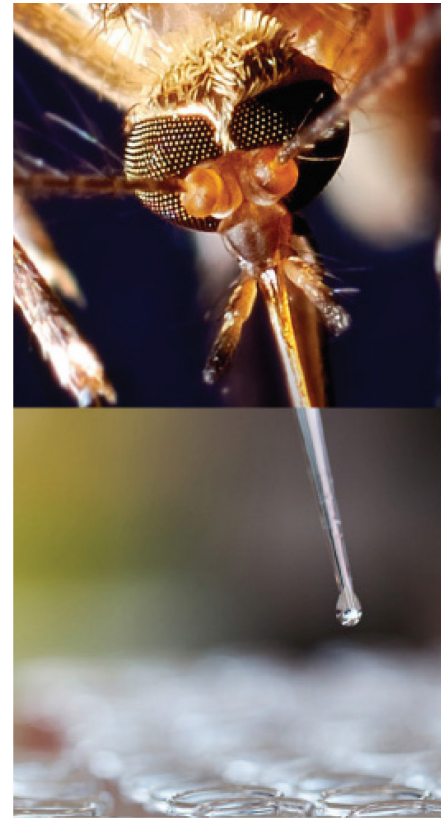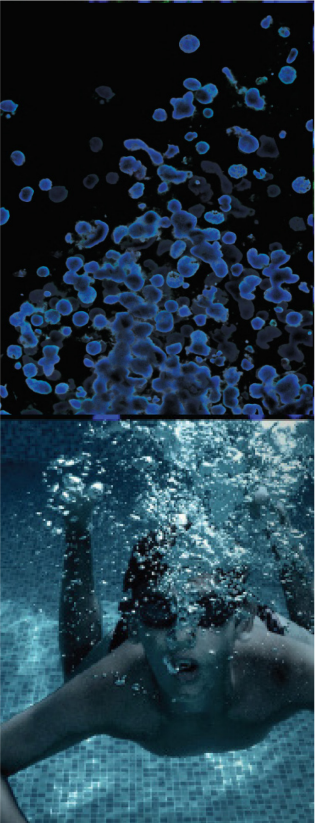# Next-Generation Cancer Models from the Human Cancer Models Initiative

James Clinton, Ph.D.

Lead Scientist, ATCC Cell Systems

Credible Leads to Incredible™

About ATCC

- Founded in 1925, ATCC is a non-profit organization with HQ in Manassas, VA, and an R&D and Services center in Gaithersburg, MD

- World's largest, most diverse biological materials and information resource for cell culture – the "gold standard"

- Innovative R&D company featuring gene editing, differentiated stem cells, advanced models

- Partner with government, industry, and academia

- Leading global supplier of authenticated cell lines, viral and microbial standards

- Sales and distribution in 150 countries, 19 international distributors

- Talented team of 450+ employees, over one-third with advanced degrees

ATCC

Outline

- Introduction to the Human Cancer Models Initiative (HCMI)

- Next generation cancer model (NGCM) technologies

- HCMI portfolio and the pipeline

- Resources to learn more about the HCMI and the models at ATCC

ATCC
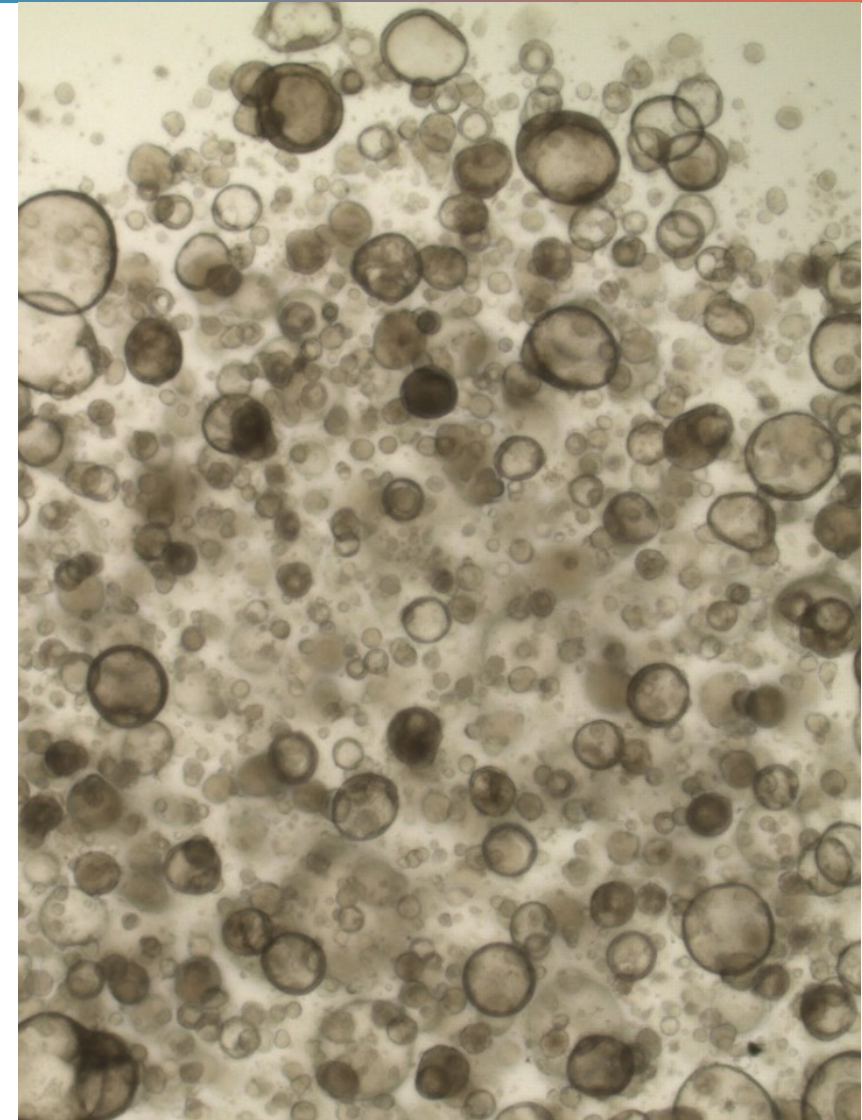
Why are new models needed?

- Poor representation of some cancer types/subtypes

- Existing lines may not be biologically/genetically representative of in vivo tumors

- Lack of patient and clinical outcome data, model history

- Lack of comparison to normal reference sample and/or directly compared to primary tumor

