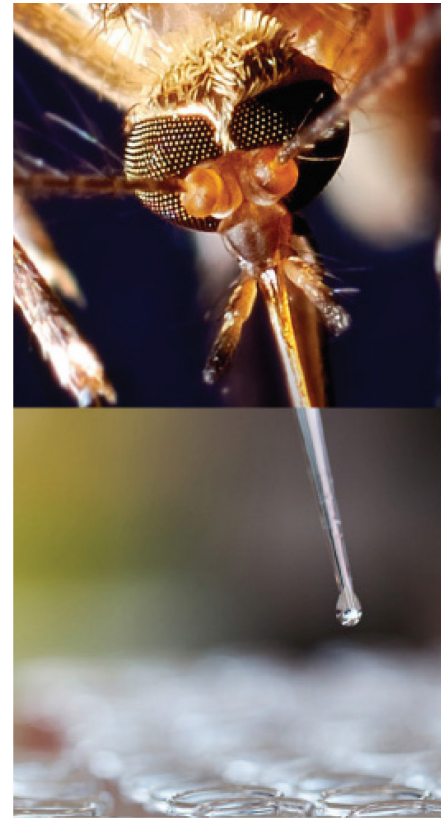
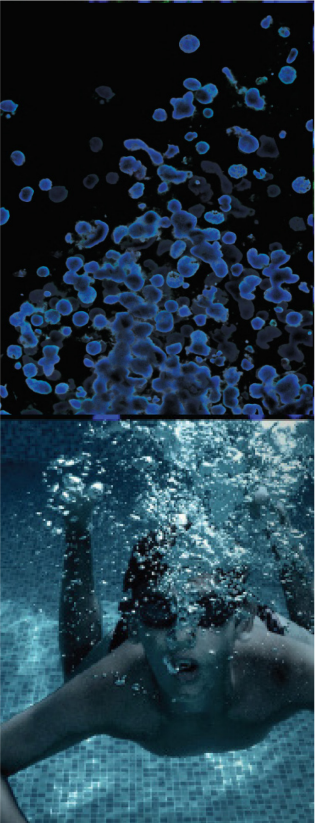




