Next-Generation Cancer Models from the Human Cancer Models Initiative

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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
- NIH National Cancer Institute
- Cancer Research UK
- Hubrecht Organoid Technology
- Wellcome Sanger Institute

Model Developers
- Broad Institute
- Cold Spring Harbor Laboratory
- Università di Verona
- Hubrecht Institute
- Stanford University
- Weill Cornell Medicine Medical College

Distribution
- ATCC
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

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

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

https://www.atcc.org/organoids
Six-day time lapse from cryopreserved primary tissue organoids.

Single ~10uL dome of extracellular matrix.

Seeded ~3x10^4 viable cells/dome.

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

Exhibits cystic morphology with single lumen.
Organoids are amenable to standard lab assays

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

- **Topotecan**
- **Cisplatin**
- **Paclitaxel**

Assayed in triplicate; results normalized to DMSO control
Organoids are more like tumors than cancer cell lines

- 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)

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%
HCMI model pipeline

More colon, esophageal, pancreatic cancer models

More rare and pediatric cancers

Double the number of breast cancer models

New cancer types

>250 models in August 2022
ATCC HCMI collection website

- 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.

https://www.atcc.org/hcmi
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

- 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

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