- Insufficient to capture the genetic diversity of cancer

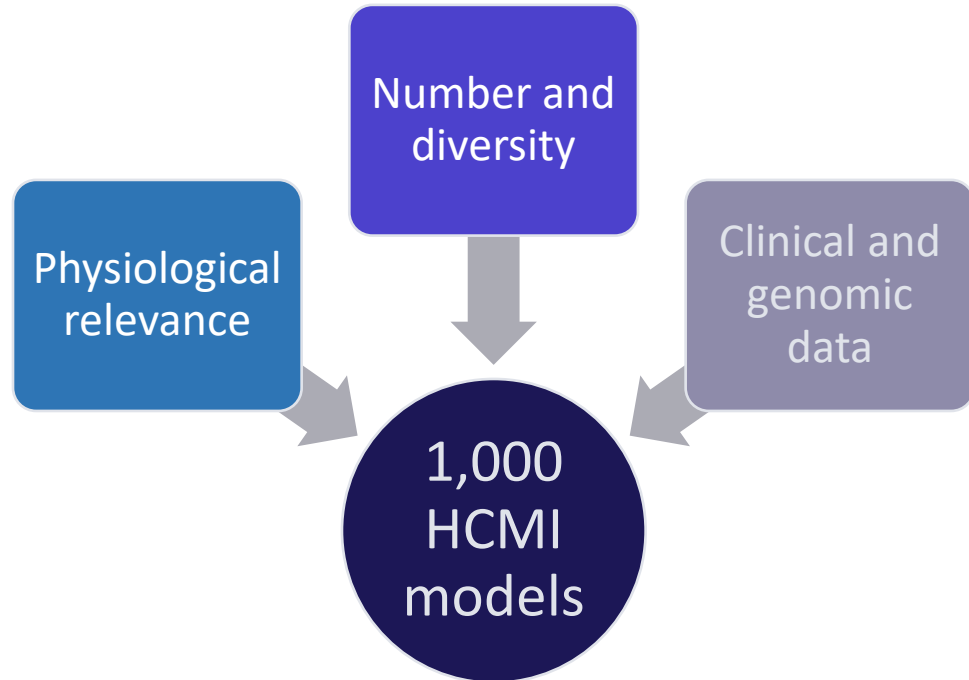ATCC
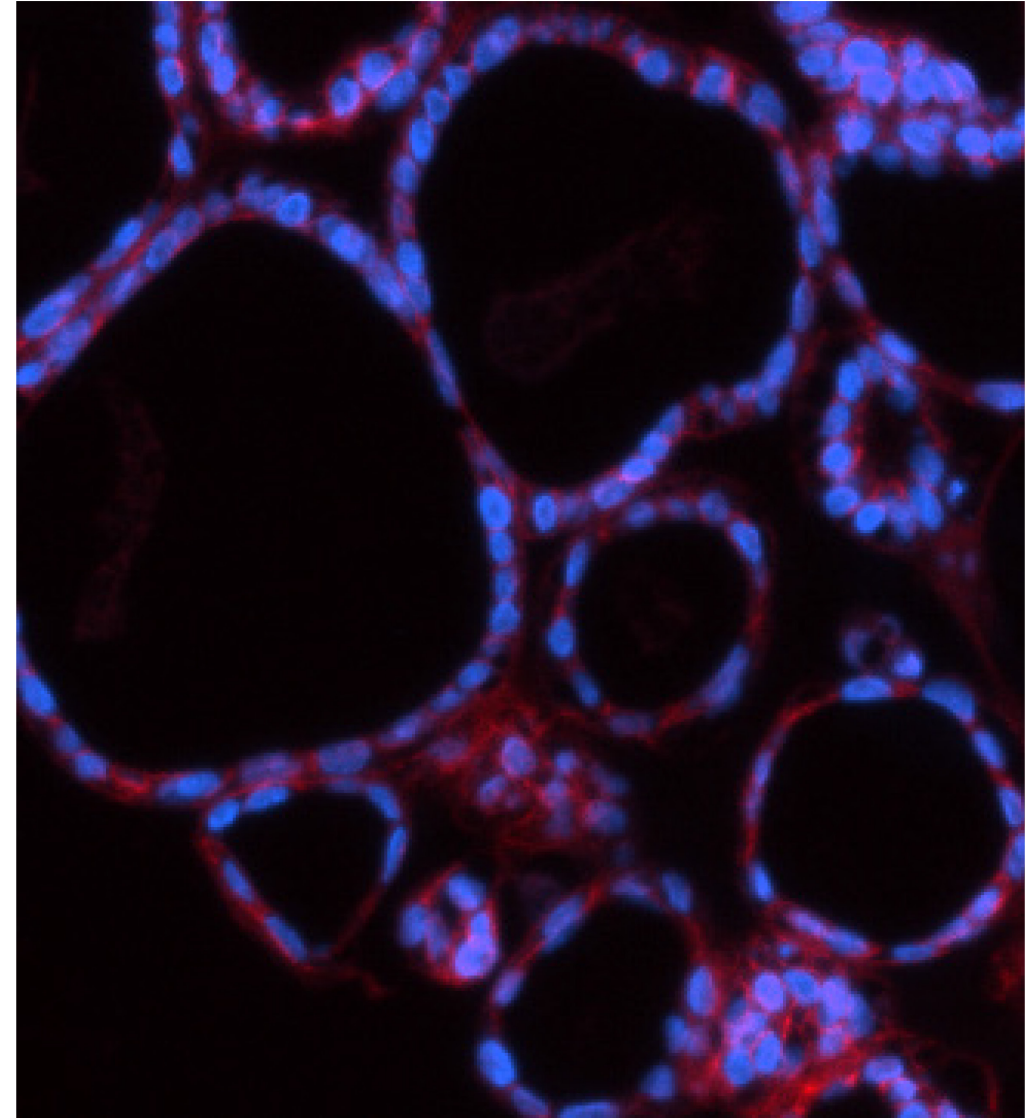
Consortium contributors

Founders

Model Developers

Distribution

HCMI approach and core principles

Physiological relevance

Number and diversity

Clinical and genomic data

1,000 HCMI models

- Models as a "community resource"

- Awareness of IP issues

- Permissive informed consent language permitting broad use

- Global distribution to ensure wide availability

- Open protocols

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Shared features of advanced culture methods

Permits growth and expansion

Limited starting material required

Genetically stable

Maintain *in vivo* phenotype

Relatively high success rate

ATCC

Characterization of models

Molecular

- 15X WGS of model, primary tumor, and normal tissue
- 150X WXS of model, primary tumor, and normal tissue
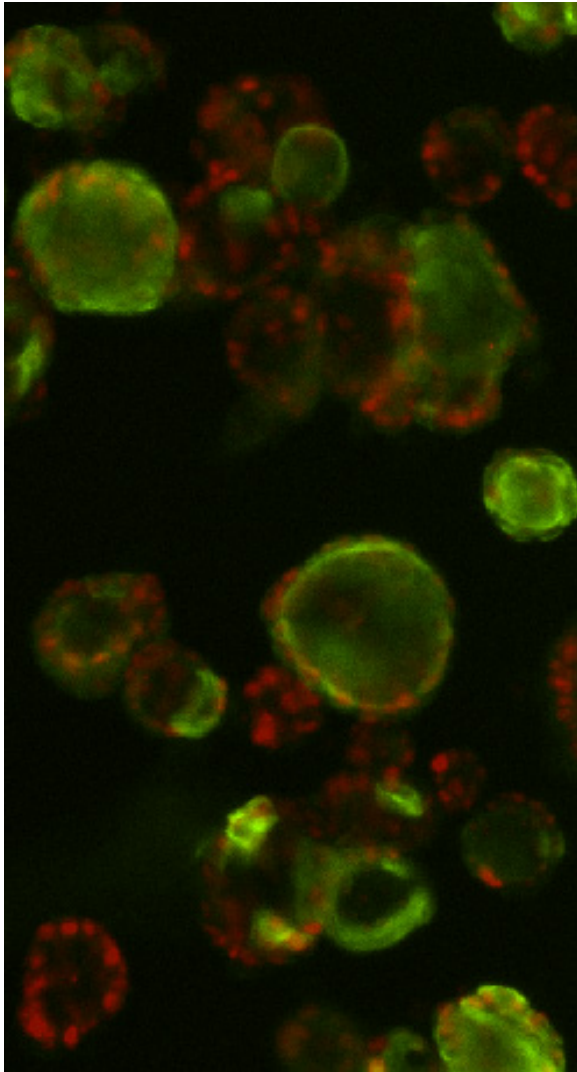- RNA-seq of model and primary tumor