# Next-Generation Cancer Models from the Human Cancer Models Initiative

James Clinton, Ph.D.  
Lead Scientist, ATCC Cell Systems

Credible Leads to Incredible™

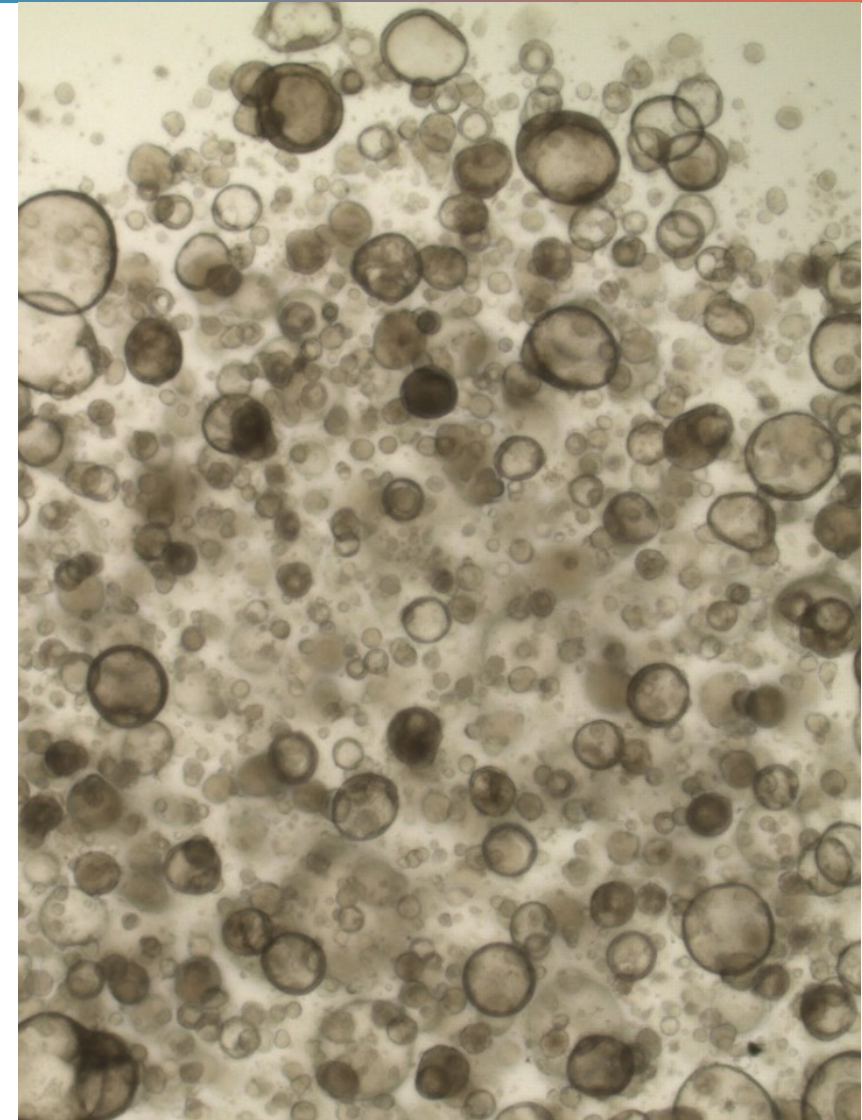


# About ATCC

- 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

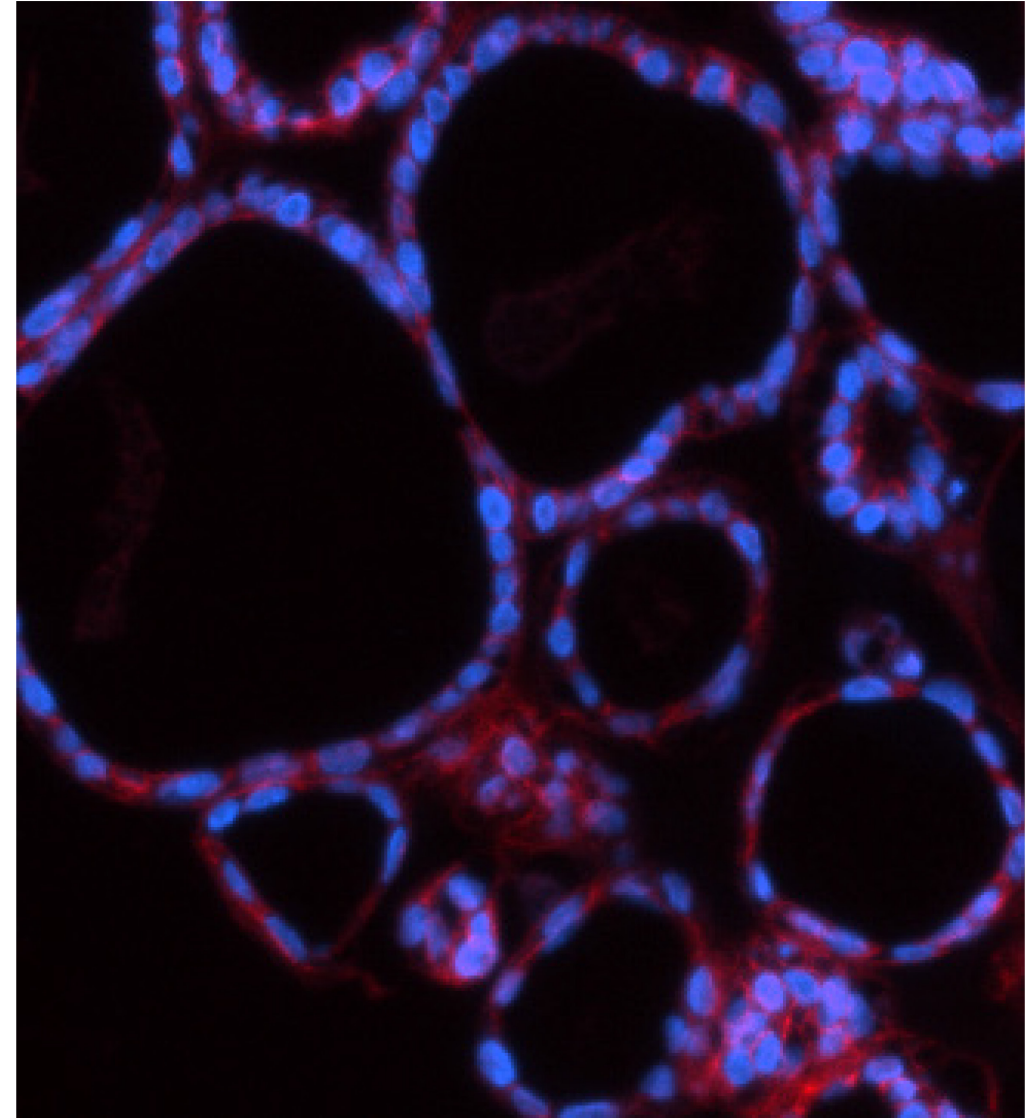
# Outline

- 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



# 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



# Consortium contributors

## Founders



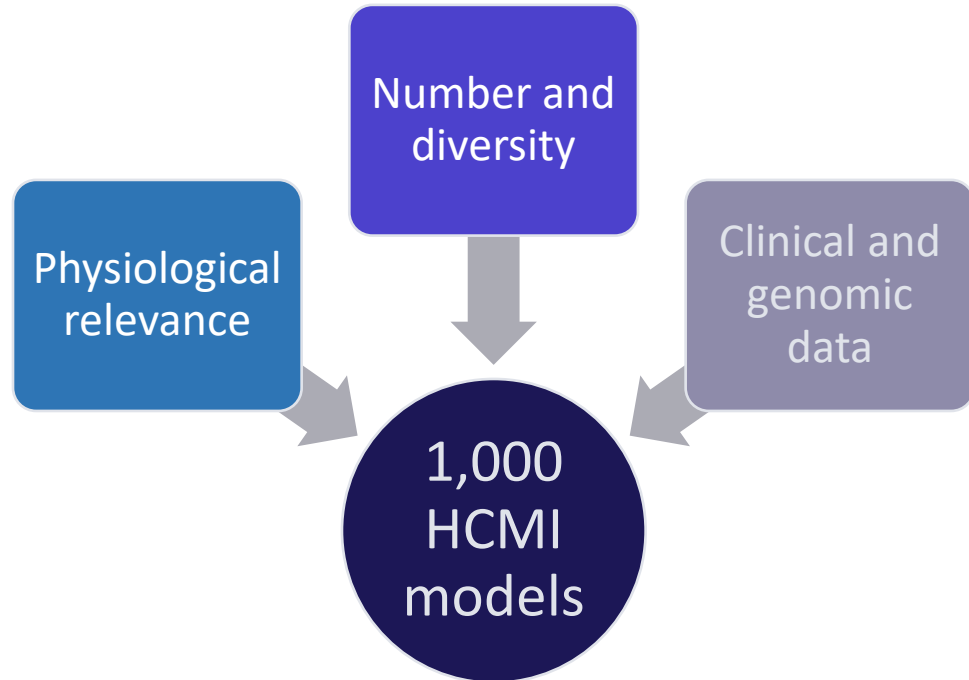
## Model Developers



## Distribution



# HCMI approach and core principles



- Models as a “community resource”
- Awareness of IP issues
- Permissive informed consent language permitting broad use
- Global distribution to ensure wide availability
- Open protocols

