirubicin and cisplatin | 5 | (yes) |
| Gastrointestinal (metastasis) | Vlachogiannis et al., 2018 | ~70% | paclitaxel[e] | 3 | yes |
| | | | TAS-102[f] | 4 | yes |
| | | | 5-FU and cisplatin[g] | 2 | yes |
| | | | cetuximab[h] | 4 | yes |
| Gastric cancer | Yan et al., 2018 | >50% | cisplatin and 5-FU | 2 | (yes) |
| | Steele et al., 2019 | | epirubicin, oxaliplatin, and 5-FU | 2 | one out of two correlated |
| Glioblastoma | Jacob et al., 2020 | ~90%[a] | radiation and temozolomide | 5[k] | |
| Mesothelioma | Mazzocchi et al., 2018 | | cisplatin and pemetrexed | 2 | yes |
| Neuroendocrine prostate CRPC-NE (metastatic) | Puca et al., 2018 | ~16% | alisertib | 2 | yes |
| Ovarian | Kopper et al., 2019 | ~65% | platinum/taxane | 1 | yes |
| | de Witte et al., 2020 | [i,a] | carboplatin and paclitaxel | 5 | yes[j] |
| | Phan et al., 2019 | | carboplatin | 2 | (yes) |
| Pancreatic cancer | Tiriac et al., 2018 | ~75% | 5-FU, gemcitabine, nab-paclitaxel, SN-38, or oxaliplatin | 9 | mostly yes five sensitive out of six longer PFS; two insensitive out of three rapid progressions; one inconsistent; one intermediate |
| | Driehuis et al., 2019 | ~62% | gemcitabine | 4 | yes |
| Rectal cancer | Ganesh et al., 2019 | ~77% | 5-FU or FOLFOX | 7 | yes |
| | Yao et al., 2020 | ~85% | 5-FU | 80 | mostly yes five exceptions to sensitive and 15 exceptions to insensitive |
| | | | irinotecan | 66 | mostly yes seven exceptions to sensitive; seven exceptions to insensitive |

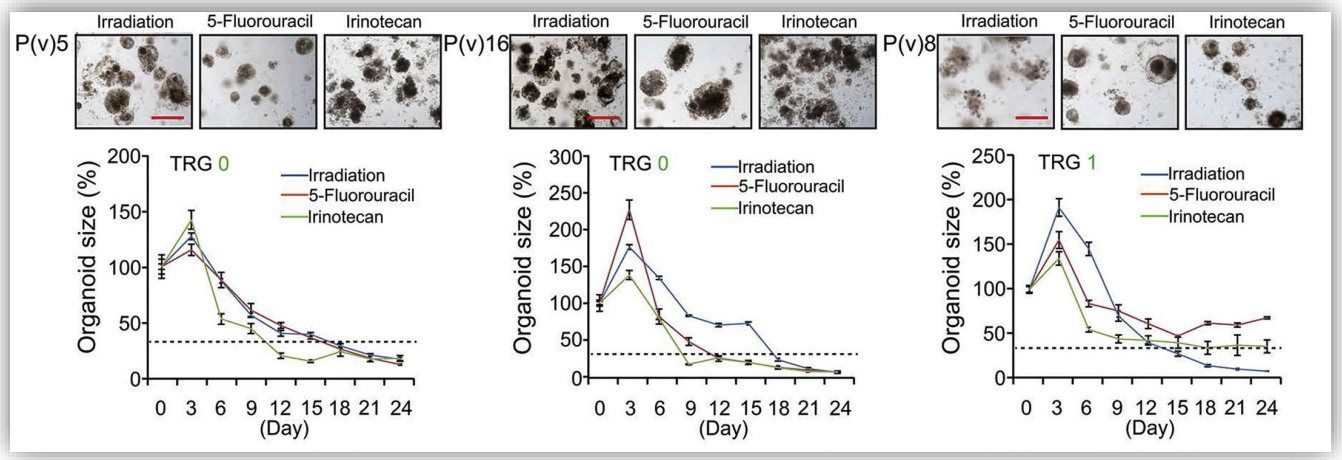
Vivanga V. and Voest E., *Cancer Cell* (2021)

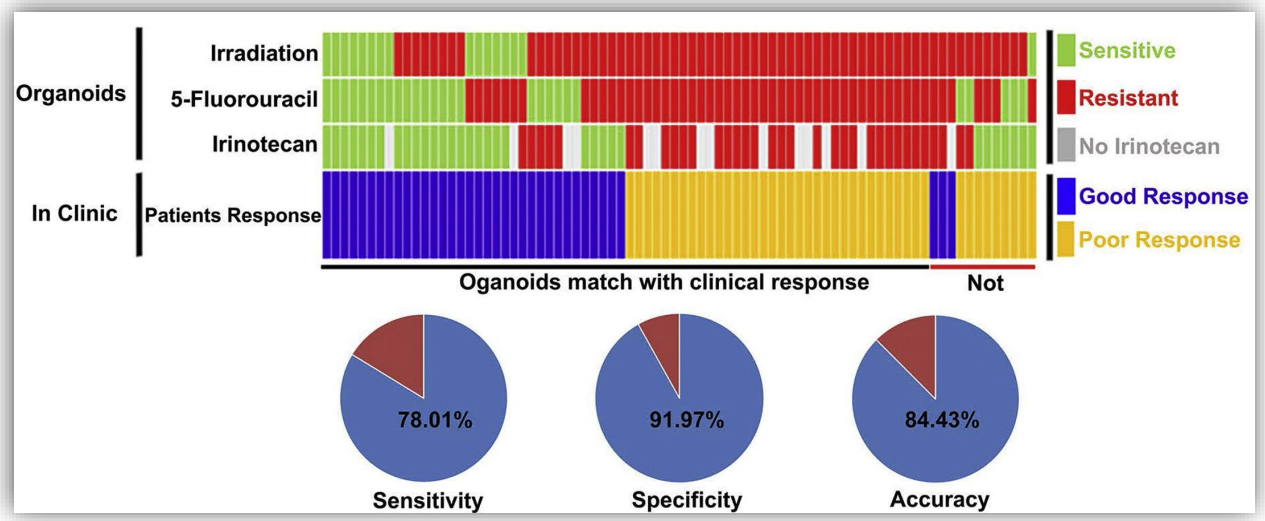
- **Encouraging correlation** between *in vitro* and clinical treatment
- Most of sample sizes of studies **too small**

# Response of patients *vs* response of tumor organoids

- **Correlation between the response of tumor organoids from rectal cancer to 5-FU, irinotecan, radiotherapy and response of the patients**