Clinical

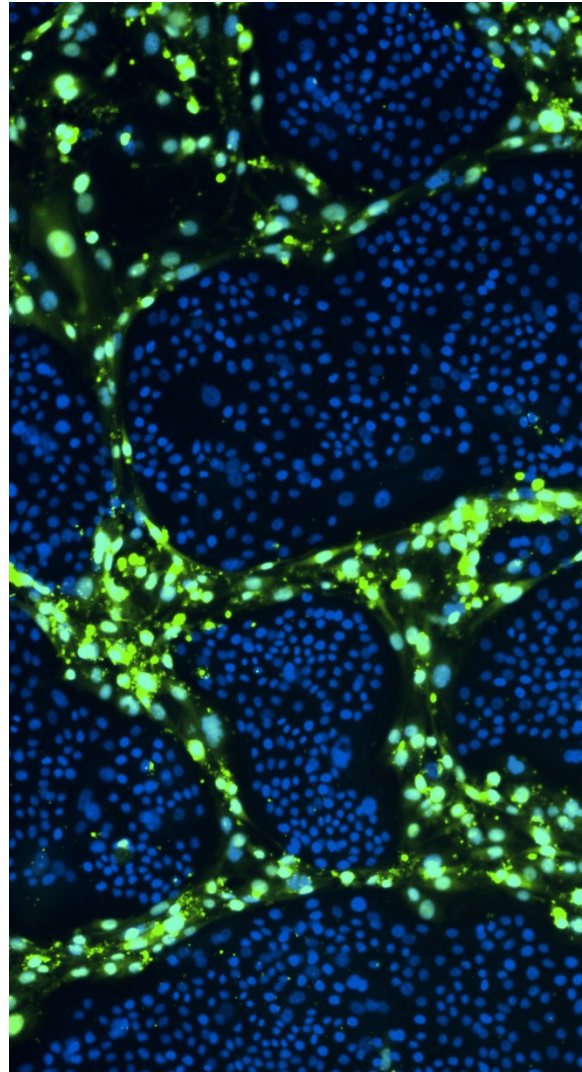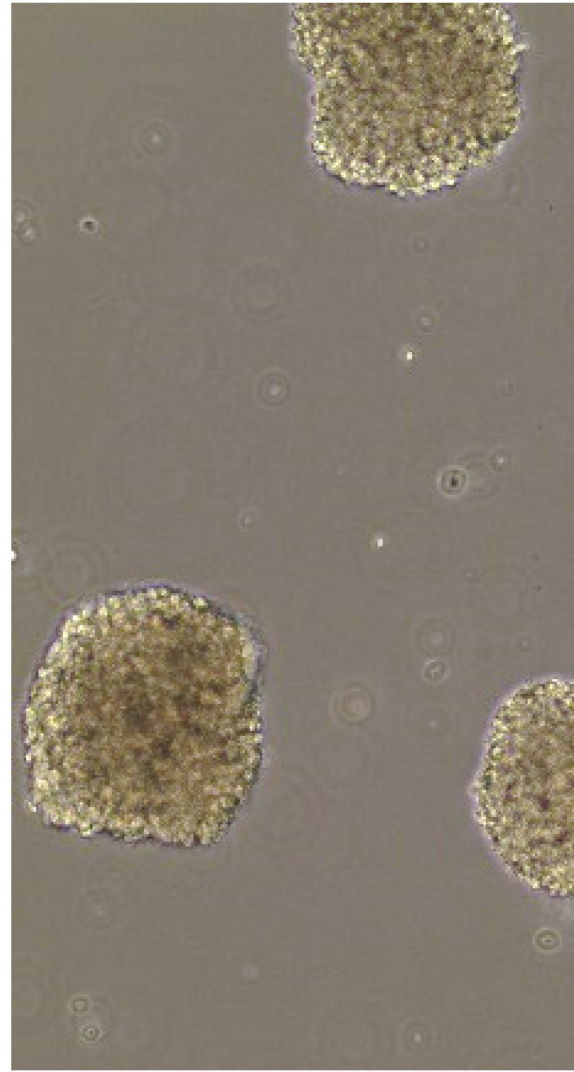- Disease diagnosis
- Patient demographics
- Treatment and outcomes
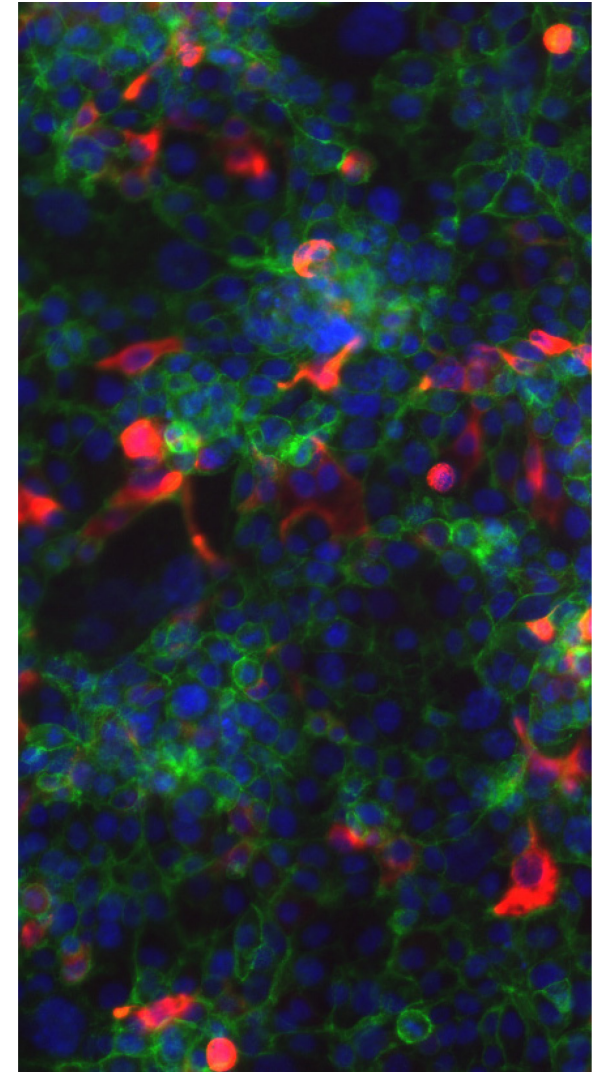
ATCC®
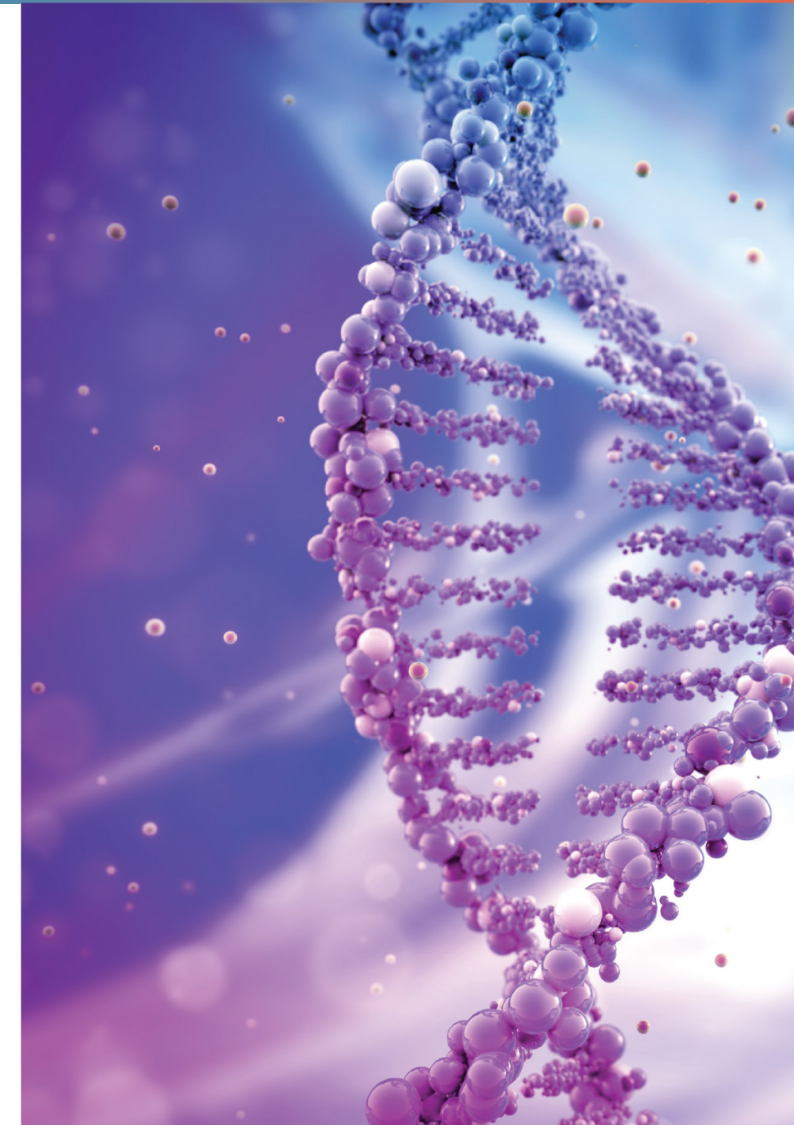
Types of patient-derived NGCMs

Organoids

Conditionally reprogrammed cells

Neurospheres
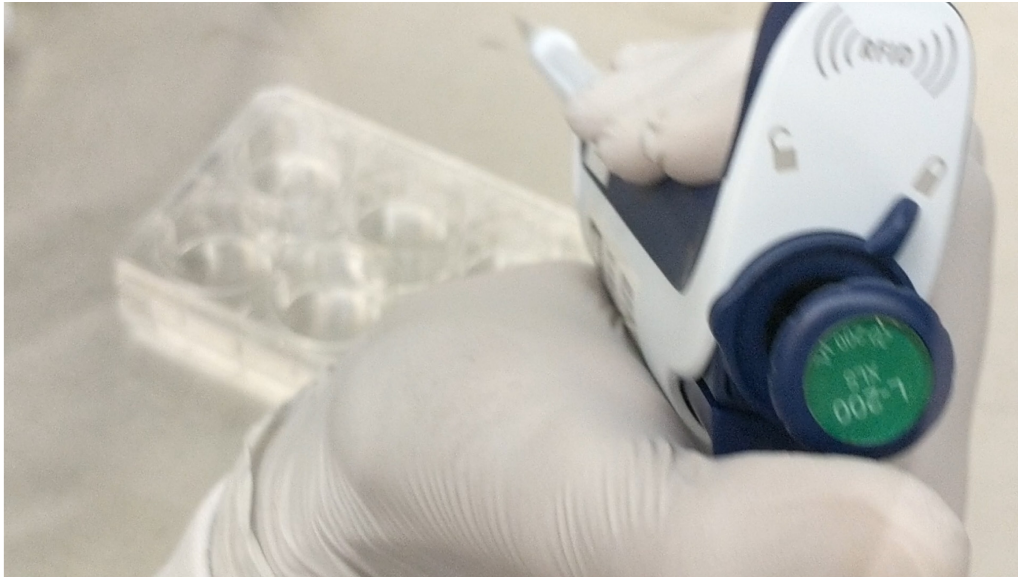
Other adherent and suspension cells

ATCC

Primary tissue-derived organoids

- Embedded three-dimensional culture technique that utilizes model-specific growth media formulations in combination with undefined extracellular matrix

- Self-organize into complex 3D structures (no intermediate differentiation steps required)

- Organoids can be dissociated, expanded, cryopreserved and recovered

⑦ Enzymatically dissociate.

⑥ Mechanically dissociate and wash to remove ECM.

⑤ Collect organoids and ECM.

passaging

① Suspend cells or fragments in ECM. Dispense as droplets.

② Incubate at 37°C to polymerize gel, forming a dome.

③ Overlay gelled dome with media containing niche factors.

④ Organoids form and enlarge.