# Shared features of advanced culture methods

Permits growth  
and expansion

Limited starting  
material  
required

Genetically  
stable

Maintain *in  
vivo* phenotype

Relatively high  
success rate

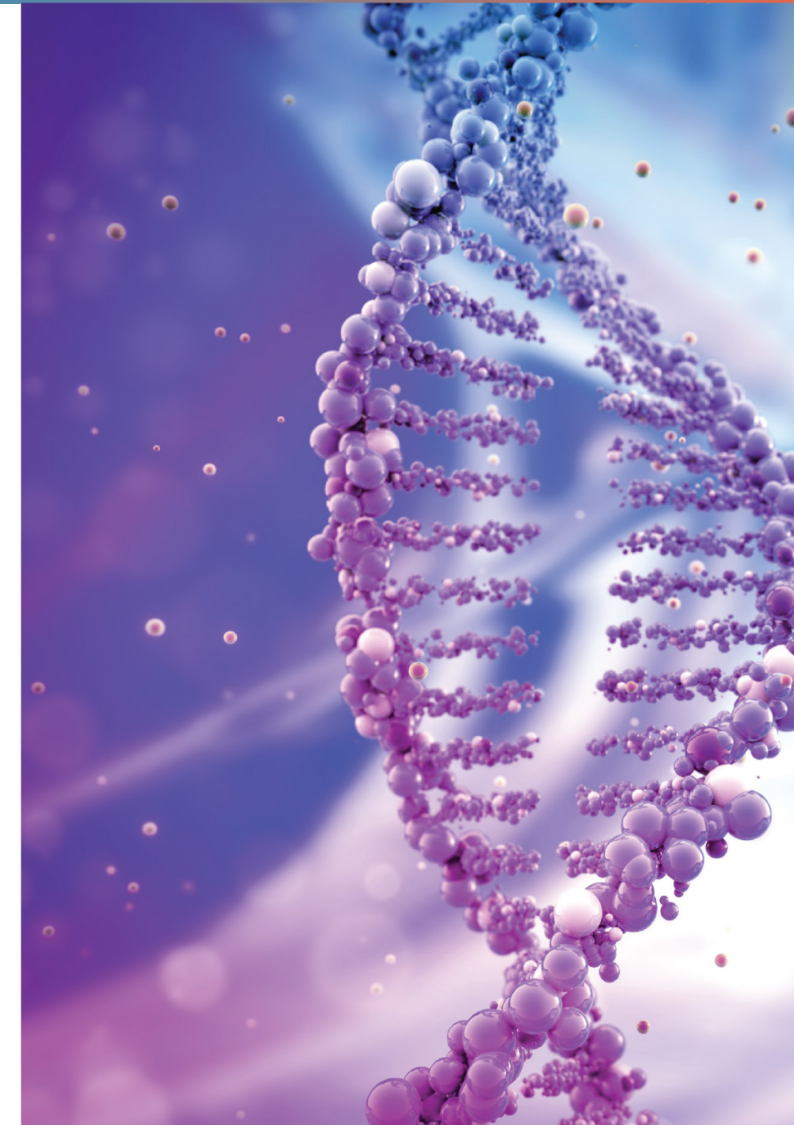
# Characterization of models

## 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

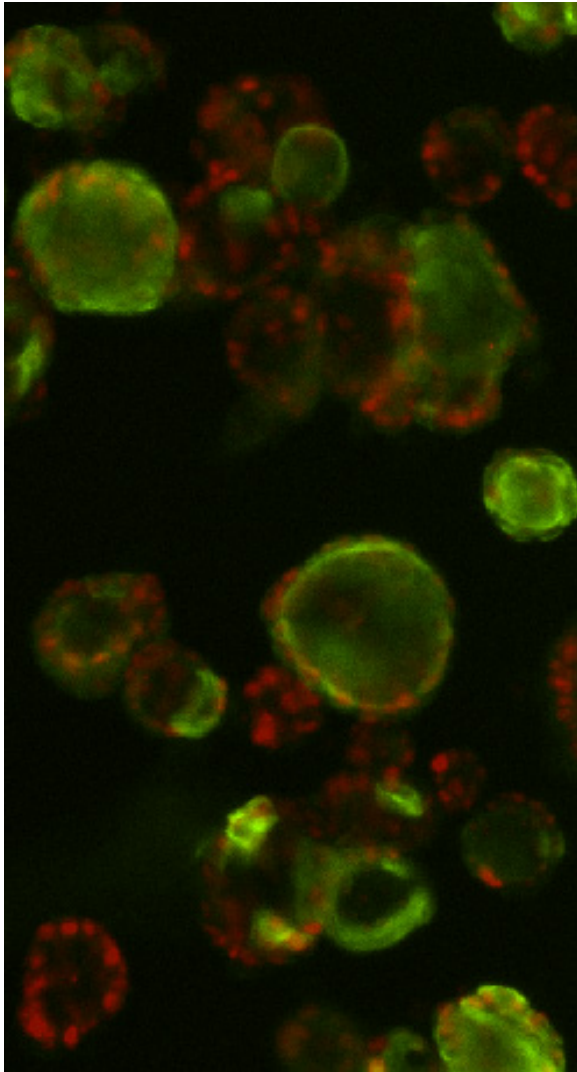
## Clinical

- Disease diagnosis
- Patient demographics
- Treatment and outcomes

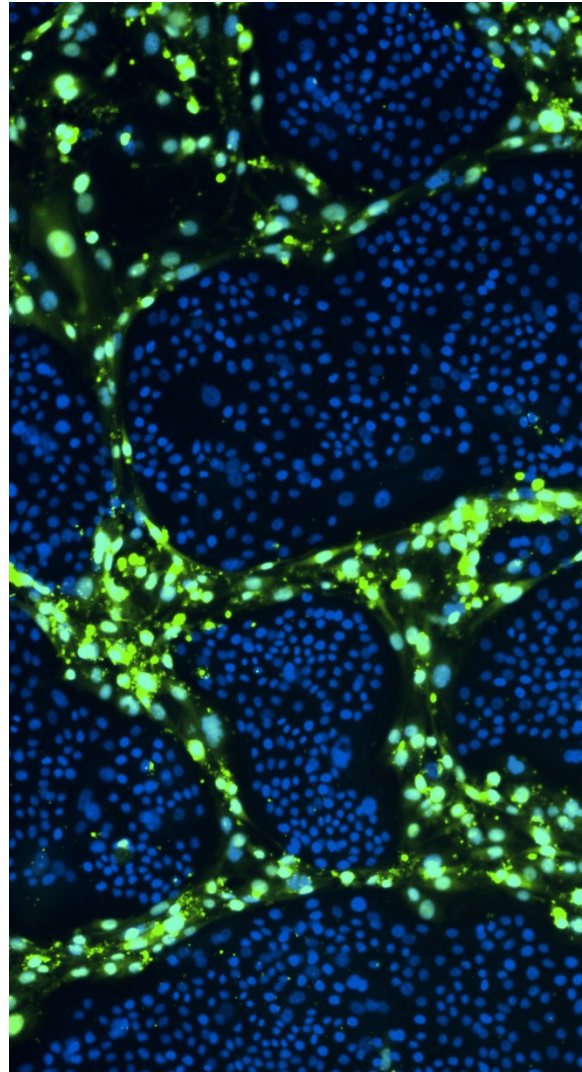




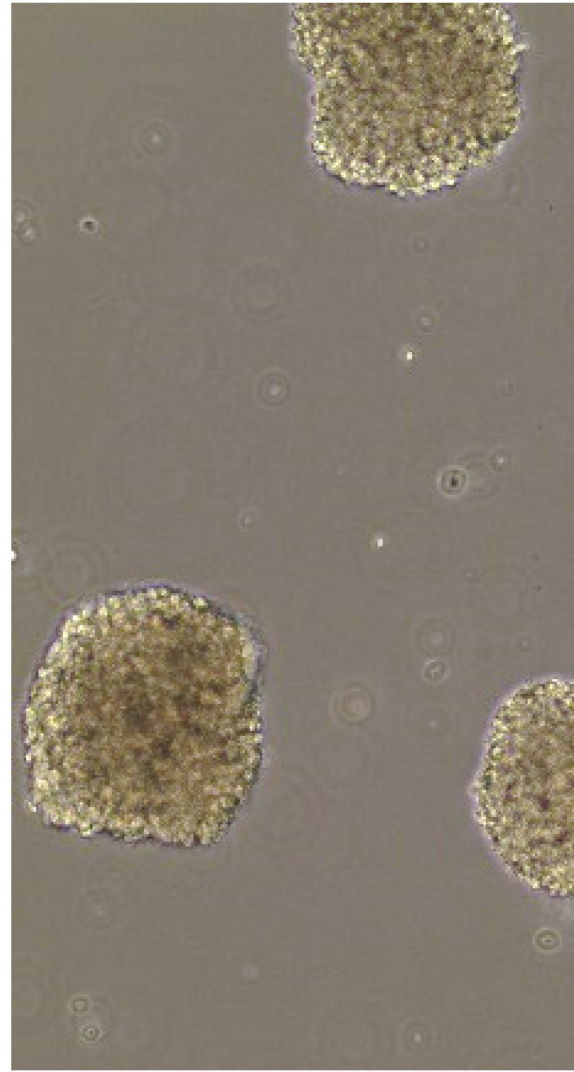
# Types of patient-derived NGCMs



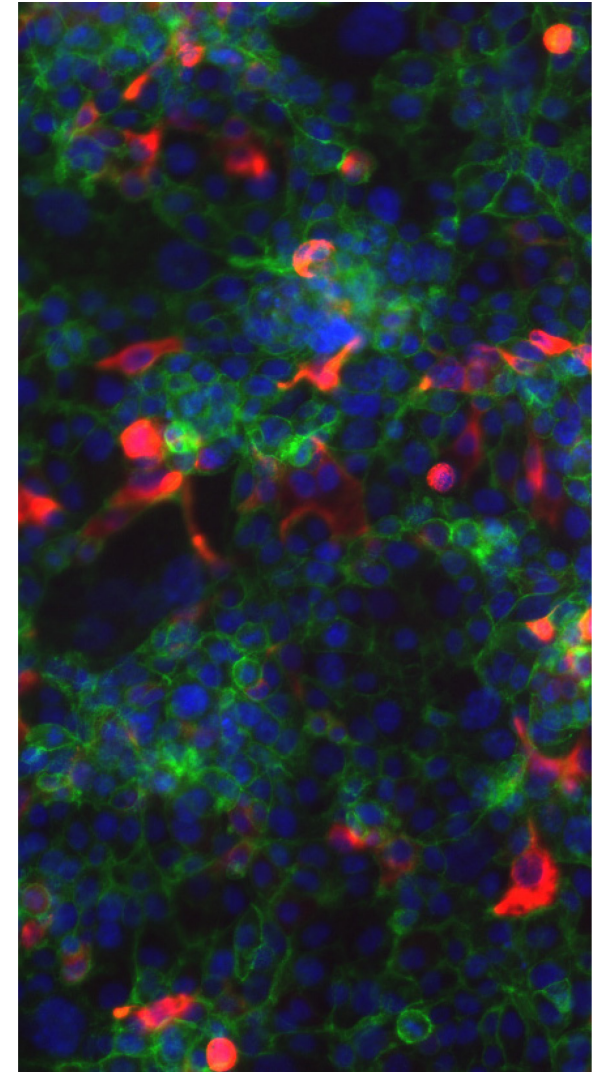