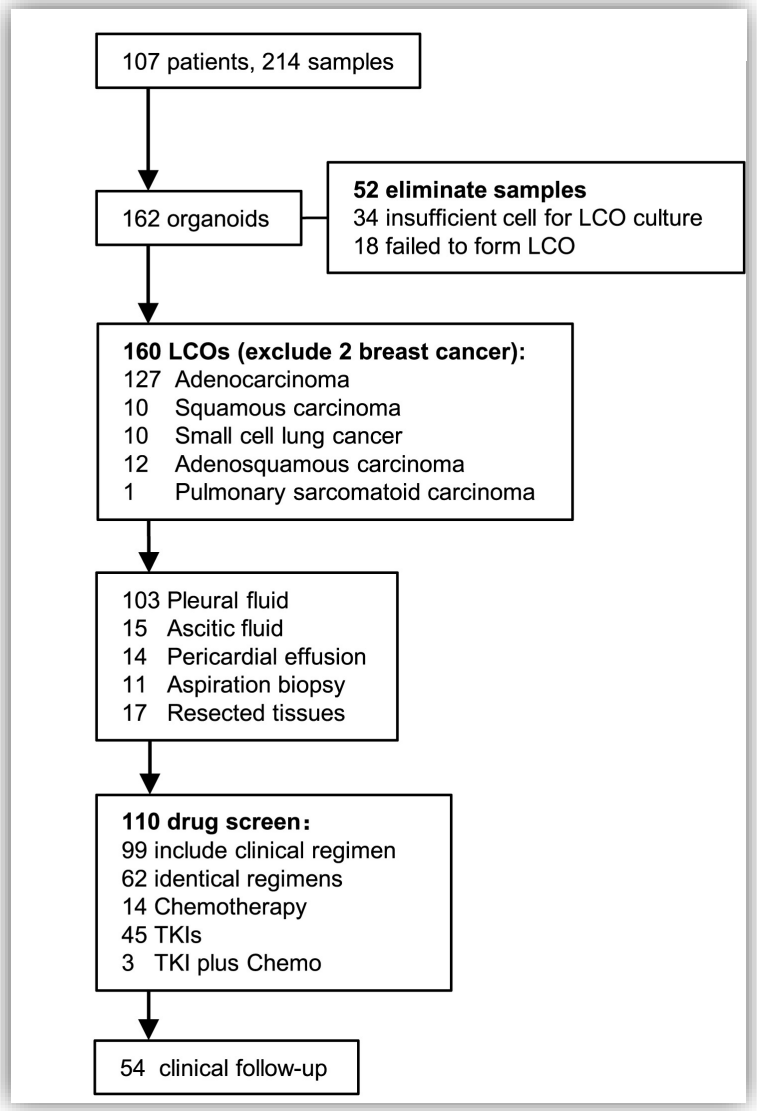


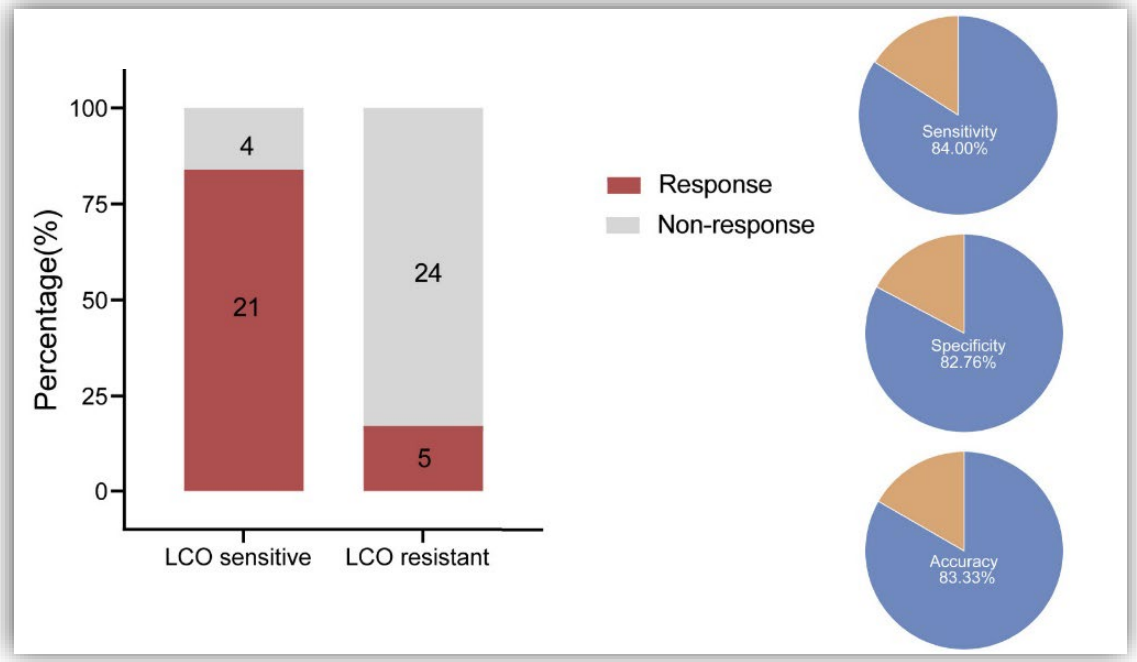

Yao Y. et al., *Cell Stem Cell* (2020)

# Response of patients vs response of tumor organoids




## Response of lung cancer organoids *versus* clinical response

- Success rate of establishment: 75%
- Targeted therapies (ALK and EGFR inhibitors, etc..)
- Chemotherapies (paclitaxel, cisplatin, etoposide, etc…)

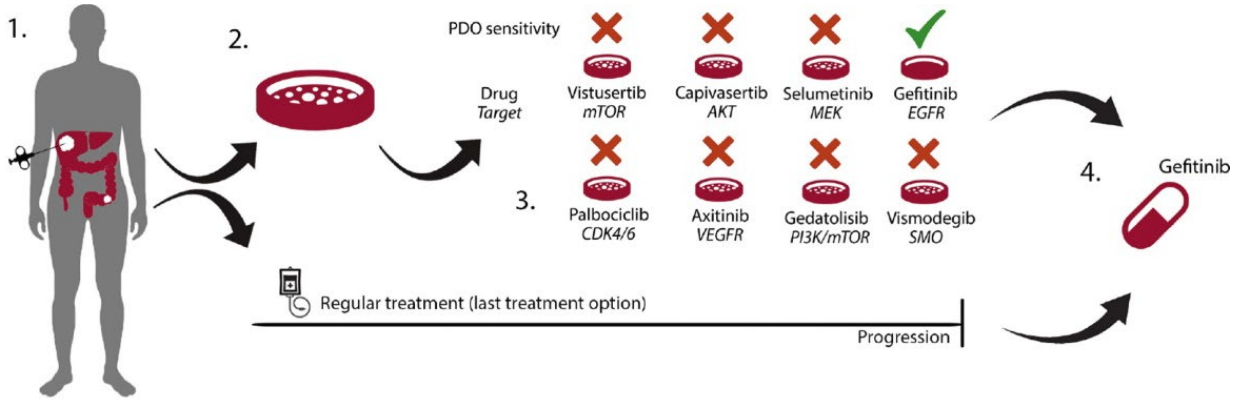



- **Prediction accuracy: 83%**

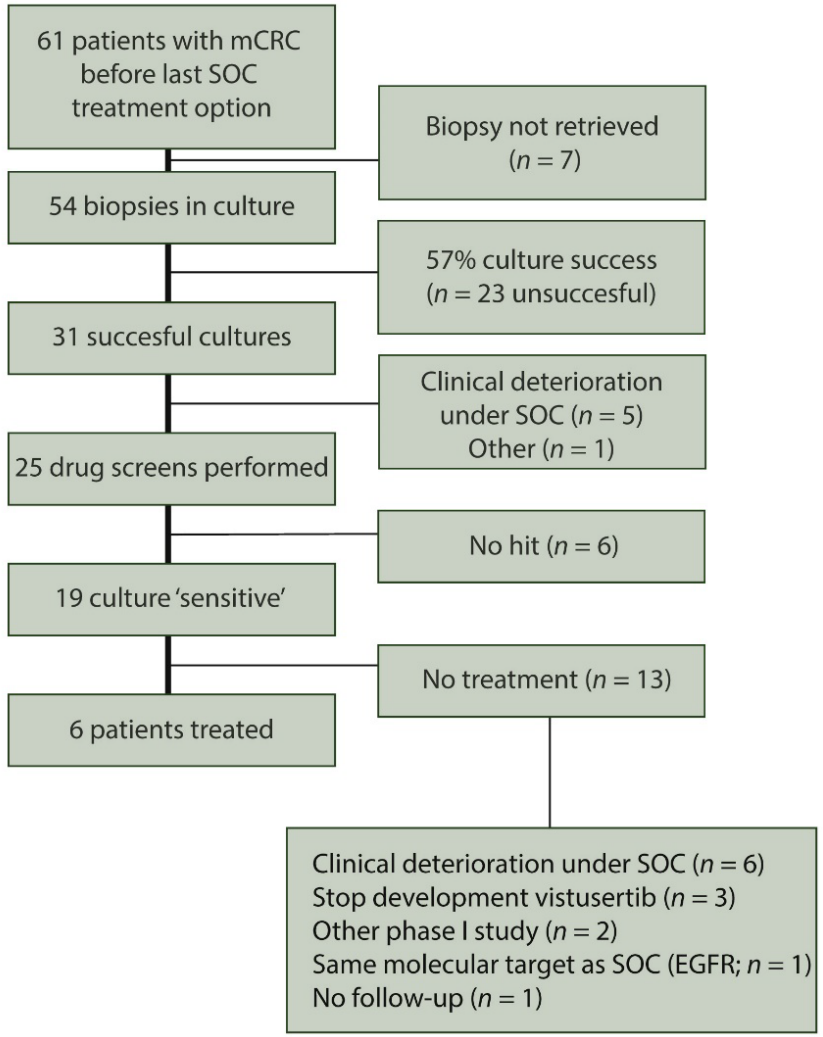
Wang HM. et al., *Cell Rep Med* (2023)