Brightfield, 10X

ATCC
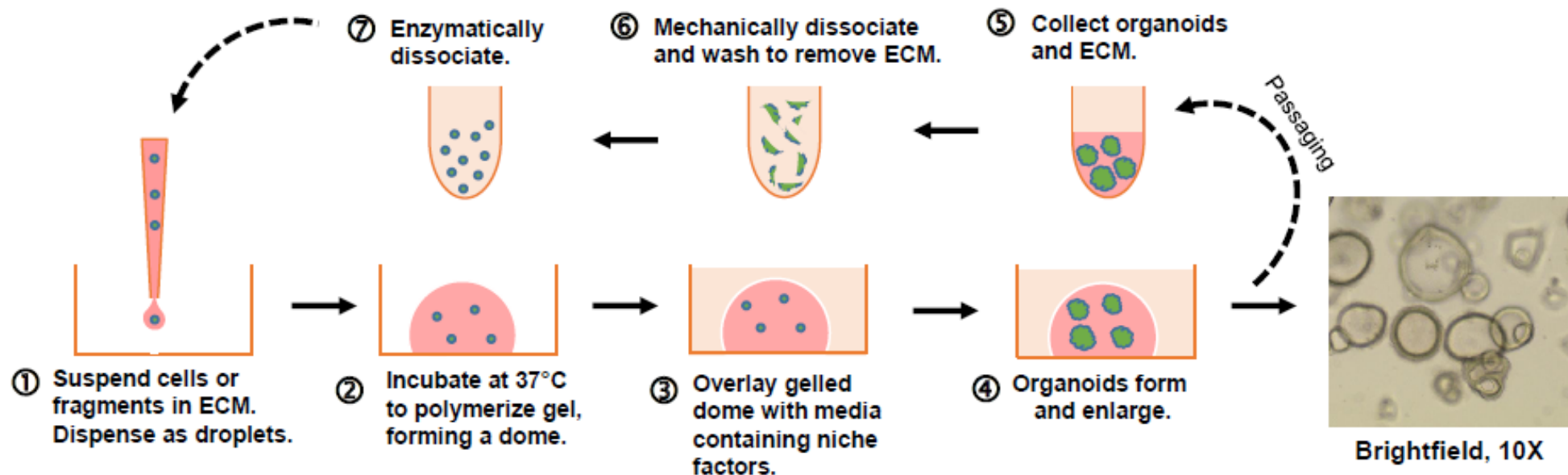
Seeding organoids in ECM droplets

Seeding a single 6-well with a P200

Seeding a dish with a multichannel pipette
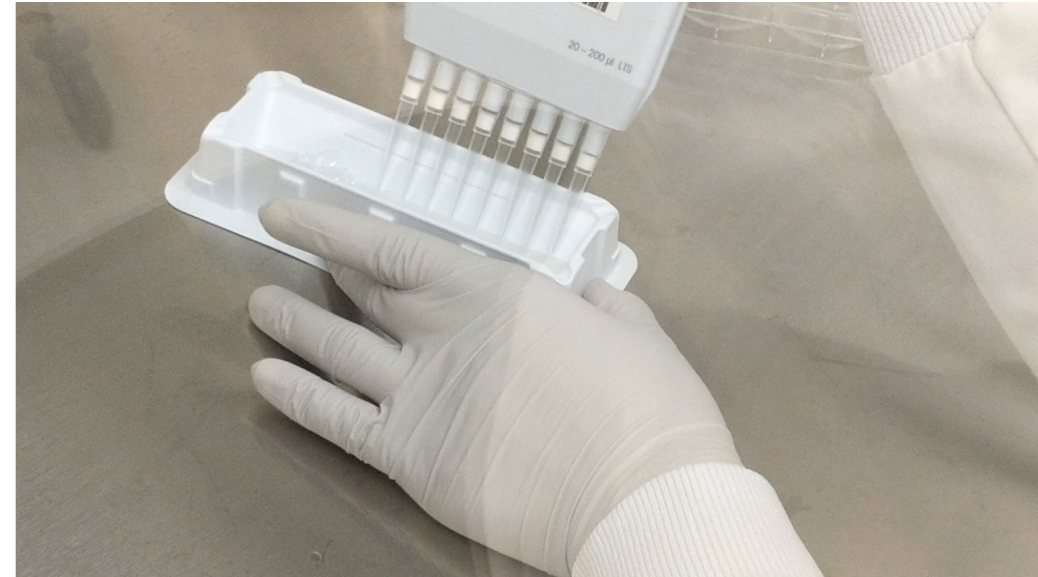
UNIT | 🔒 Free Access

Initiation, Expansion, and Cryopreservation of Human Primary Tissue-Derived Normal and Diseased Organoids in Embedded Three-Dimensional Culture
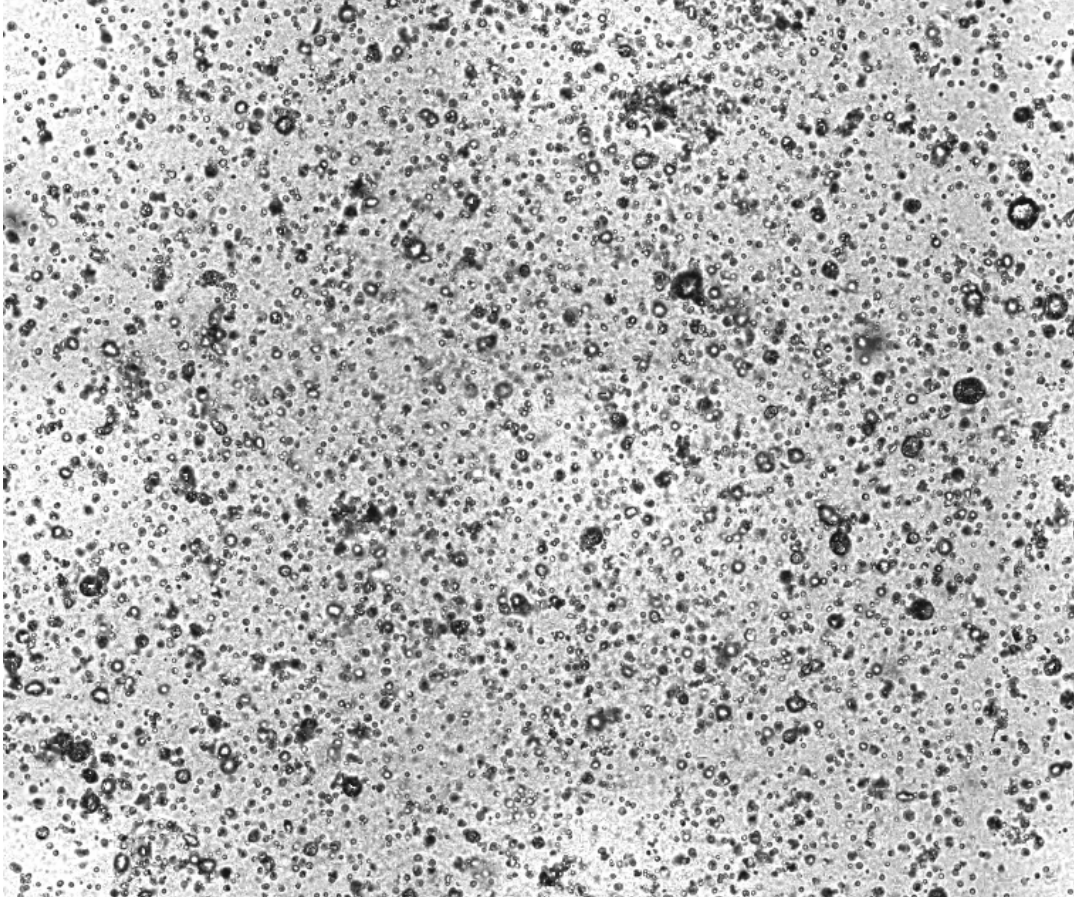
https://doi.org/10.1002/cpcb.66

ATCC Video tutorial on thawing, culturing, and cryopreserving human organoids (~20 minutes)

https://www.atcc.org/organoids

Organoid growth and expansion

ATCC® PDM-90™
Pancreatic cancer organoid

- Six-day time lapse from cryopreserved primary tissue organoids.

- Single ~10uL dome of extracellular matrix.

- Seeded ~3×10^4 viable cells/dome.

- Individual organoids increase in size by ~2-5X.

- Exhibits cystic morphology with single lumen.