**Organoids**



**Conditionally reprogrammed cells**



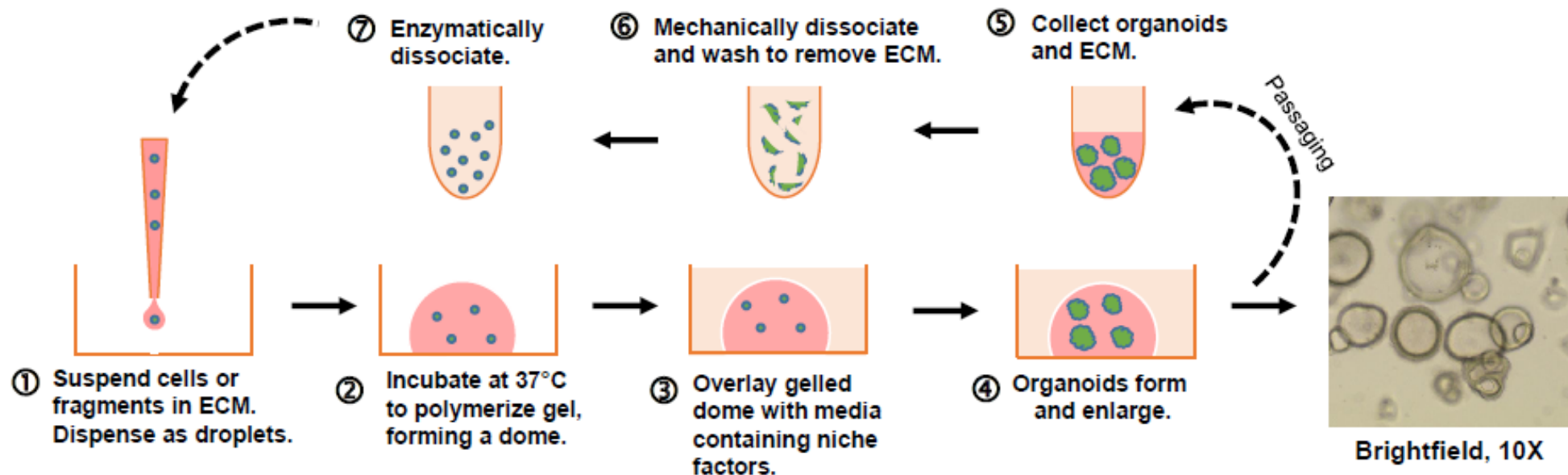
**Neurospheres**



**Other adherent and suspension cells**

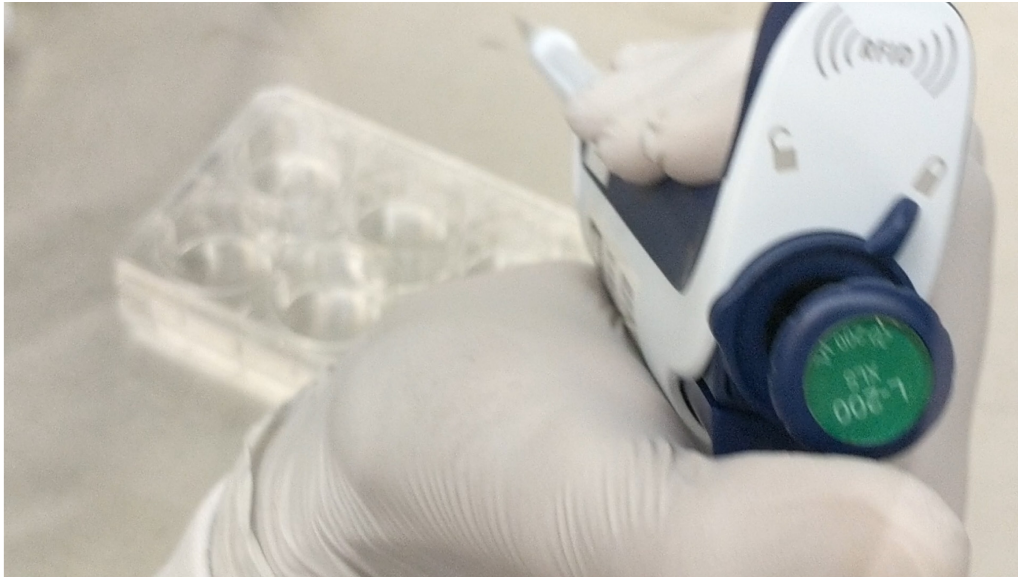
# Primary tissue-derived organoids

- 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

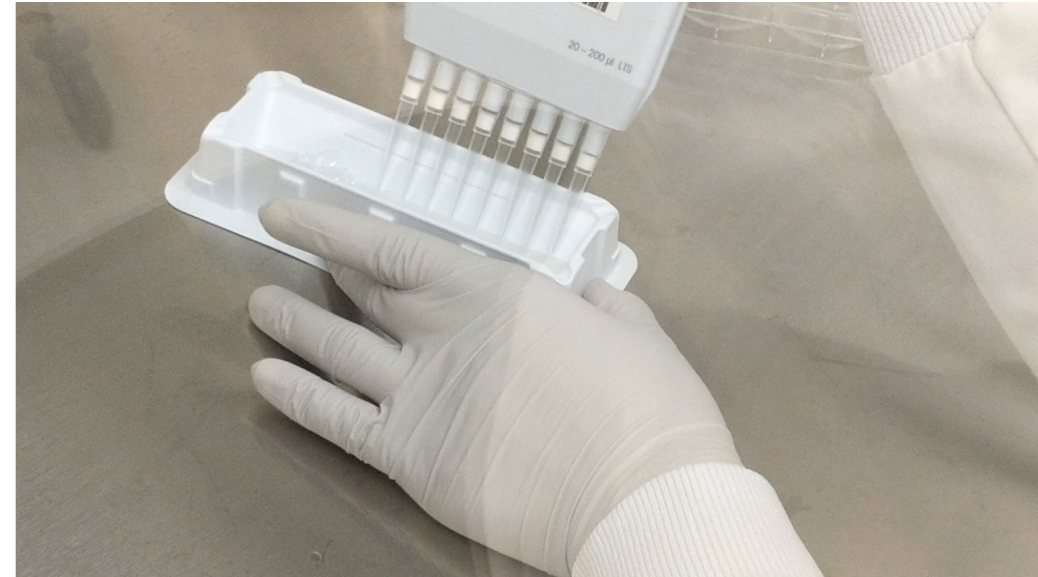


# Seeding organoids in ECM droplets

Seeding a single 6-well with a P200



Seeding a dish with a multichannel pipette



**CURRENT PROTOCOLS**  
A Wiley Brand

in Cell Biology

UNIT |  Free Access |

Initiation, Expansion, and Cryopreservation of Human Primary Tissue-Derived Normal and Diseased Organoids in Embedded Three-Dimensional Culture