# Tumor organoids: a tool for guiding treatment decision-making

## Prospective clinical trial: use of tumor organoids to guide treatment decision-making



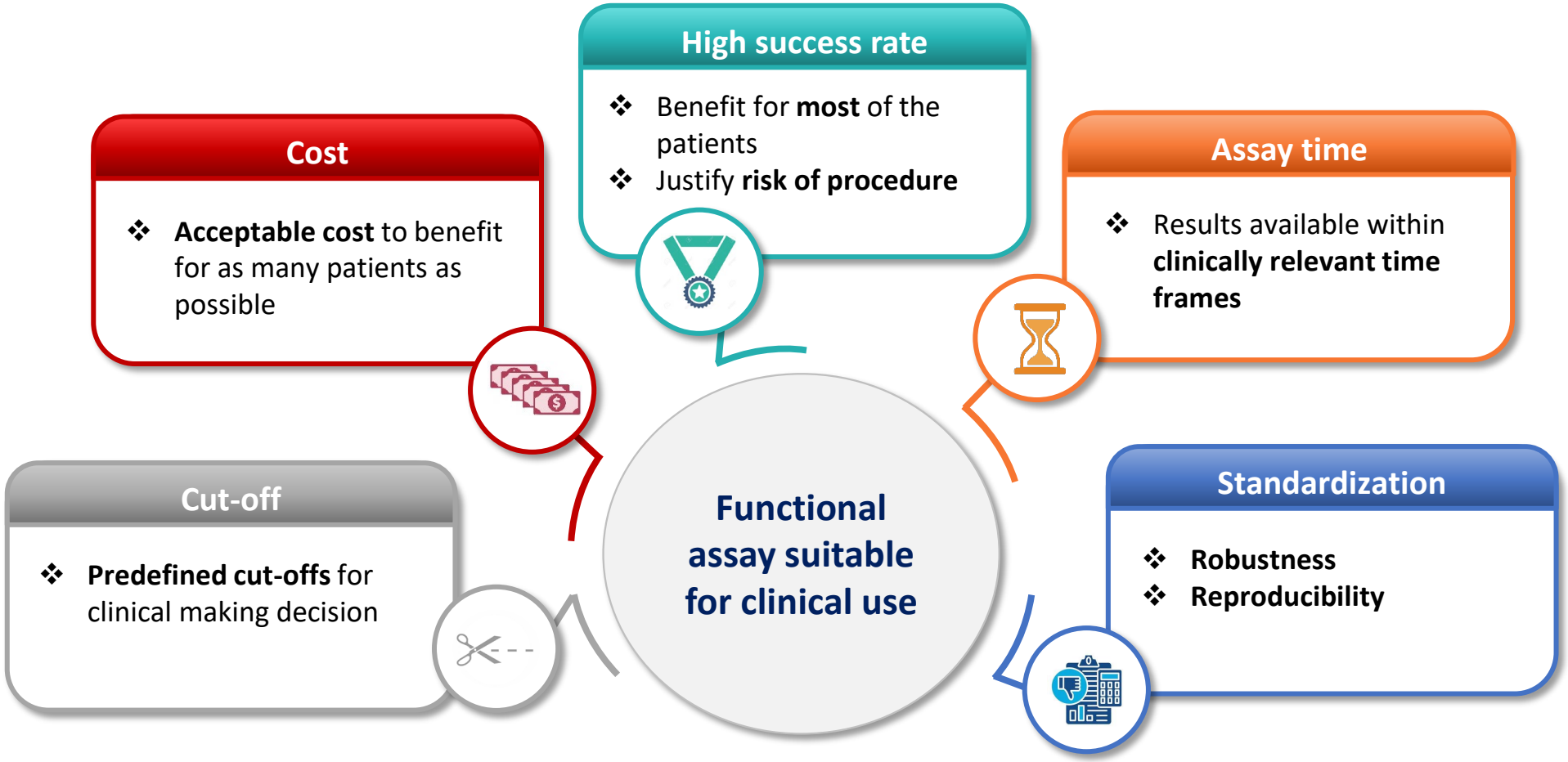

**Metastatic colorectal cancer**
**8 targeted therapies**




- **Only 6 patients (on 61 enrolled) treated based on the response of tumor organoids**
- **No clinical response**

Ooft F. et al., *ESMO Open* (2021)

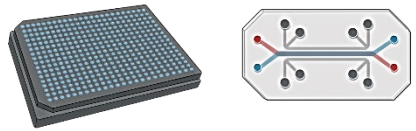
# Quality criteria for the development of functional assays



# Challenges associated with clinical implementation

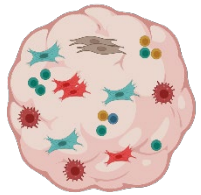
## Challenges
**for the routine use of tumor organoids in clinical oncology**

### Implementation of fast track protocols
*Miniaturization, microfluidic*

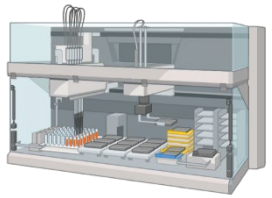


### Improve representativeness of the biological sample collected
- **Selection of sampling area**
- **Selection of sampling time**
- **Selection of culture method**

### Co-culture of tumor organoids
- *Immune cells*
- *CAF*
- *Endothelial cells*
- *…*



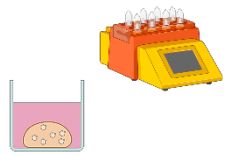
### Implement high-throughput procedures
- *Production and culture*
- *Treatment et analysis*



- *Histological characterization*

*(TMA, multiplexing)*

### Increase success rate of establishment, standardize the protocols
- ***Optimize and standardize protocols of culture***
  - dissociation method
  - extracellular matrix
  - media