Organoids are amenable to standard lab assays
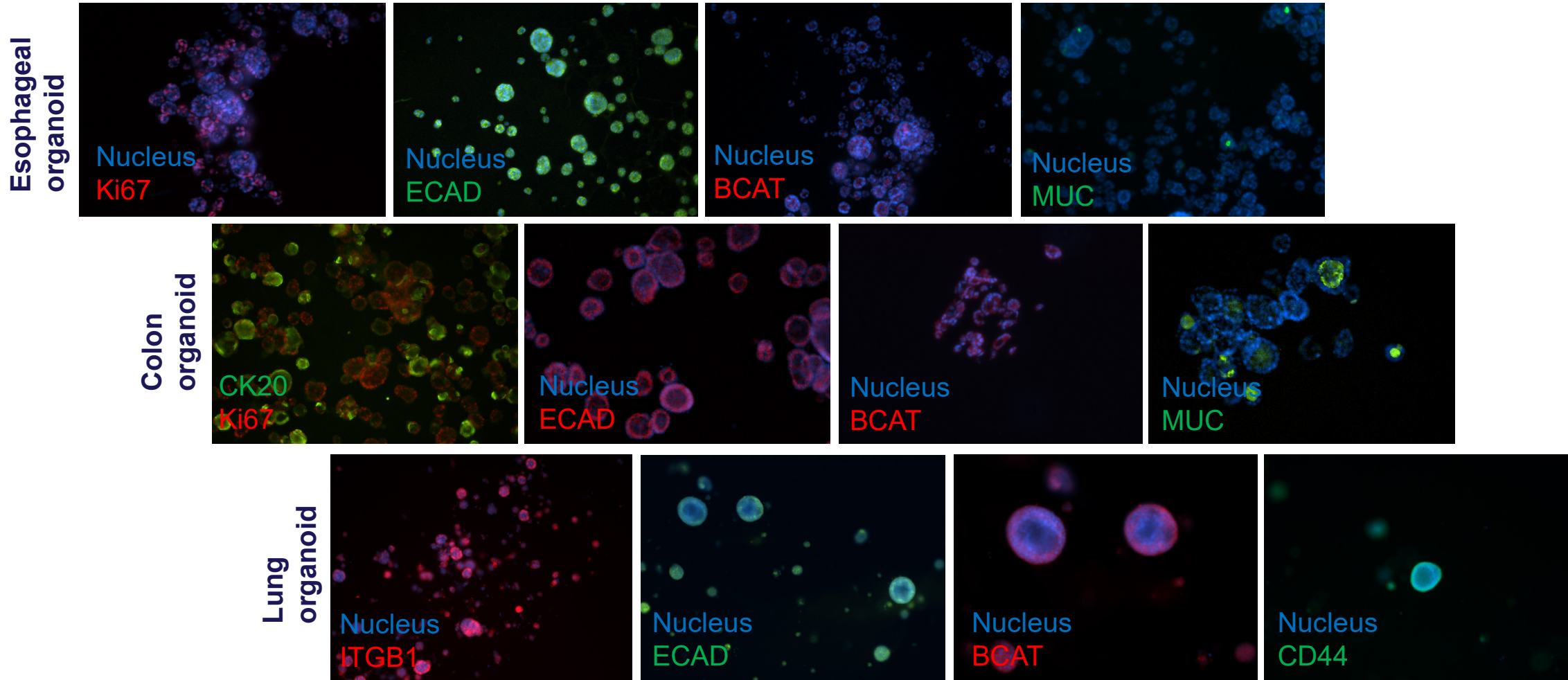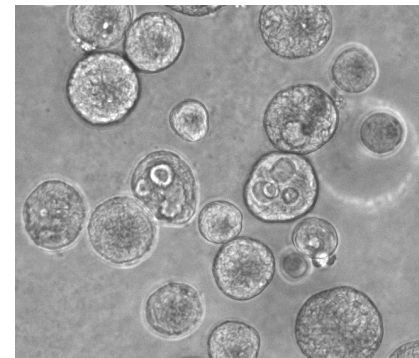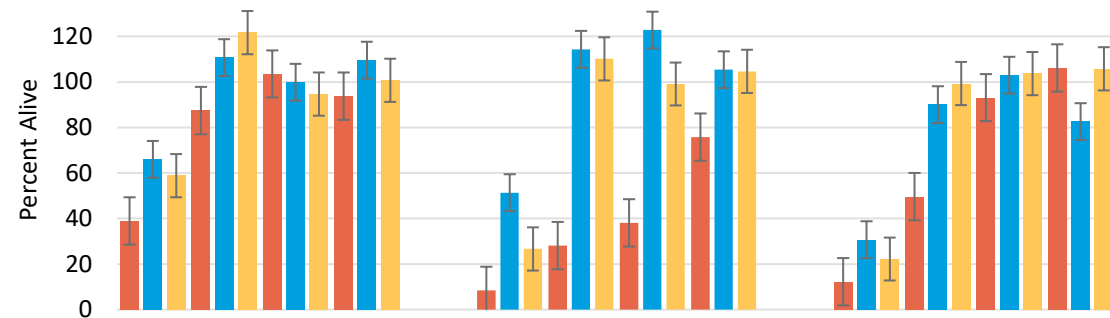

Esophageal organoid

Nucleus
Ki67

Nucleus
ECAD

Nucleus
BCAT

Nucleus
MUC

Colon organoid

CK20
Ki67

Nucleus
ECAD

Nucleus
BCAT

Nucleus
MUC

Lung organoid

Nucleus
ITGB1

Nucleus
ECAD

Nucleus
BCAT

Nucleus
CD44

Primary human organoids embedded within Cell Basement Membrane Gel (ATCC® ACS-3035™) and subjected to standard immunofluorescent staining and imaging.

Organoids are amenable to standard lab assays
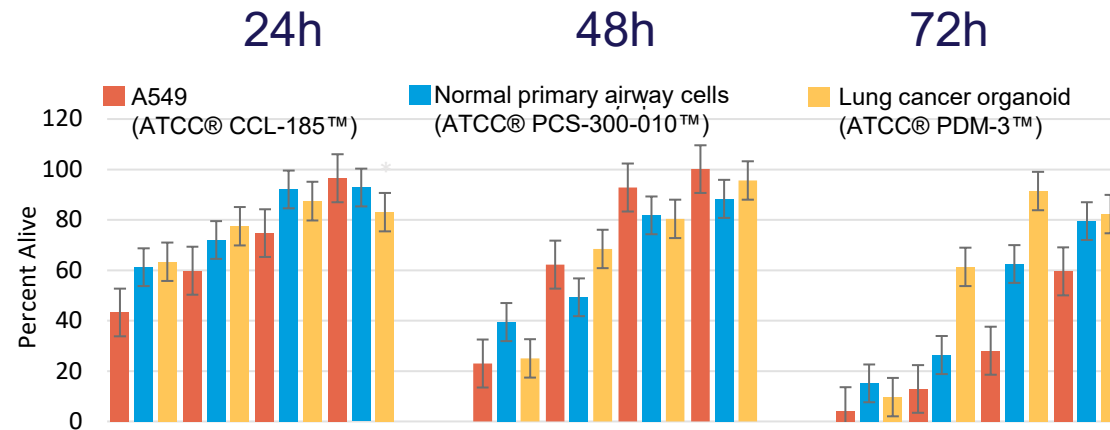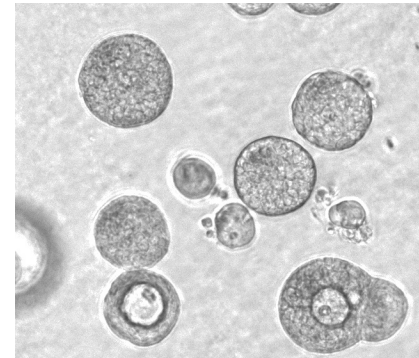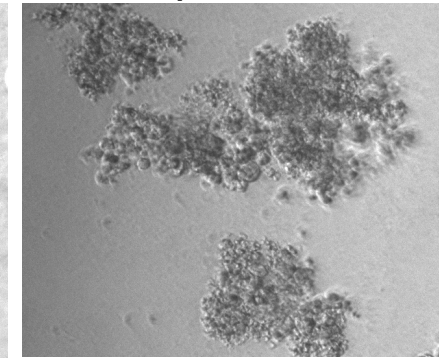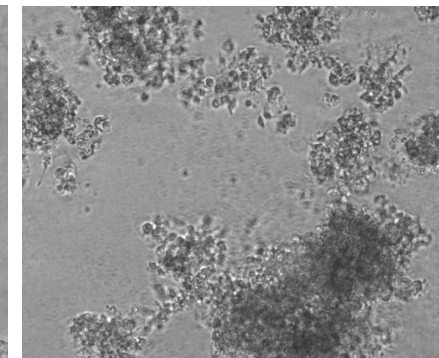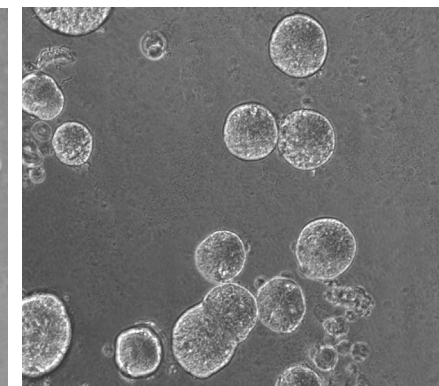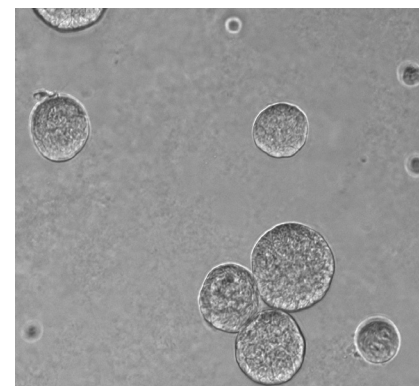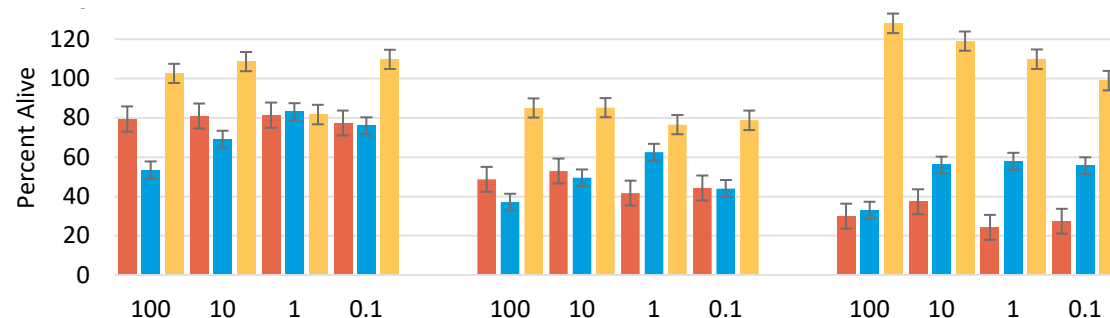
10X brightfield images of PDM-3 organoids in suspension