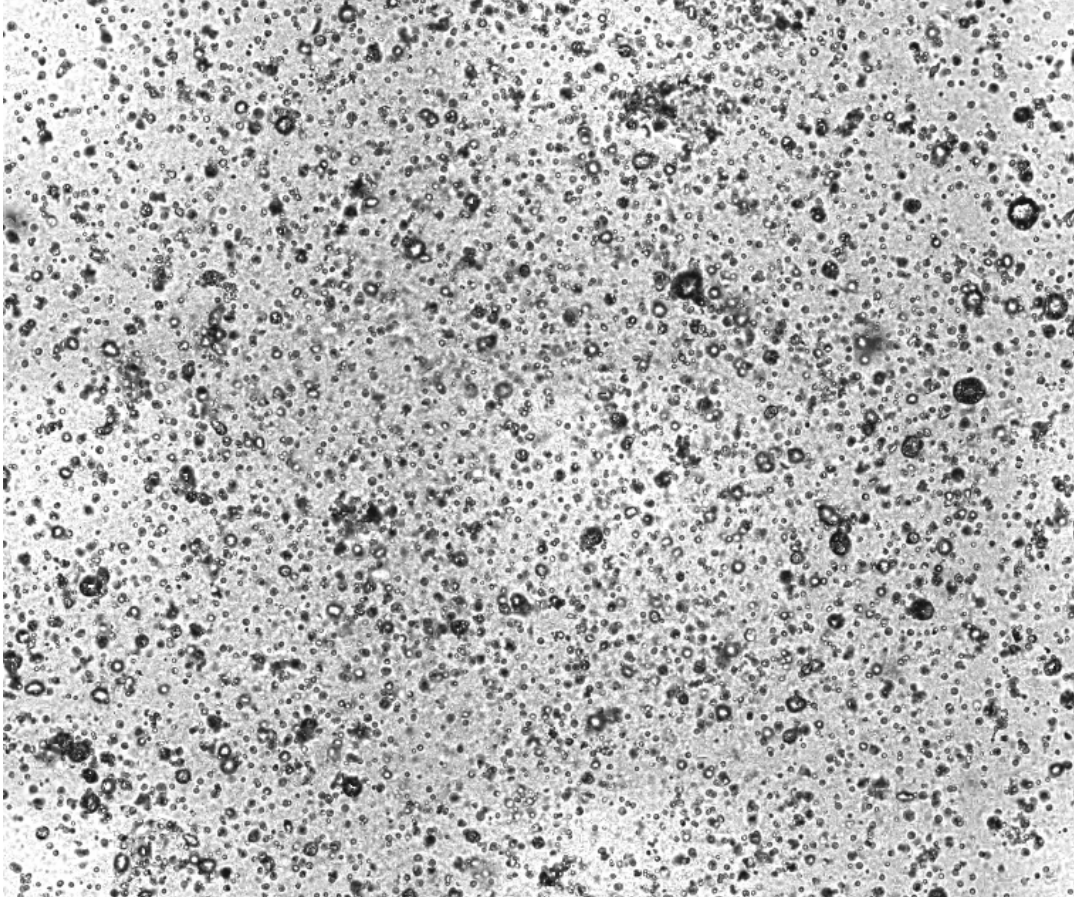
<https://doi.org/10.1002/cpcb.66>

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



<https://www.atcc.org/organoids>

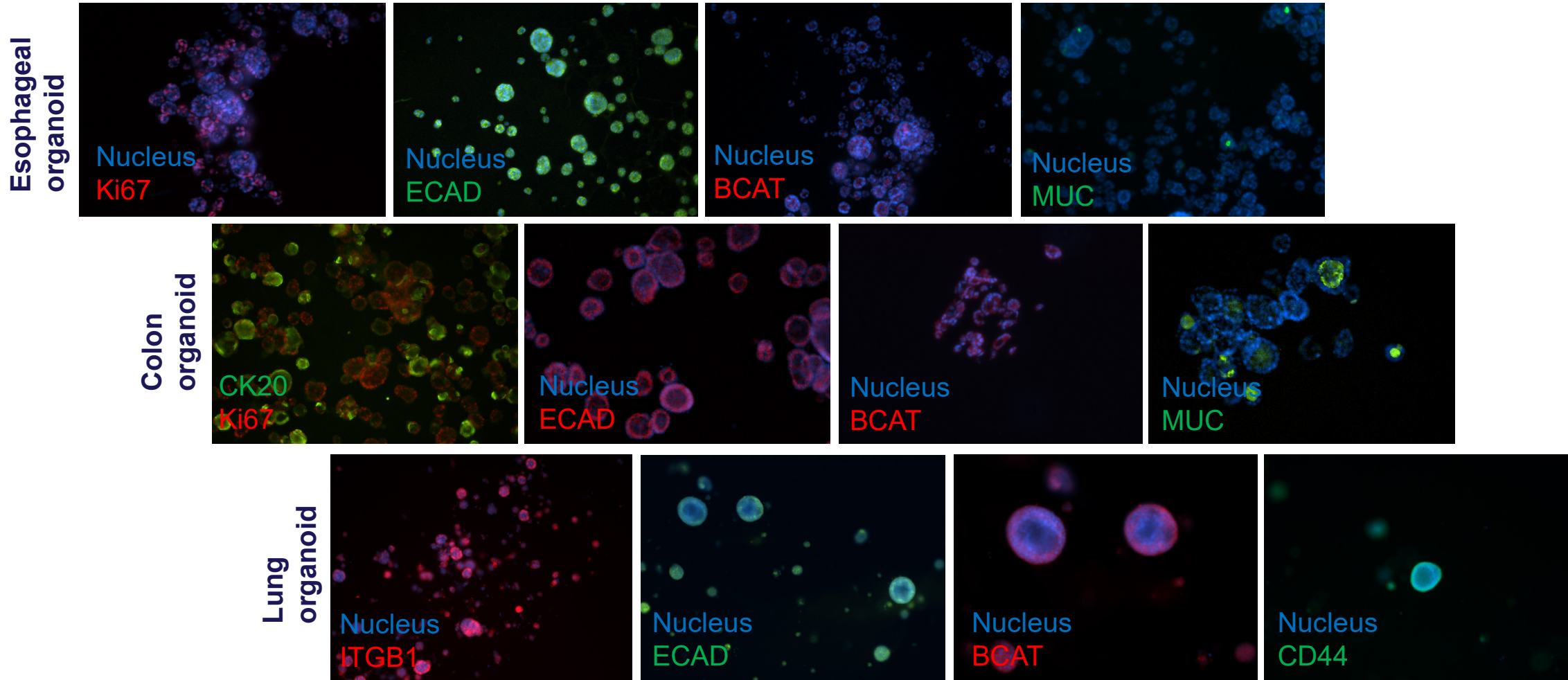
# Organoid growth and expansion



ATCC® PDM-90™  
Pancreatic cancer organoid

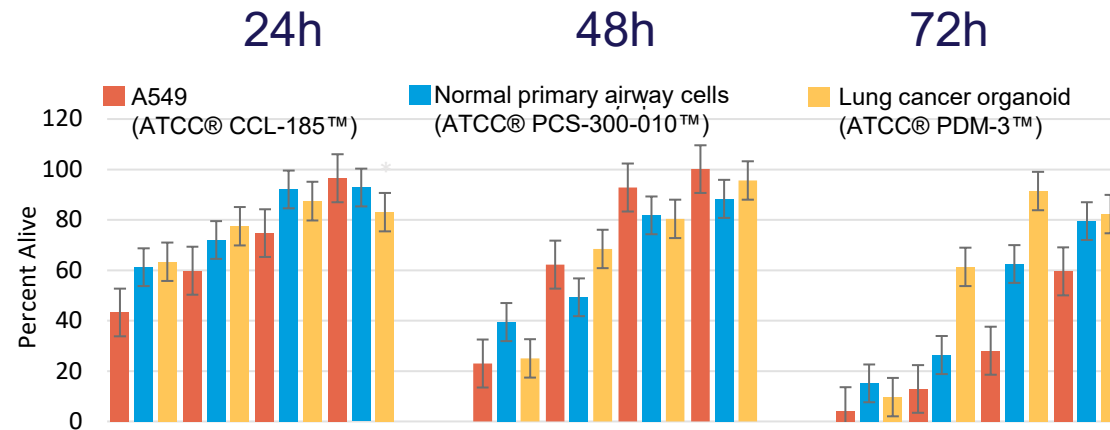
- Six-day time lapse from cryopreserved primary tissue organoids.
- Single ~10uL dome of extracellular matrix.
- Seeded  $\sim 3 \times 10^4$  viable cells/dome.
- Individual organoids increase in size by ~2-5X.
- Exhibits cystic morphology with single lumen.

# Organoids are amenable to standard lab assays

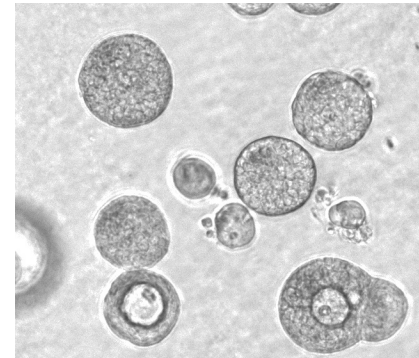


# Organoids are amenable to standard lab assays

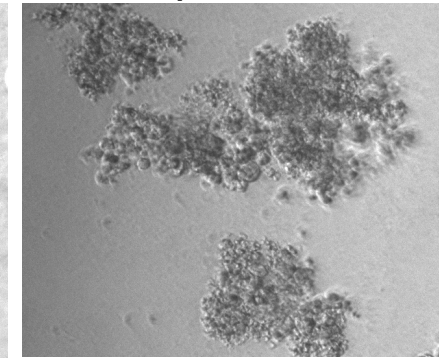
## Topotecan



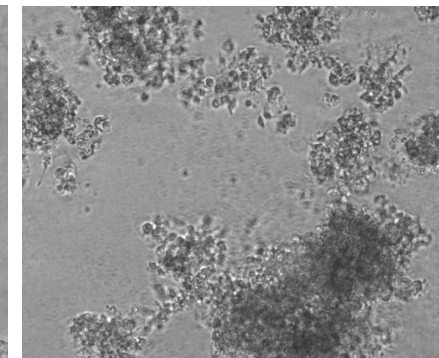
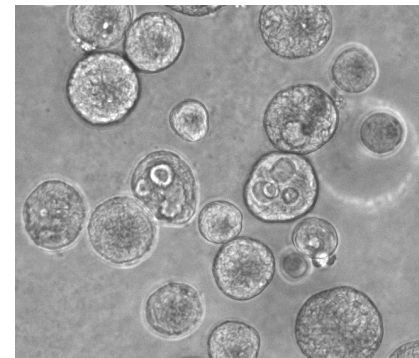
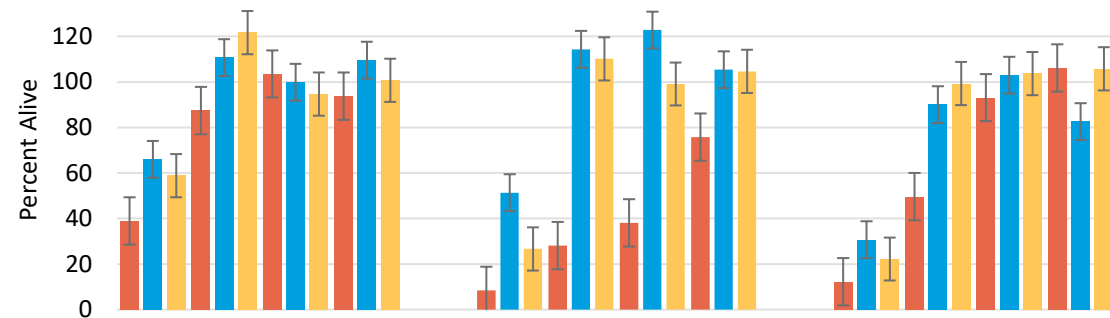
Control at 72h



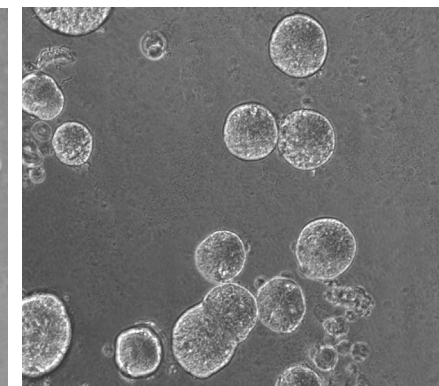
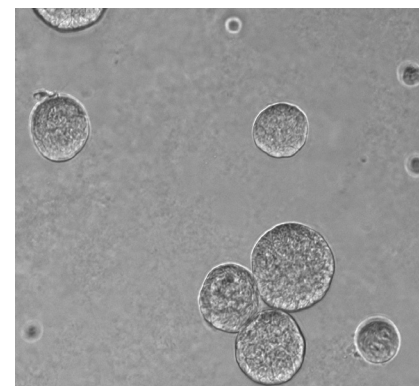
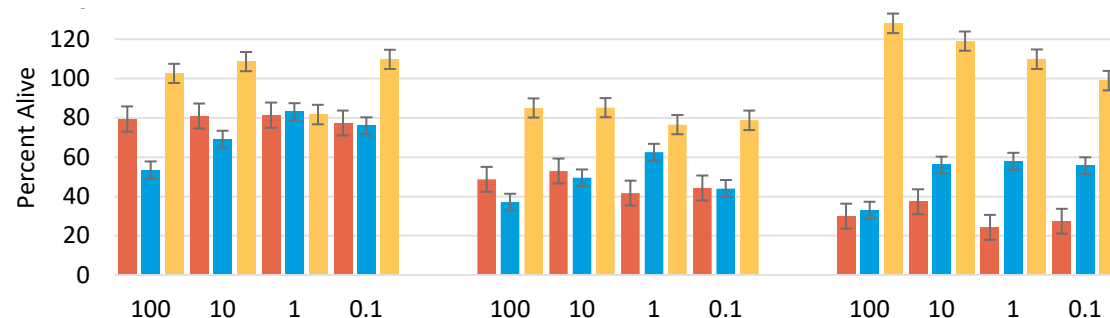
100 μM at 72h