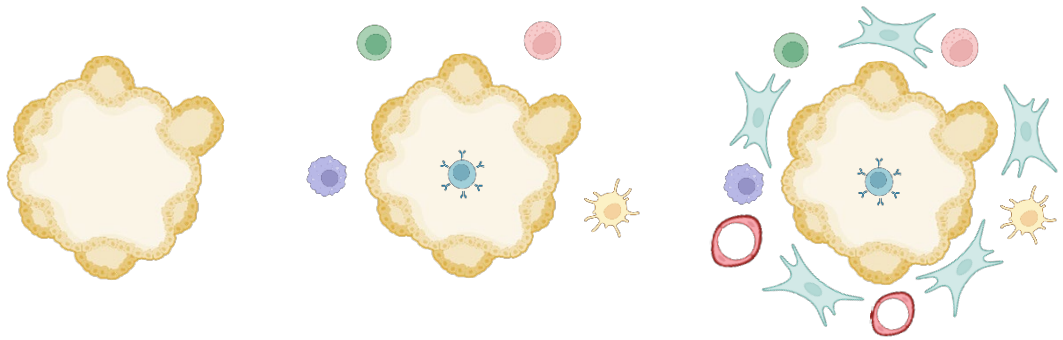


- ***Check the number and the quality of the cells in the sample***

Adapted from Perréard M. et al., *Médecine/Sciences* (2022)