Assayed in triplicate; results normalized to DMSO control

Organoids are more like tumors than cancer cell lines

Taylor & Francis
Taylor & Francis Group

BRIEF REPORT

OPEN ACCESS | Check for updates

The DNA methylation landscape of human cancer organoids available at the American type culture collection

Ricky Joshi[a], Manuel Castro De Moura [b]a, David Piñeyro [b]a, Damiana Alvarez-Errico[a], Carles Arribas[a], and Manel Esteller [b]a,b,c,d

[a]Josep Carreras Leukaemia Research Institute (IJC), Badalona, Barcelona, Spain; [b]Institucio Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain; [c]Centro de Investigacion Biomedica en Red Cancer (CIBERONC), Madrid, Spain; [d]Physiological Sciences Department, School of Medicine and Health Sciences, University of Barcelona (UB), Barcelona, Spain

- Joshi, et al. used microarrays to probe methylation of HCMI organoids.
- 25 models from 5 tissue types were examined.
- Tumor organoids clustered with themselves, not normal tissue.
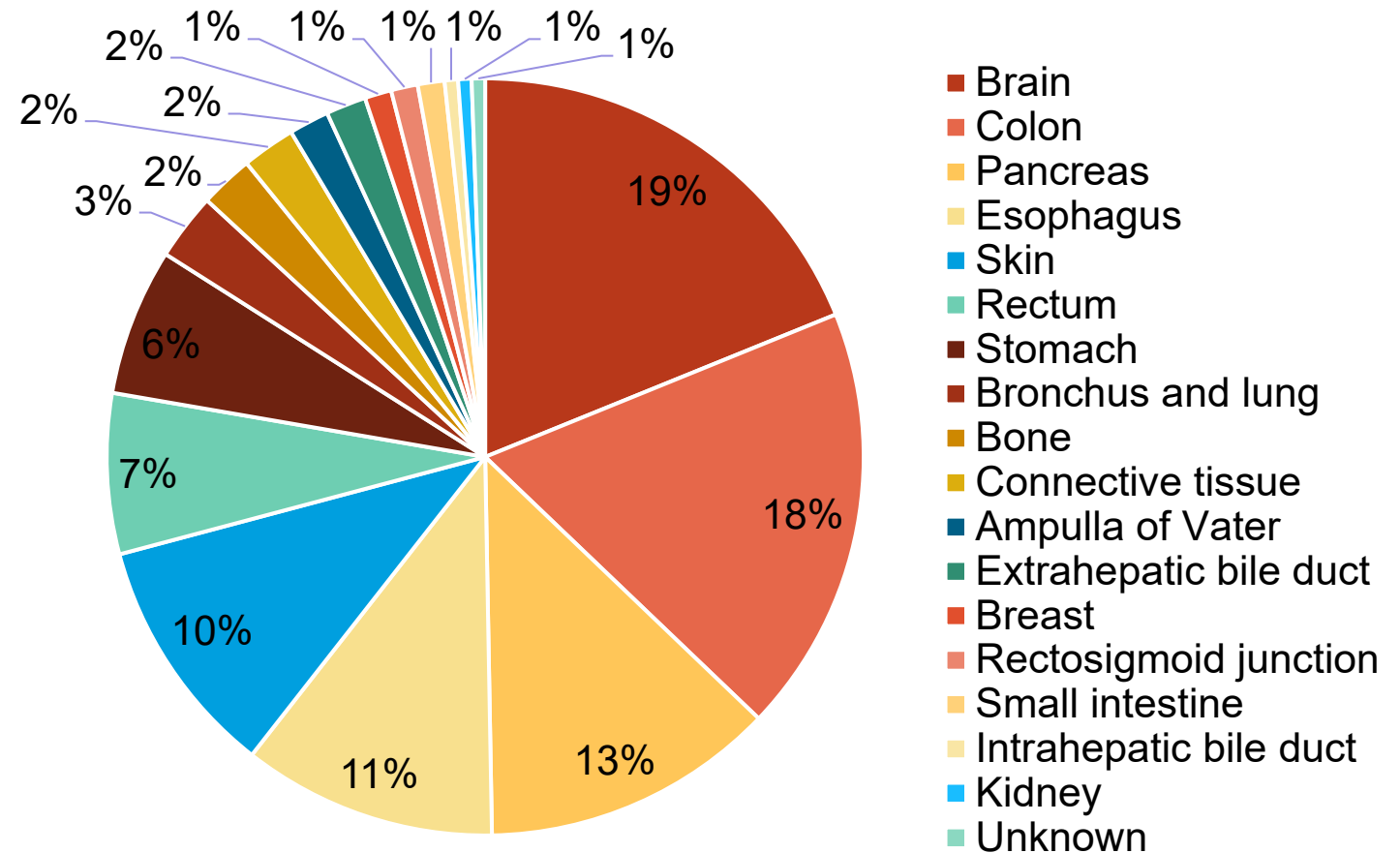- Organoids clustered with primary tumor tissue, not cancer cell lines.
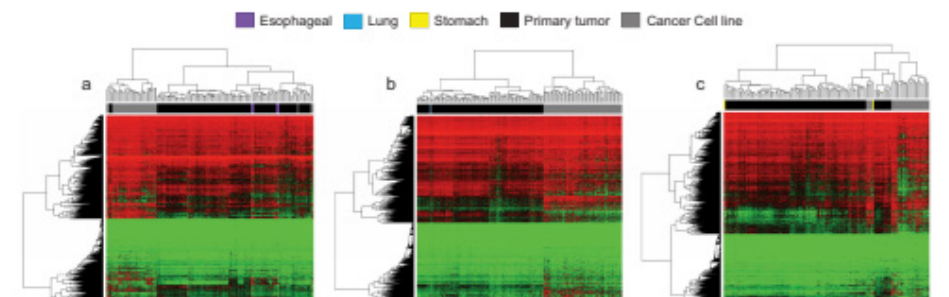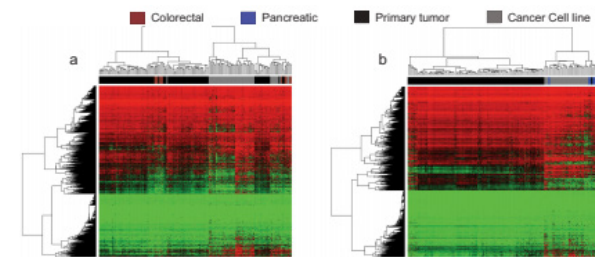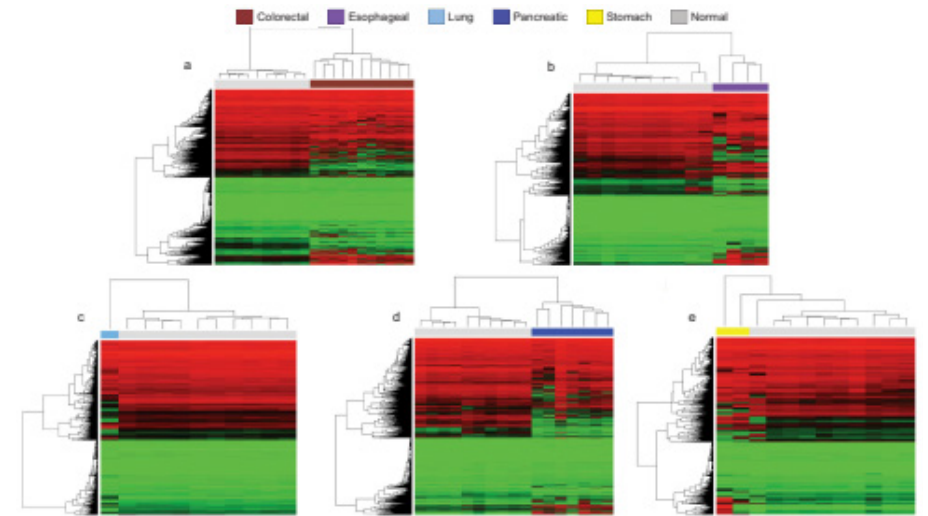
Currently available models (177)