## Cisplatin



## Paclitaxel



10X brightfield images of PDM-3 organoids in suspension

# Organoids are more like tumors than cancer cell lines

EPIGENETICS  
<https://doi.org/10.1080/15592294.2020.1762398>



BRIEF REPORT

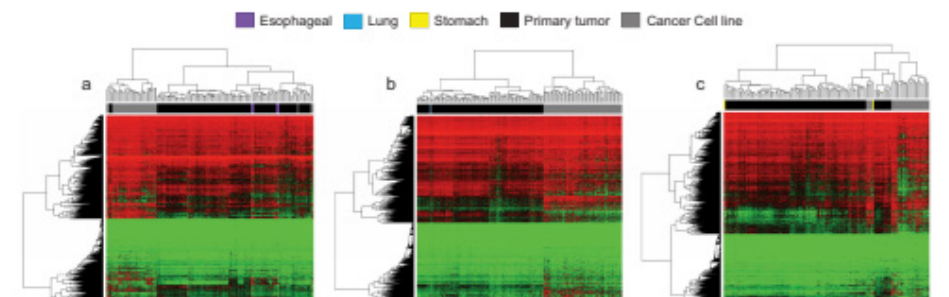
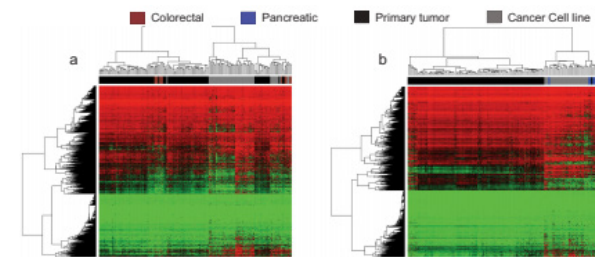
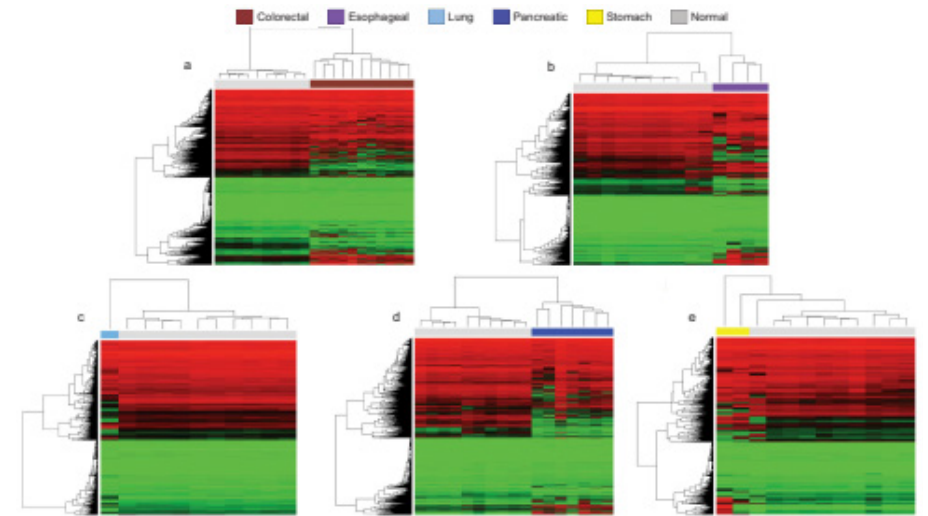
OPEN ACCESS Check for updates

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

Ricky Joshi<sup>a</sup>, Manuel Castro De Moura<sup>b\*</sup>, David Piñeyro<sup>b\*</sup>, Damiana Alvarez-Errico<sup>a</sup>, Carles Arribas<sup>a</sup>, and Manel Esteller<sup>a,b,c,d</sup>

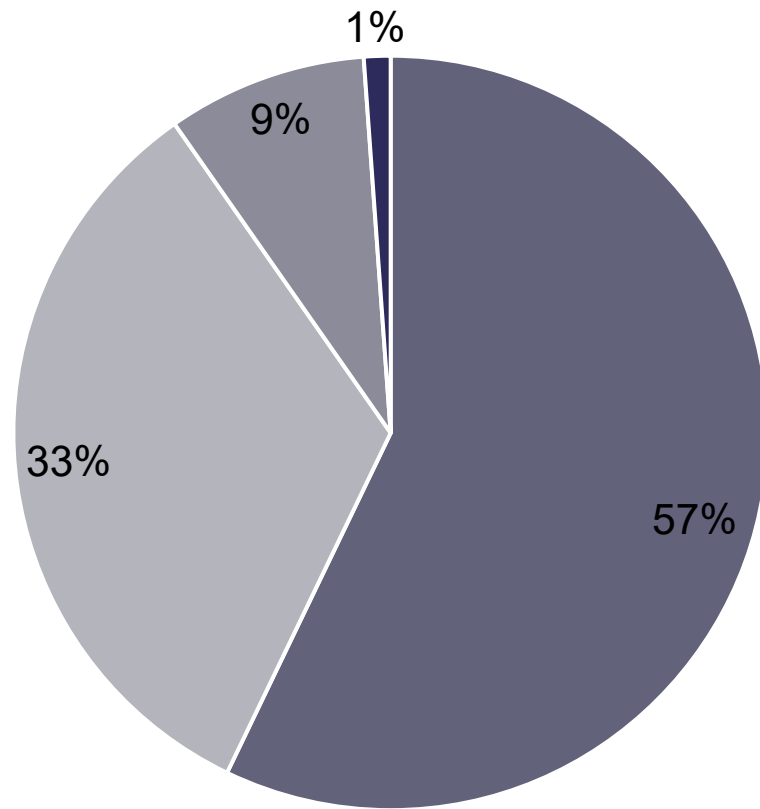
<sup>a</sup>Josep Carreras Leukaemia Research Institute (IJC), Badalona, Barcelona, Spain; <sup>b</sup>Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain; <sup>c</sup>Centro de Investigación Biomedica en Red Cancer (CIBERONC), Madrid, Spain; <sup>d</sup>Physiological Sciences 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.



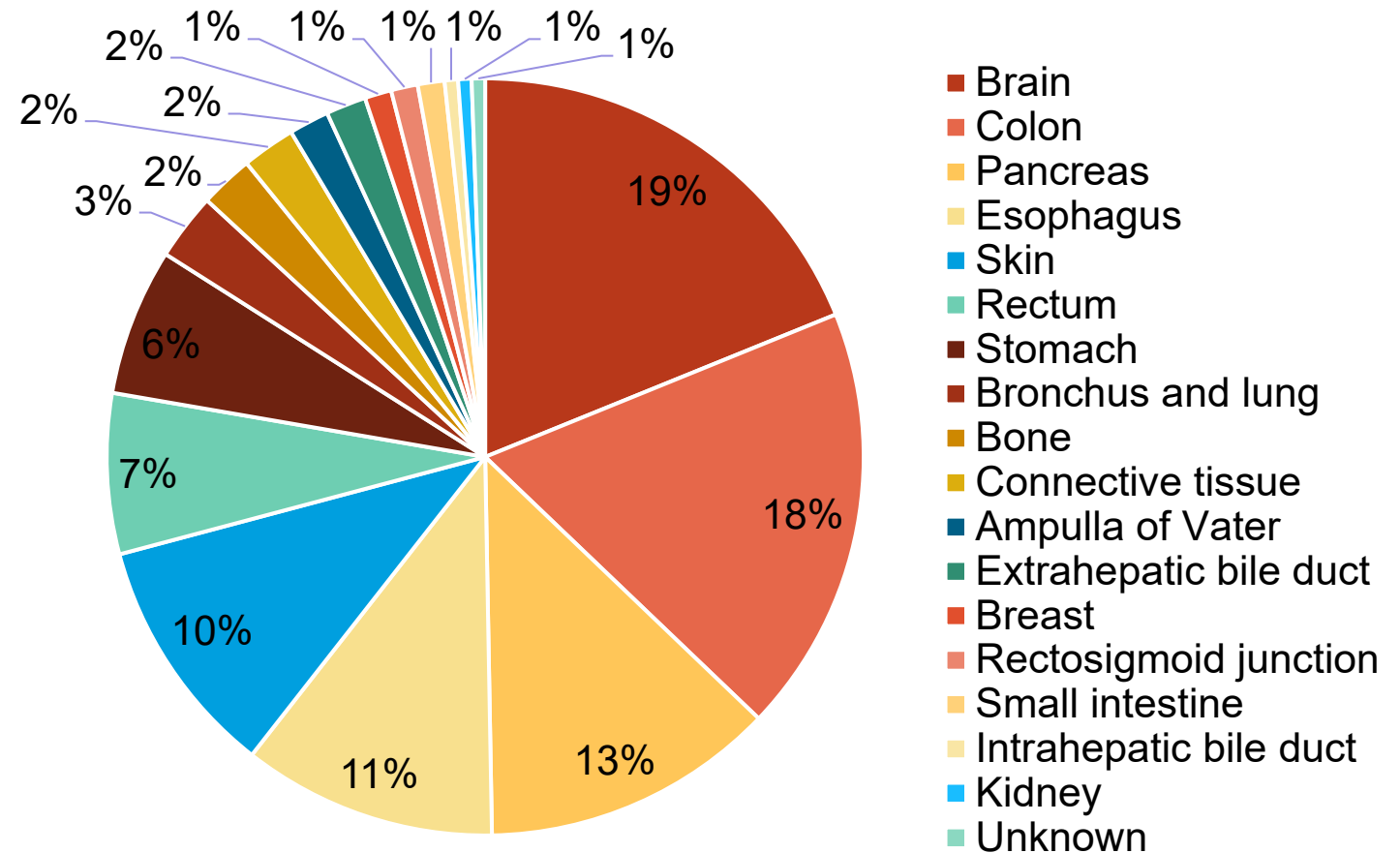
# Currently available models (177)