# Modeling tumor microenvironment using tumor organoids

## *What?*



Complexity

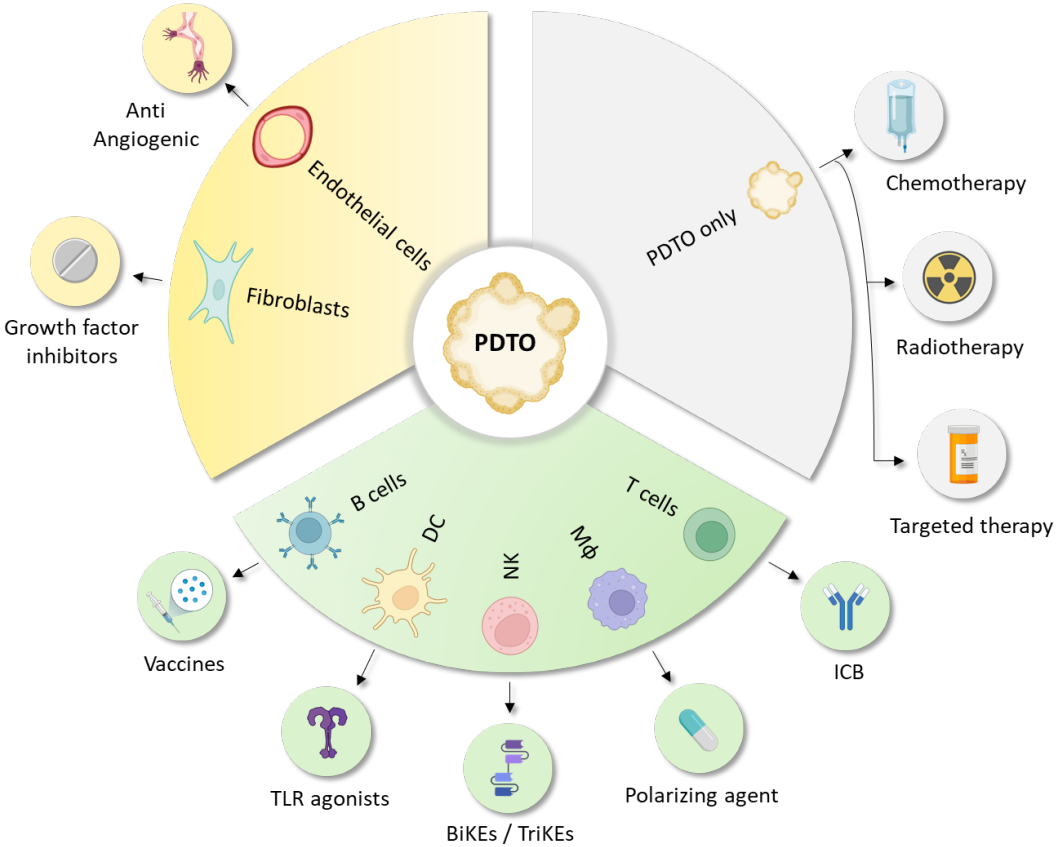
: Immune cells

: Fibroblasts

: Endothelial cells

Tumor organoids co-cultured with stromal cells

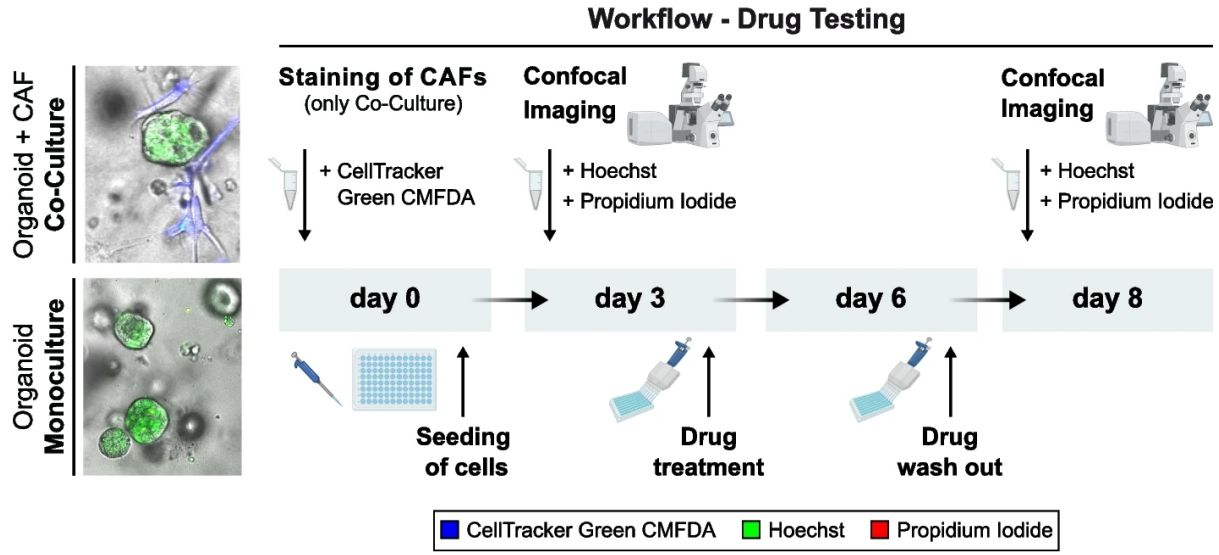
## *Why?*

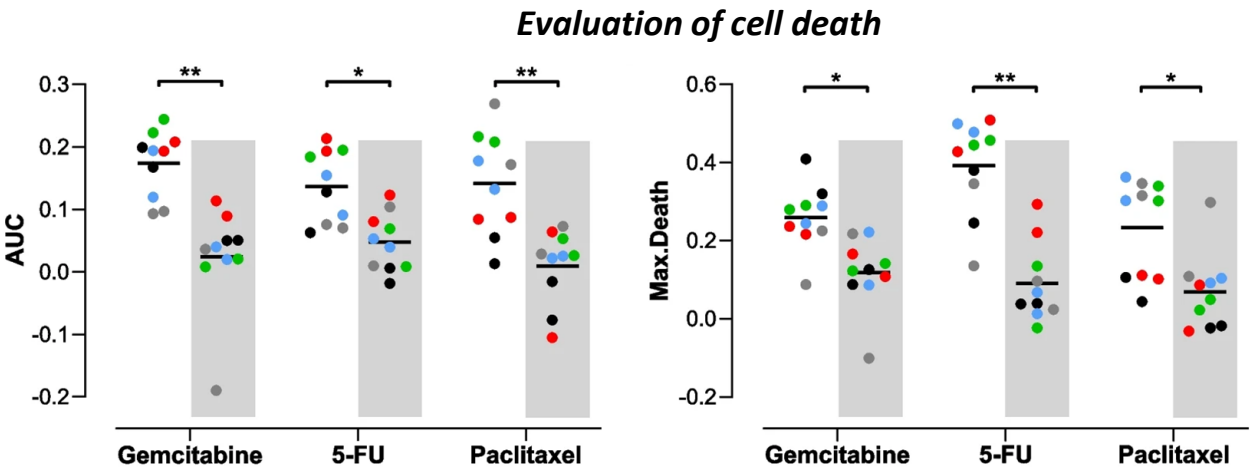



1. Broaden spectrum of treatments
2. Improve relevance of the model

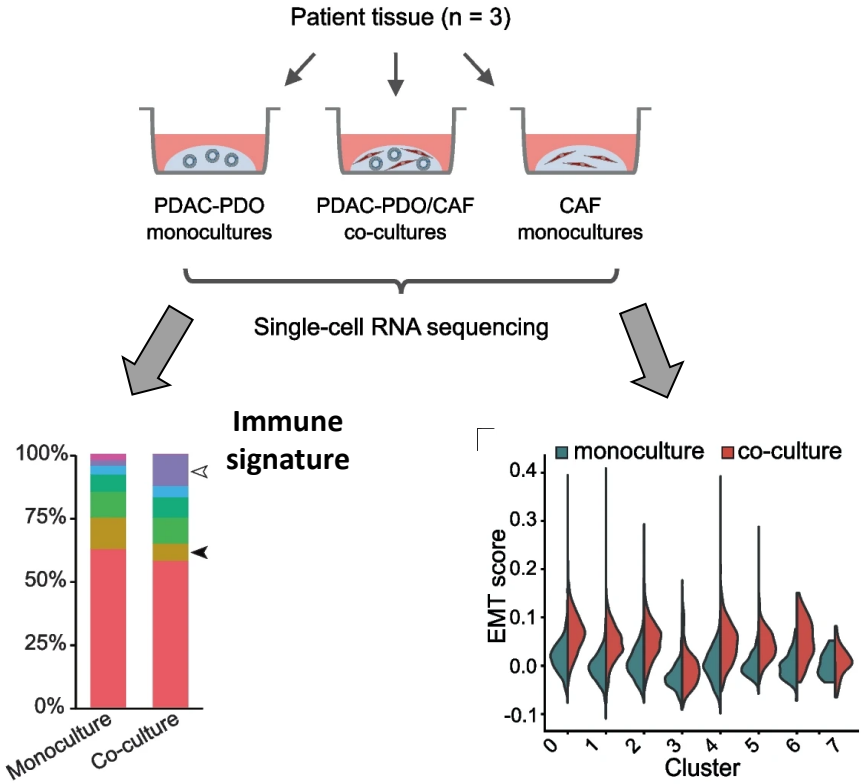
Florent R. et al., (in preparation)

# Co-culture of pancreatic cancer organoids with fibroblasts



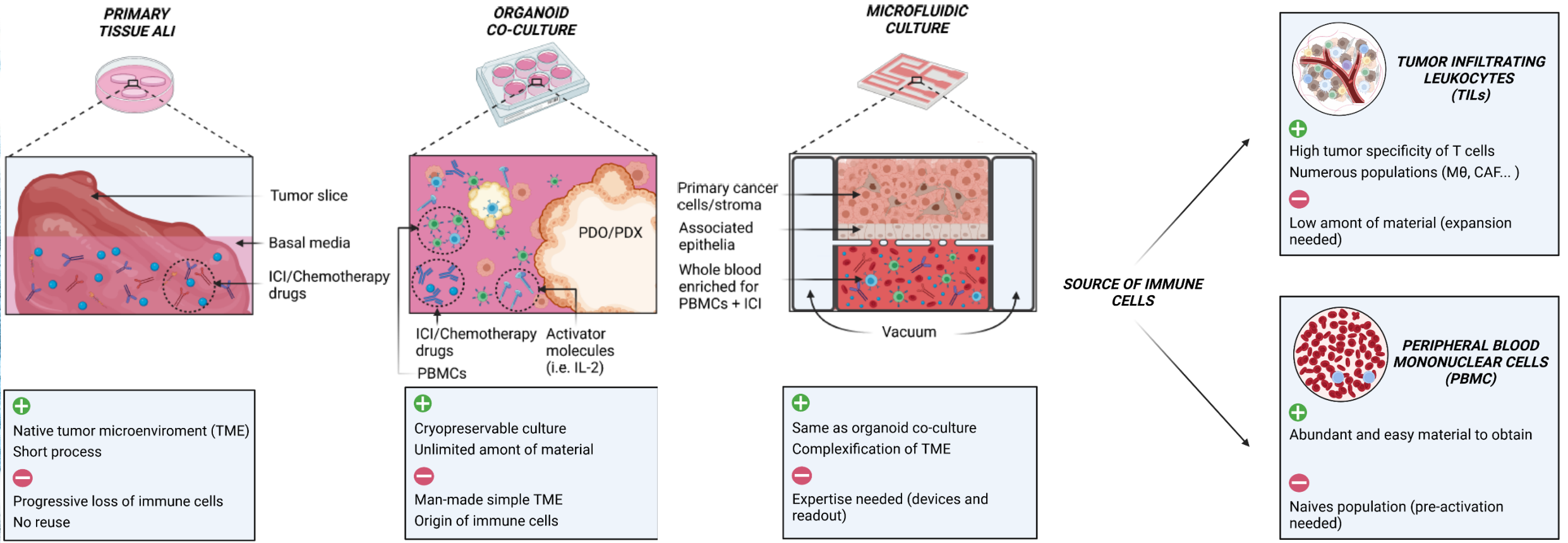




Shuth S. et al., *J Exp Clin Cancer Res* (2022)




- ✓ Increase of resistance to treatments in presence of CAFs
- ✓ Upregulation of inflammatory and EMT pathways

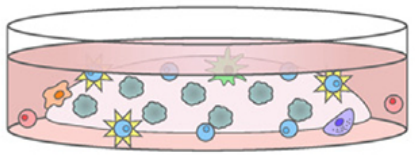
# Culture systems modeling the tumor immune microenvironment



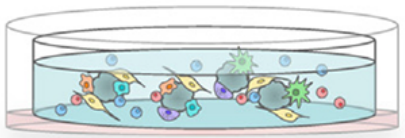

Adapted from Mackenzie NJ. et al., *Clinical & Translational Immunology* (2022)

# Co-culture for personalized cancer immunotherapy

## Tumor organoid culture with immune cells

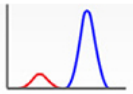


Reconstituted TME organoid culture



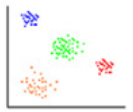
Native TME organoid culture

## Tumor/immune cell characterization



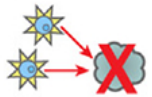
Flow cytometry

Histological analysis
(i.e., immunofluorescence staining)

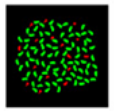


Single cell analysis
(i.e., RNA-seq)

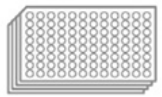
Cytokine profiling



T cell cytotoxicity



Live/dead imaging



Immunotherapy drug screens
(i.e., small molecules and immune checkpoint inhibitors)

## Therapeutic applications

**Assessment of ICB response determination of combination therapy**
(e.g., Immunotherapy agents: anti-PD-1, CTLA-4, LAG-3, TIM-3, etc., chemotherapy drugs and targeted therapy drugs)