Tissue type

Primary tissue site
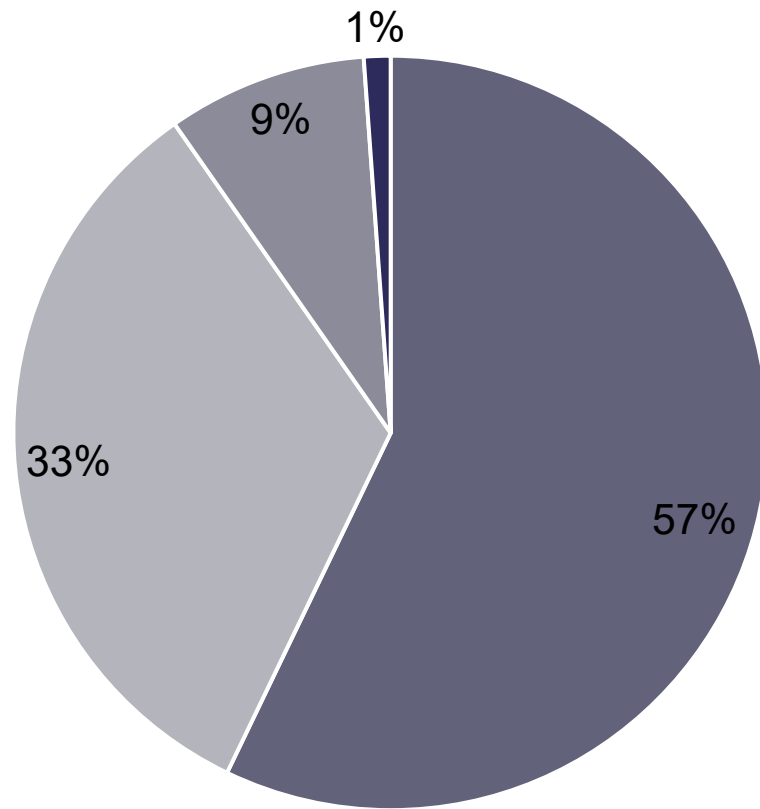
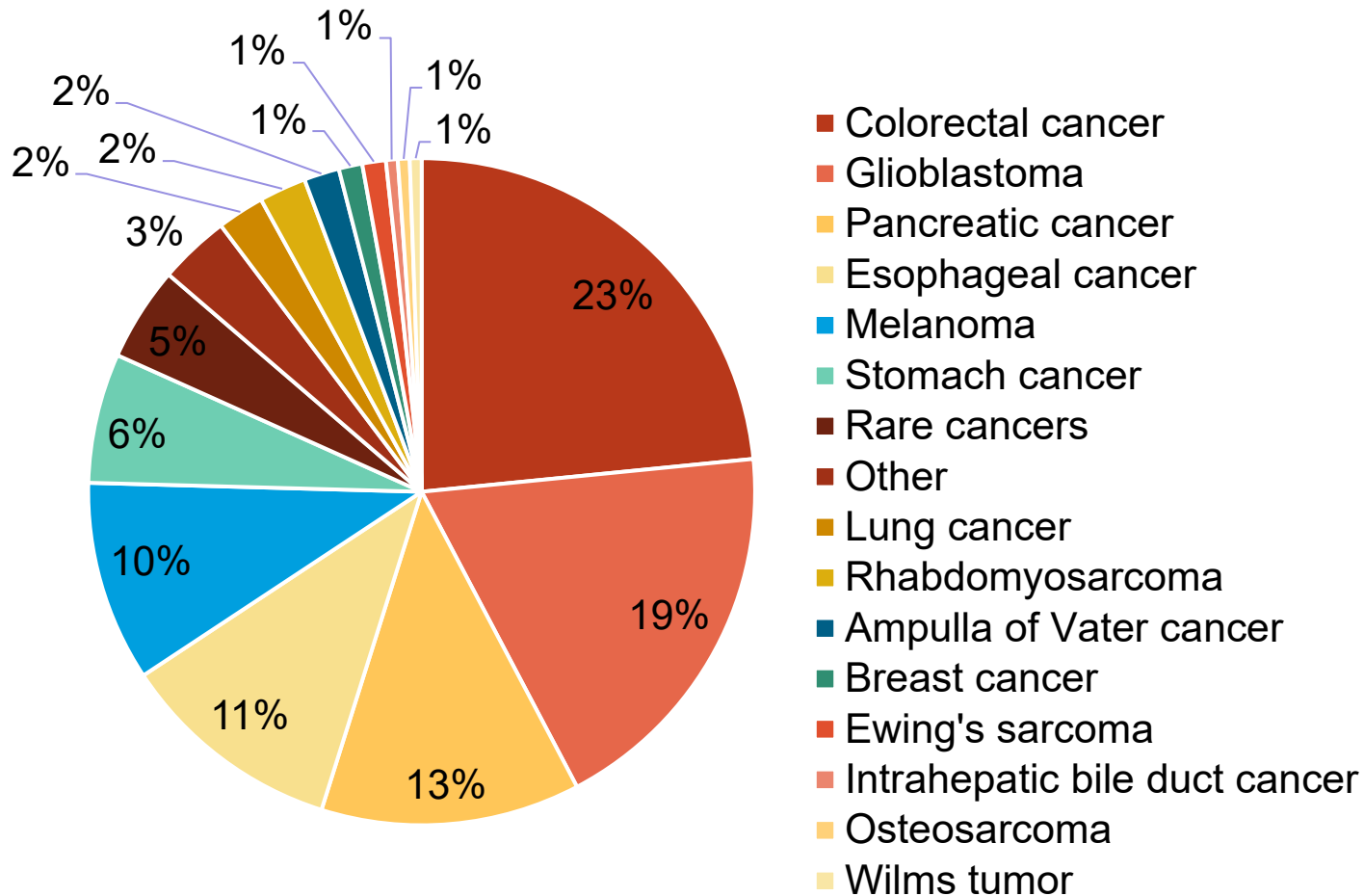Legend (Tissue type): Primary, Metastasis, Recurrent, Pre-malignant