## Tissue type



■ Primary ■ Metastasis ■ Recurrent ■ Pre-malignant

## Primary tissue site

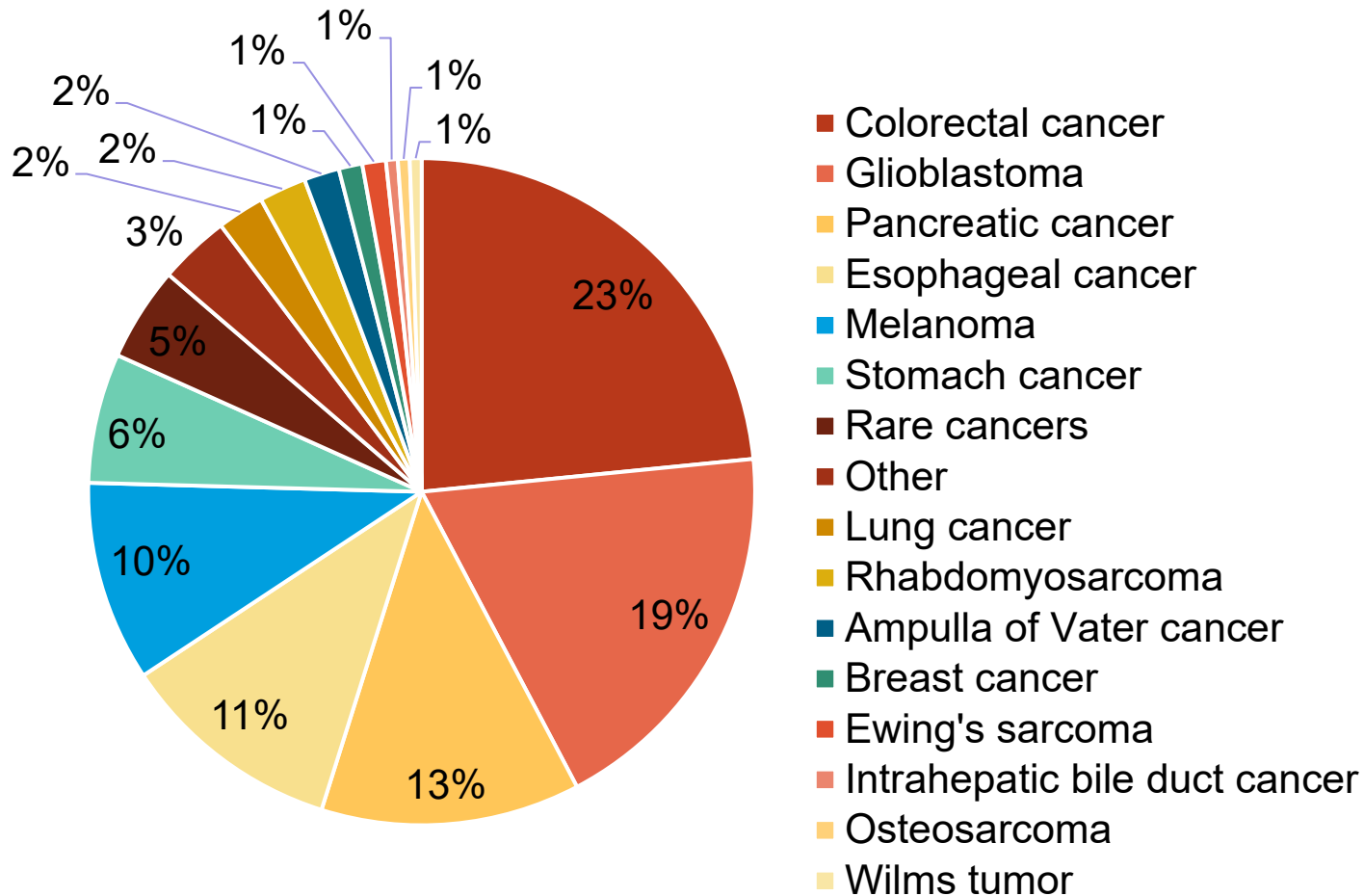


- Brain
- Colon
- Pancreas
- Esophagus
- Skin
- Rectum
- Stomach
- Bronchus and lung
- Bone
- Connective tissue
- Ampulla of Vater
- Extrahepatic bile duct
- Breast
- Rectosigmoid junction
- Small intestine
- Intrahepatic bile duct
- Kidney
- Unknown

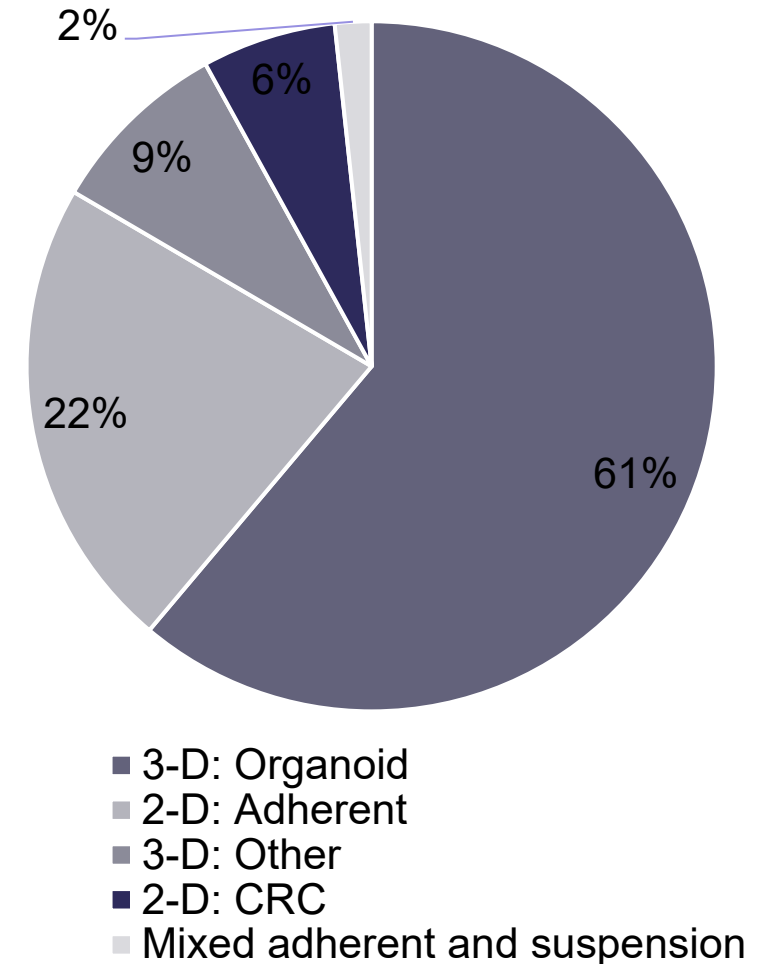


# Currently available models (177)

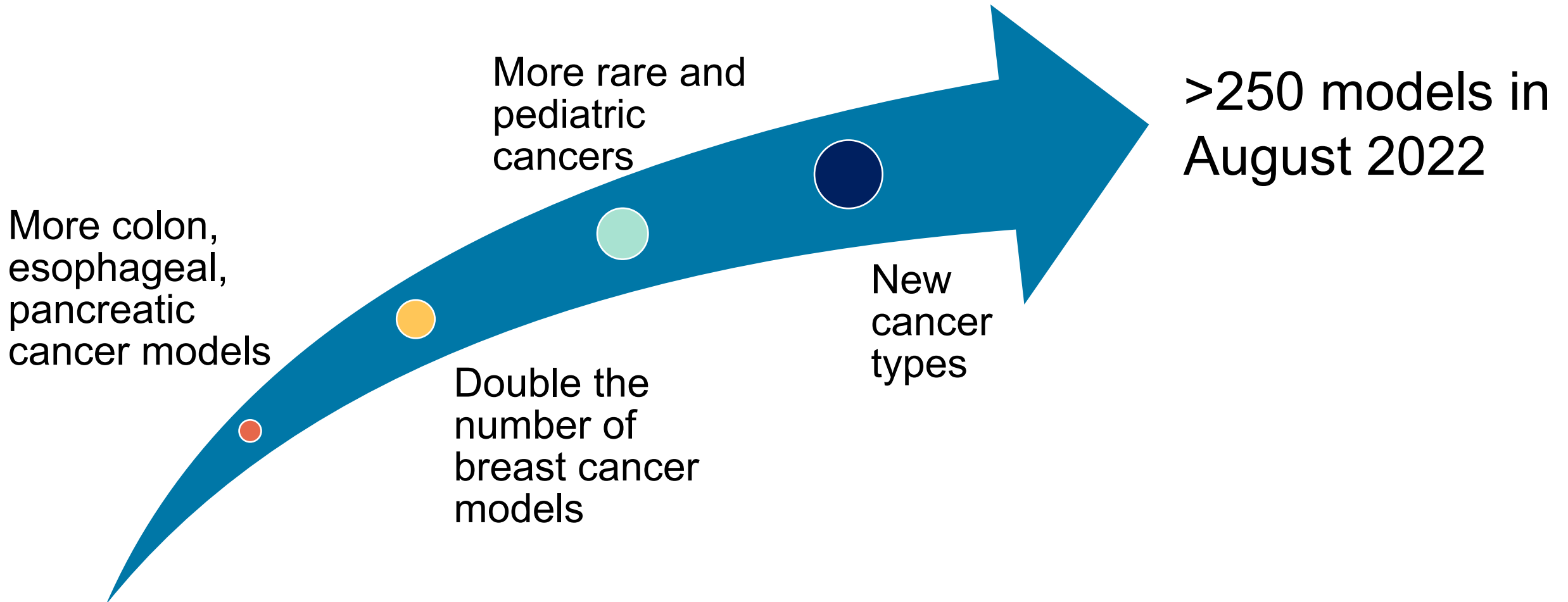
## Clinical tumor diagnosis



## Type of model



# HCMI model pipeline



# ATCC HCMI collection website

The screenshot displays the ATCC HCMI collection website interface. At the top, there is a navigation bar with links for Resources, Support, and United States. Below this is the ATCC logo and a search bar. The main heading is "Human Cancer Models Initiative". A banner image features the text "Revolutionizing cancer research with next-generation 2-D and 3-D patient-derived cancer models". Below the banner, there are 172 products listed. The first three products are:

- HCM-CSHL-0057-C18**: PDM-2, BSL 1, Price: \$3,328.00 ea. Product format: Frozen. Organism: *Homo sapiens*. Tissue: Large intestine; Sigmoid colon. Disease: Adenocarcinoma; Primary.
- HCM-CSHL-0085-C24-01A**: PDM-218, BSL 1, Price: \$3,328.00 ea. Product format: Frozen. Organism: *Homo sapiens*. Tissue: Small intestine; Ampulla of water. Disease: Carcinoma; Primary.
- HCM-CSHL-0366-C50**: PDM-195, BSL 1, Price: \$3,328.00 ea. Product format: Frozen. Organism: *Homo sapiens*. Tissue: Breast. Disease: Carcinoma; Primary.

On the left side, there is a "Refine by" section with filters for Product category, Product type, Product application, and Product format. The "Product category" filter shows "Human cells" with 172 results. The "Product type" filter shows "Cell model" with 172 results and "Organoid" with 93 results. The "Product application" filter shows "3D cell culture" with 171 results, "Cancer research" with 141 results, and "Neuroscience" with 30 results. The "Product format" filter shows "Frozen" with 172 results.

<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

**Human Cancer Models Initiative** Searchable Catalog

Use the filter panel on the left to customize your model search.

Showing 1 - 20 of 172 models

Name	Primary Site	Clinical Tumor Diagnosis	Tissue Status	Age At Acquisition (Years)	Age At Diagnosis (Years)	Has Multiple Models	Expansion Status	# Mutated Genes	# Research Somatic Variants	# Clinical Variants	# Histo-Pathological Biomarkers
HCM-BROD-0001-C18	Rectum	Colorectal cancer	Metastasis	49	47	No	EXPANDED	1	0	1	0
HCM-BROD-0002-C71	Brain	Glioblastoma	Primary	66	66	No	EXPANDED	112	112	0	1
HCM-BROD-0003-C71	Brain	Glioblastoma	Primary	82	82	No	EXPANDED	100	100	0	1
HCM-BROD-0005-C41	Bone	Ewing's sarcoma	Metastasis	8	7	No	EXPANDED	34	31	1	1
HCM-BROD-0007-C49	Bronchus and lung	Rhabdomyosarcoma	Metastasis	13	12	No	EXPANDED	30	29	1	0
HCM-BROD-0008-C15	Pancreas	Pancreatic cancer	Metastasis	64	63	No	EXPANDED	2	0	1	1
HCM-BROD-0009-C15	Pancreas	Pancreatic cancer	Metastasis	49	49	No	EXPANDED	1	0	0	1
HCM-BROD-0010-C15	Pancreas	Pancreatic cancer	Metastasis	53	53	No	EXPANDED	2	0	1	1
HCM-BROD-0011-C21	Brain	Glioblastoma	Primary	54	54	No	EXPANDED	66	59	0	1
HCM-BROD-0012-C21	Brain	Glioblastoma	Recurrent	56	56	No	EXPANDED	70	70	0	1
HCM-BROD-0013-C21	Brain	Glioblastoma	Recurrent	62	59	No	EXPANDED	1	0	0	1
HCM-BROD-0014-C71	Brain	Glioblastoma	Primary	68	68	No	EXPANDED	91	92	0	1
HCM-BROD-0015-C15	Esophagus	Esophageal cancer	Primary	68	67	No	EXPANDED	356	380	0	0
HCM-BROD-0016-C16	Stomach	Stomach cancer	Primary	74	73	No	EXPANDED	1301	1404	0	0
HCM-BROD-0017-C34	Bronchus and lung	Lung cancer	Metastasis	66	65	No	EXPANDED	2907	2854	0	0
HCM-BROD-0018-C71	Brain	Glioblastoma	Recurrent	60	58	No	EXPANDED	105	105	0	1
HCM-BROD-0019-C71	Brain	Glioblastoma	Recurrent	58	58	No	EXPANDED	1	0	0	1
HCM-BROD-0020-C49	Bone	Rare cancers	Metastasis	11	9	No	EXPANDED	0	0	0	0
HCM-BROD-0026-C41	Bone	Ewing's sarcoma	Metastasis	26	13	No	EXPANDED	88	88	1	1

**Human Cancer Models Initiative** Searchable Catalog

Model: HCM-BROD-0002-C71 EXPANDED

Model Details:

- Type: 2D: Conditionally reprogrammed cells
- Split Ratio: N/A
- Time to Split: N/A
- Doubling Time: N/A
- Tissue Status: Primary

Patient Details:

- Tissue Status: Primary
- Gender: Male
- Race: White
- Age At Diagnosis (Years): 66
- Age At Acquisition (years): 66
- Disease Status: Progressive disease
- Vital Status: Dead
- Neoadjuvant Therapy: No
- Therapy:
  - Cytotoxic chemotherapy
  - Targeted therapy (small molecule inhibitors and targeted antibodies)
  - Radiation therapy
- Chemotherapeutic Drug List Available: Yes
- Clinical Tumor Diagnosis: Glioblastoma
- Histological Subtype: Gliosarcoma
- Primary Site: Brain
- Acquisition Site: Brain
- TNM Stage: N/A
- Clinical Stage Grouping: N/A
- Histological Grade: N/A

Repository Status:

- Date Updated: October 05, 2020
- Date of Availability: February 28, 2019
- Licensing Required For Commercial Use: Yes
- Date Created: February 04, 2019

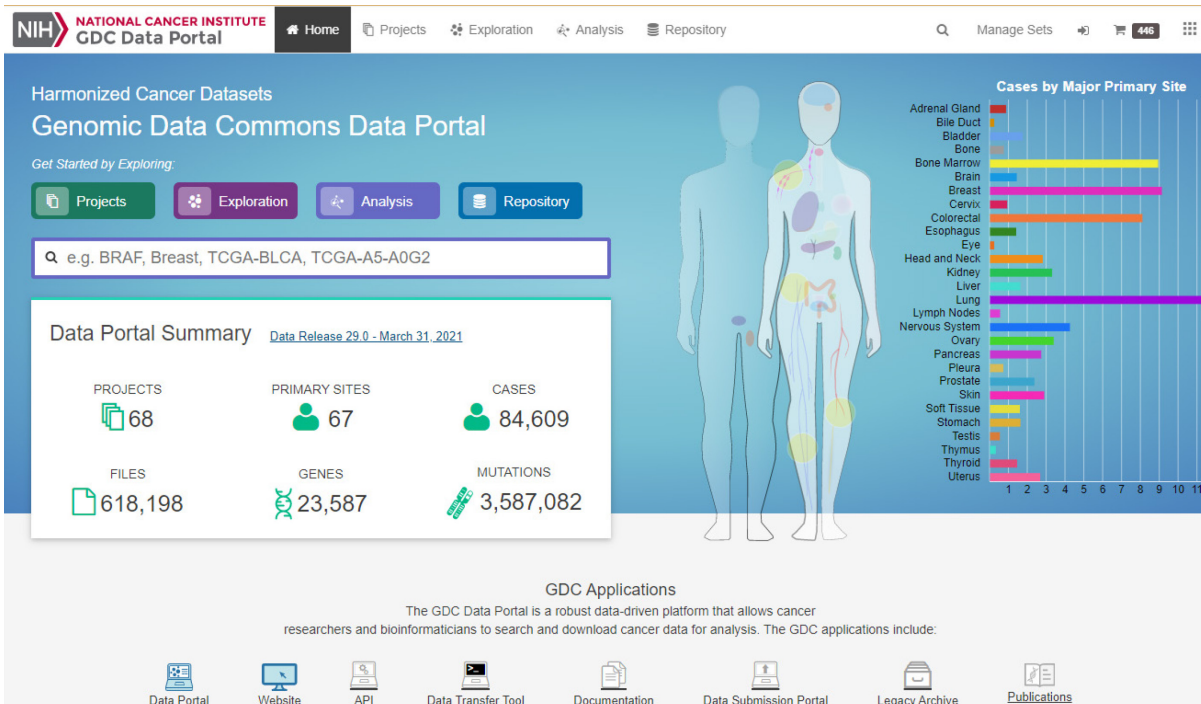
External Resources:

- Sequencing Files
- Model Source
- Masked Somatic Map
- Visit PDM-16 to Purchase

- 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