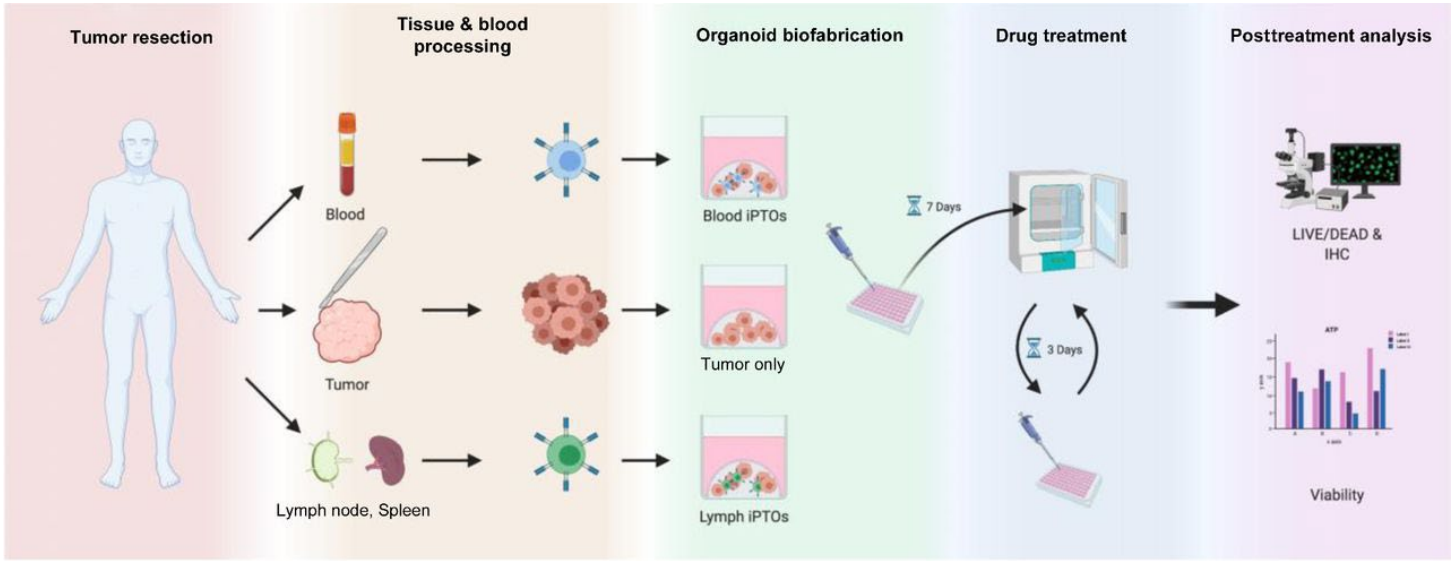
**Generation of tumor-reactive T cells for adoptive cell therapy**
(e.g., TILs, CAR-T, CAR-NK cells)

**Biomarker identification to predict patient response**

**Exploration of potential targets to enhance immune therapy**

Yuki K. et al., *Trends Immunol* (2020)

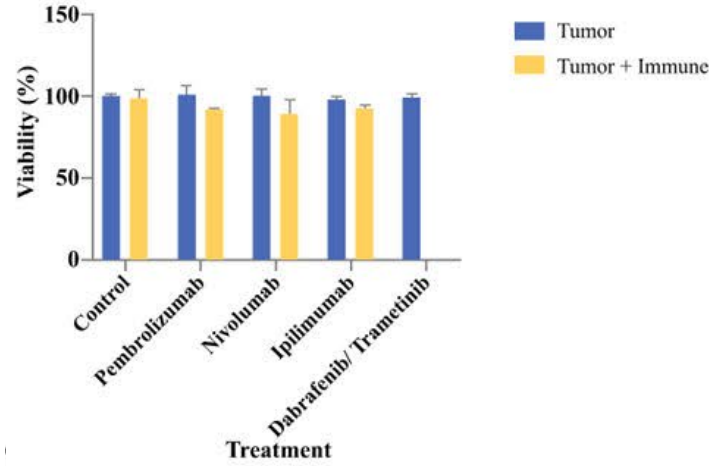
# Response to immunotherapy: tumor organoids *versus* patients



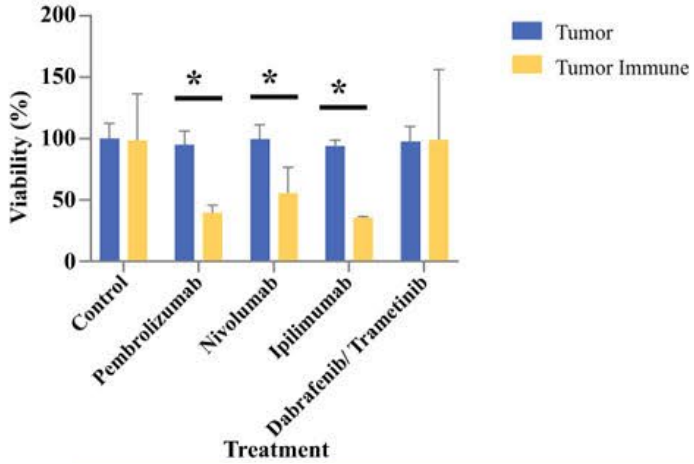

| Patient | Immune component Node/blood | Response to CPIs | | Response to D/T | | *BRAF* | Clinical info |
|---|---|---|---|---|---|---|---|
| | | Organoid | Tumor | Organoid | Tumor | | |
| 4017010-1 | Node | No | No | Yes | Yes | Wild | *MEK* mutation |
| 4017010-2 | Blood | No | No | No | No | Wild | Recurrence on Trametinib |
| 4017011 | Node | No | NT | No | NT | – | Denied Treatment |
| 4017025-1 | Node | No | No | No | NT | V600E | Local recurrence on nivo |
| 4017025-2 | Blood | No | No | No | NT | V600E | Resected local recurrence No new lesions on nivo |
| 4017026 | Node | No | No | No | NT | Wild | Resected tumor progressed on pembro. Stable stage IV disease 10 months later on pembro |
| 4017029 | Node | – | – | – | – | – | Cauterized specimen. No available organoids. |
| 4017032 | Node | Yes | No | No | NT | V600K | Local recurrence at 2.5 months while on nivo. No further distant disease |
| 4017033 | Node | Yes | Unknown | NA | NT | – | NED post resection |
| 4017035 | Blood | No | No | No | NT | Wild | Resected tumor progressed on pembro. Stable stage IV disease 5 months later on pembro |

85% (6/7)

***Non responder***




***Responder***

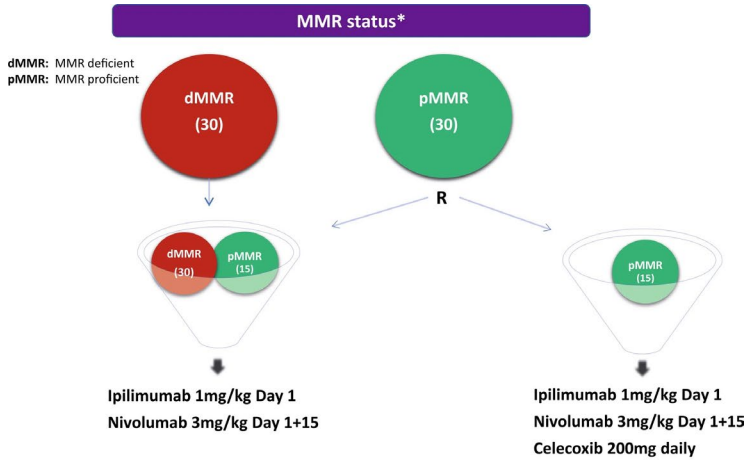



Forsythe SD. et al., *Clin Cancer Res* (2021)

