Organoid Culture Fundamentals: Critical Steps for Success

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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
- cGMP biorepository

- 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
Agenda

- HCMI Background
- Model Descriptions
- HCMI Support / GDC and HCMI Catalog
- ATCC Cell Culture Support
- Organoid Culture Educational Video
Why are new models needed?

- Poor representation of some cancer types/subtypes
- 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
- Existing lines may not be biologically/genetically representative of in vivo tumor

There is a need for better preclinical models to predict therapeutic outcomes
Overview of HCMI and ATCC

Founders
- National Cancer Institute
- Cancer Research UK
- Hubrect Organoid Technology Foundation
- Wellcome Sanger Institute

Model Development
- Broad Institute
- Cold Spring Harbor Laboratory
- Wellcome Sanger Institute
- Hubert Organoid Technology Foundation
- University of Verona
- Hubrecht Institute
- Stanford University
- Weill Cornell Medical College

Distribution
Cancer model development centers

Primary biopsy sample

Anonymized patient/clinical data captured

Sequencing

In vitro model

Subset will be sequenced

Expand, cryopreserve and perform quality control testing

Global distribution to cancer research and biomedical community
Characterization of models

**Molecular**
- 15X Whole Genomic Sequencing (WGS) of model, primary tumor, and normal tissue
- 150X Whole Exosome Sequencing (WXS) of model, primary tumor, and normal tissue
- RNA-seq of model and primary tumor

**Clinical**
- Disease diagnosis
- Patient demographics
- Treatment and outcomes
Advanced culture technologies

Organoids

Conditionally Reprogrammed Cells, Neurospheres, other 2D Models
What is an HCMI Organoid?

Organoids are complex, self organizing microtissues embedded within a 3D extracellular matrix

- Patient derived
- Multiple cell types
- Cellular polarization
- In vivo like architectural features (lumen)
- Long term expansion
- Phenotypically and genetically stable
Organoid technology

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

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.
5. Collect organoids and ECM.
6. Mechanically dissociate and wash to remove ECM.
7. Enzymatically dissociate.

Model resources and data access

- NCI managed website
- Integrates clinical, model, and genomic information
- Search for models of interest using various filters
  - Primary tumor site/acquisition site
  - Model type
  - Tumor diagnosis/stage/grade/histological type
  - Gender/age/ethnicity
- Links out to clinical and genomic data, ATCC model product page

hcmi-searchable-catalog.nci.nih.gov
Model resources and data access

- NCI managed website
- Search and download cancer related datasets for analysis
- Navigate to the “HCMI-CMDC” project for HCMI specific datasets
- Download WGS/WXS/RNAseq data
  - Aligned reads, gene expression, SNVs

portal.gdc.cancer.gov
Model resources and data access

- View all models available or grouped by tissue
- Model specific information such as:
  - Culture images
  - Seeding densities
  - Media change frequencies
- Individual model product pages include detailed culture protocols
  - Complete media formulation
  - Thawing/subculturing/freezing guides
- Model pages link to other resource pages that host clinical and sequencing data
- Frequently asked questions

www.atcc.org/HCMI
Detailed Support for Organoid Culture

Protocols
- Subculturing
- Thawing
- Freezing

Formulations
- Complete list of components
- Medium – Reagents

CoreKits
- Reagents specific to models
- Recombinant proteins / chemicals

Healthy organoid growth

Coming Soon!
Where we are now

Over the past two years, ATCC has worked with NCI and the model developers to launch 150 next generation models including **80 organoid models**

**Types**
- Adenocarcinoma
- Carcinoma

**Stages**
- Primary
- Recurrent
- Metastatic
- Pre-malignant

**Tissues**
- Lung
- Colon
- Rectum
- Mammary
- Esophagus
- Pancreas
- Liver
- Stomach
Summary

- Information on models is available:
  - HCMI searchable catalog
  - GDC Data Portal
  - ATCC offers organoid culture protocols, formulations, and materials needed
  - Coming soon: Core growth kits to with pre-aliquoted supplements to make organoid culture easy

- ATCC currently offers 150 models with approximately 40 more models being launched in upcoming months

- For more information, download the Organoid Culture guide or re-watch the organoid cell culture video available on the ATCC website

www.atcc.org/organoids
Upcoming events

- **Webinars:**
  - The Importance of Using Next-Generation Sequencing to Further Authenticate the ATCC Microbial Collections
  - Presented by: Briana Benton
  - April 8
  - ATCC offers organoid culture protocols, formulations, and materials needed
  - Coming soon: Core growth kits to with pre- aliquoted supplements to make organoid culture easy

- **Tradeshow:** AACR2021

www.atcc.org/organoids
AACR Annual Meeting 2021
American Association for Cancer Research
4/10/2021 – 4/15/2021

Primary NK Cells and Luciferase Expressing Reporter Cell Lines for Use in Developing ADCC Assays for Immuno-oncology Drug Screening
Presenter: Haiyun Liu, PhD, Scientist, ATCC
Poster Number: 1306

Checkpoint Molecule Profiling in Tumor Cell Lines and Immune Cell Lines for Applications in Immuno-oncology Drug Screening
Presenter: Brian Della Fera, Biologist, ATCC
Poster Number: 1648

www.atcc.org/AACR2021