Legend (Primary tissue site): Brain, Colon, Pancreas, Esophagus, Skin, Rectum, Stomach, Bronchus and lung, Bone, Connective tissue, Ampulla of Vater, Extrahepatic bile duct, Breast, Rectosigmoid junction, Small intestine, Intrahepatic bile duct, Kidney, Unknown
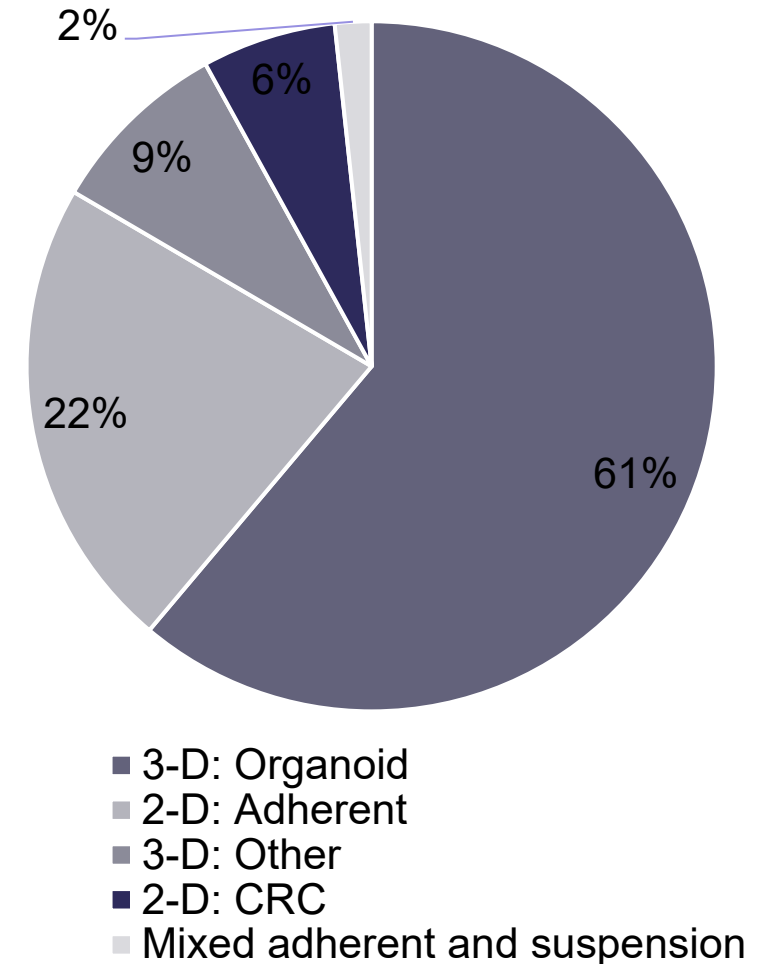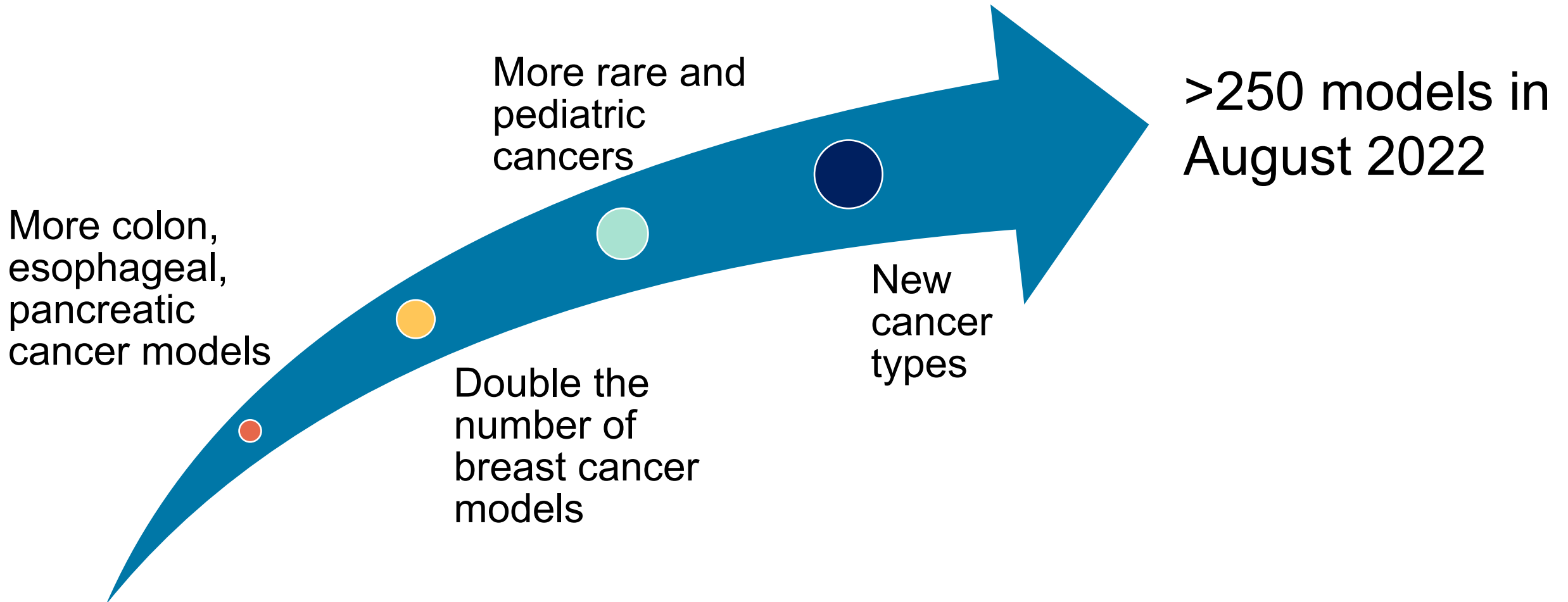
Currently available models (177)

Clinical tumor diagnosis

- Colorectal cancer — 23%
- Glioblastoma — 19%
- Pancreatic cancer — 13%
- Esophageal cancer — 11%
- Melanoma — 10%
- Stomach cancer — 6%
- Rare cancers — 5%
- Other — 3%
- Lung cancer — 2%
- Rhabdomyosarcoma — 2%
- Ampulla of Vater cancer — 2%
- Breast cancer — 1%
- Ewing's sarcoma — 1%
- Intrahepatic bile duct cancer — 1%
- Osteosarcoma — 1%
- Wilms tumor — 1%

Type of model

- 3-D: Organoid — 61%
- 2-D: Adherent — 22%
- 3-D: Other — 9%
- 2-D: CRC — 6%
- Mixed adherent and suspension — 2%

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HCMI model pipeline

More colon, esophageal, pancreatic cancer models

Double the number of breast cancer models

More rare and pediatric cancers

New cancer types

>250 models in August 2022

ATCC

ATCC HCMI collection website

https://www.atcc.org/hcmi

- View all models released or grouped by tissue.

- Model specific information such as images, STR profiles, and culture recommendations.

- Individual model product pages include detailed culture protocols.

- Growth media information.

- Thawing/subculturing/freezing guides.

- Model pages link to other resource pages that host clinical and sequencing data.

- Frequently asked questions.

- Links to webinars and organoid culture guide and videos.

HCMI Searchable Catalog

- NCI managed website dedicated to HCMI models

- Integrates clinical, model, and genomic information.

- Download model lists with available non-controlled data.

- Search for models of interest using various filters.

- Links out to clinical and genomic data, ATCC model product page.

https://hcmi-searchable-catalog.nci.nih.gov

NCI GDC Data Portal

https://portal.gdc.cancer.gov/projects/HCMI-CMDC
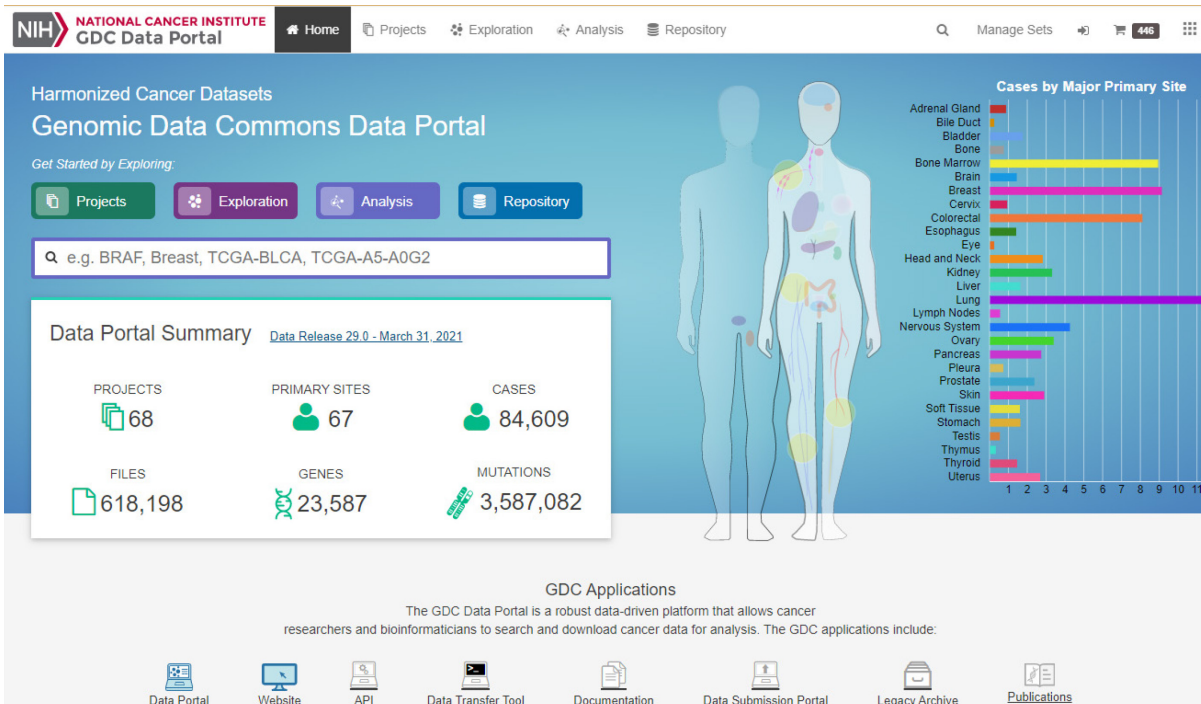
- NCI managed website

- Search and download cancer related datasets for analysis

- Navigate to the "HCMI-CMDC" project for HCMI specific datasets

- Download clinical/biospecimen data

- Access WGS/WXS/RNAseq data
  - Aligned reads, gene expression, SNVs, etc.
  - BAM files, etc.

- Controlled data requires dbGaP access
  - https://gdc.cancer.gov/access-data/obtaining-access-controlled-data
  - https://ocg.cancer.gov/flowchart/guide-accessing-data

Summary

- HCMI portfolio consists of patient derived cancer models is currently ~177 expected to hit 250+ in a year

- Includes a large variety of cancer types

- Includes a variety NGCM including organoids, neurospheres, and others

- Models are supported with clinical and molecular characterization

- ATCC has supporting resources including video culture guides, published protocols and other supporting information available

ATCC®