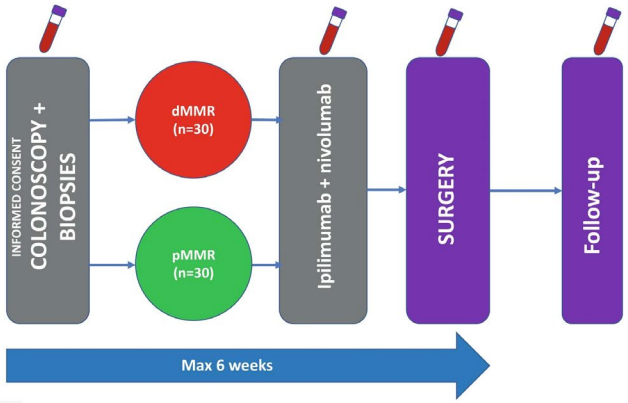
Votanopoulos KI. et al., *Ann Surg Oncol* (2020)

# Response to immunotherapy: tumor organoids *versus* patients

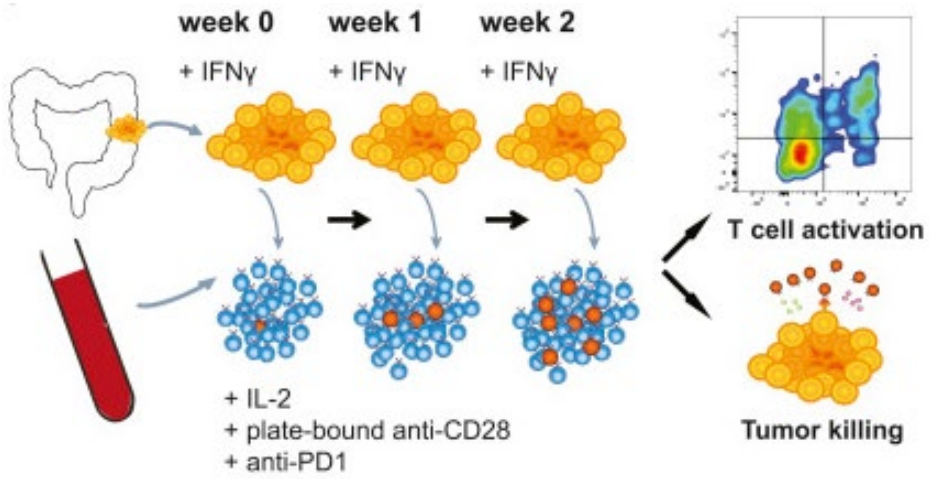
## Neoadjuvant immunotherapy in MMR-proficient and MMR-deficient early-stage colon cancers



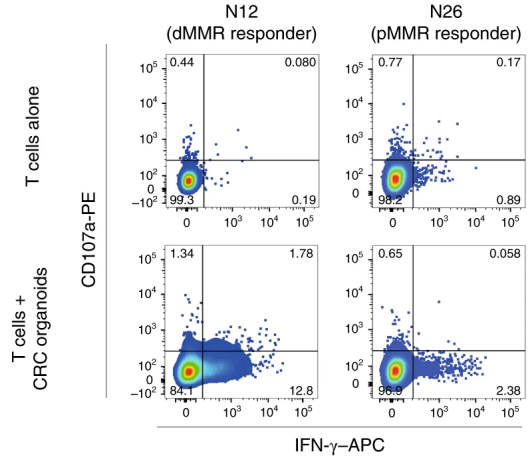

**MMR protein staining for MLH1, PMS2, MSH2, MSH6*

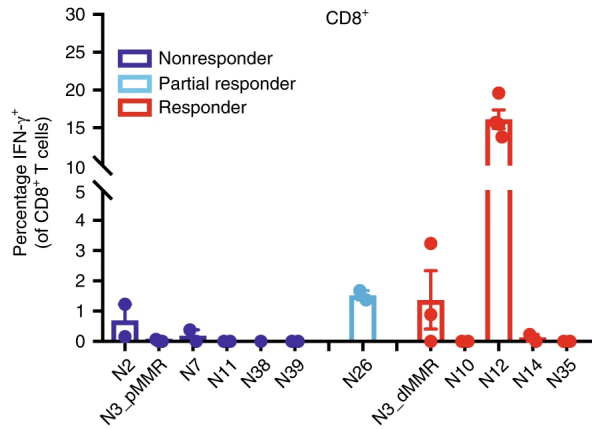



Chalabi M. et al., *Nature Med* (2020)




Dijkstra KK. et al., *Cell* (2018)

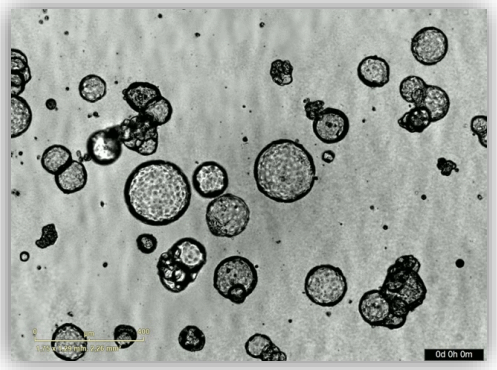


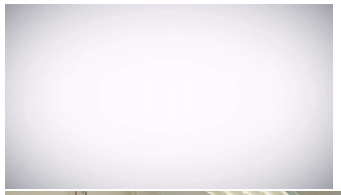




- **Reactivity in 3/6 responders**
- **No reactivity in non-responders**

Vaincrabe

Réseau OrgaNO






lb.weiswald@baclesse.unicancer.fr
l.poulain@baclesse.unicancer.fr

Laurent POULAIN
Louis-Bastien WEISWALD
Jérémie LE GOFF
Romane FLORENT
Jordane DIVOUX
Guillaume DESMARTIN
Lucie LECOUFLET

# Ribbon network

GDR Groupement de recherche Organoïdes

Research workshop

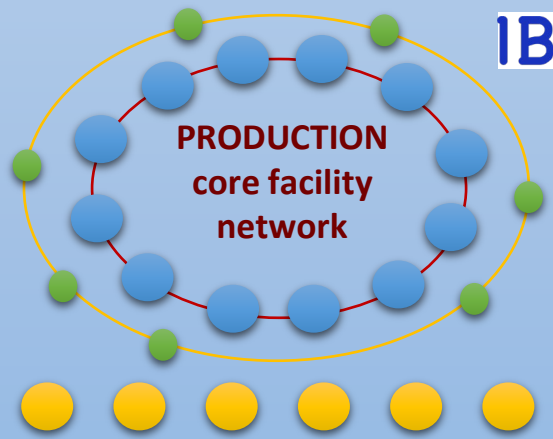
Valorization workshop

Training workshop

Ethic workshop

**Core facility workshop**

RIBBON* network (CF / BRC)




IBiSA

⇔ **Research units**

« Support » or « post-production » core facilities

## *RIBBON :*

***National network of productions core facilities and organoid biobanks***

**Aim (2024)**

Network of Core Facilities

Associated with certified Biological Ressource Center

Common web portal :
Catalogs of available organoid models and presentation of how to access them

FC3R centre français

Call for projects
« Collective initiative and
And sharing network »

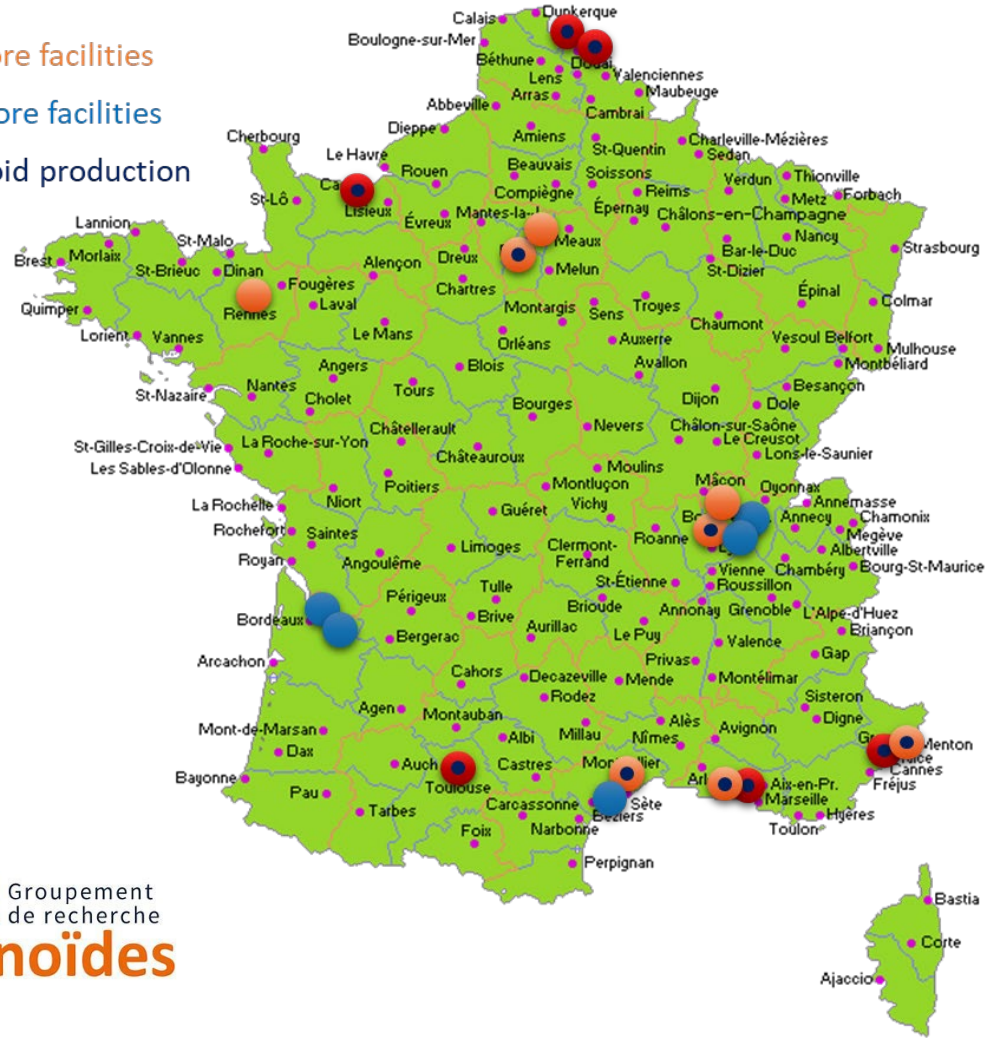
# Organoid core facilities in France

IBiSA-certified production core facilities

Production core facilities

« Support » core facilities

Tumor organoid production core facilities




cnrs GDR Groupement de recherche Organoïdes

## ❑ 6 IBiSA-certified production core facilities

- Caen / OrgaPred (Laurent Poulain, L-B Weiswald)
- Lille / OrgaRES (Audrey Vincent)
- Marseille / 3D-Hub-O (Géraldine Guasch)
- Nice / 3D-Hub-S (Cédric Gaggioli)
- Toulouse / POT (Nathalie Vergnolles, David Sagnat)
- Lille / ORGANOMICS (Isabelle Fournier, Marie Duhamel)

IBiSA Infrastructures en Biologie Santé et Agronomie

## ❑ 7 other production core facilities

- Rennes / Numecan (Bruno Clément)
- Montpellier / POM (Albano Meli, John DeVos)
- Lyon / SBRI (Bertrand Pain, Colette Dehay)
- Lyon / 3D-Onco (Véronique Maguer-Satta)
- Nice-Marseille / PETRA (Aurélie Tchoghandjian)
- Paris / IP-PTBM (Samy Gobaa)
- Paris / IGR (Fanny Jaulin, Karelia Lipson)

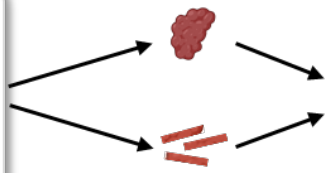
## ❑ 5 « support » core facilities (encapsulation, bioprinting…)

- Bordeaux / VoxCell (Laetitia Andrique)
- Bordeaux / ART-BioPrint (Hugo de Oliveira)
- Montpellier / CARTIGEN (Emeline Groult / Matthieu Simon)
- Lyon / 3D Fab
- Lyon / C3D

# Objectives of ORGAPRED core facility

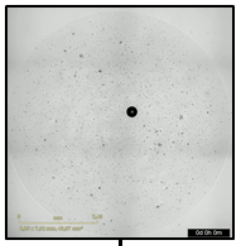
**Setting up of clinical studies and biological collections** *

Head & neck
Breast
Ovarian
Gastroesophageal
...
Tumors



Dissociation

**Production of tumor organoids** *



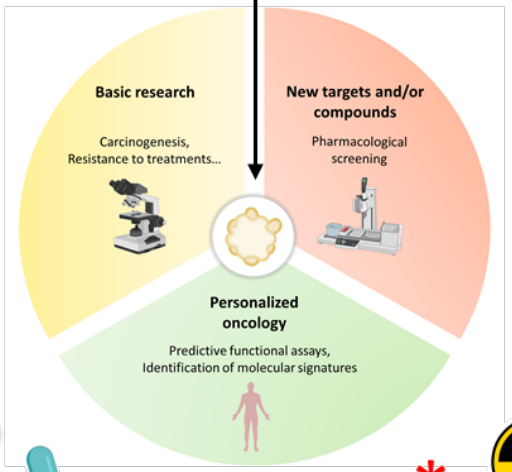
**Available models:**

- 25 ovarian cancers
- 15 breast cancers
- 15 head & neck cancers
- 3 gastroesophageal cancers

**Biobanking** *


*Local biological resource centers*

**Research teams**




**Research teams & Industries**

ChemBioFrance
de petites molécules pour comprendre et soigner le vivant

**Education and training** *

**Advice and support** *

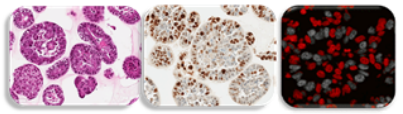
**Partner hospitals**

IBiSA Infrastructures en Biologie Santé et Agronomie

**Histological and molecular characterization**

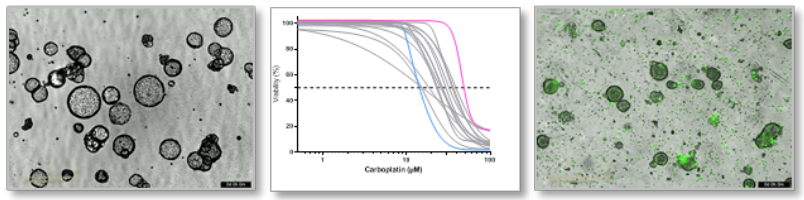
PLATON ONCOLOGY SERVICES UNIT

IHC, STR,
NGS ADN & ARNs, CGH array...
*Collaborations with other facilities*



**Predictive aspects: Precision oncology**

**Functional assays** *



**Morphology** (IncuCyte S3)

**Viability** (CellTiterGlo-3D)

**Cell death** (CellTox Green)

**Molecular signature, Companion diagnostic test**

CLASSIFICATION OF PDTO (sensitive, resistant, intermediate)

* **Proposed services**

# Conditions of access to organoid core facilities

**Tumor organoid culture:**


**€**

**Collaboration**

- Academic partners
- Potential contribution of users to experiments
- Common grant funding application
- IP sharing (eventually)

**€€€**

**Service provision**

- Private/academic partners
- No contribution to experiments
- No IP sharing

**Get in touch with the core facility!!**