Model Matters: Human Cell Strategies for ADME, DMPK, and Safety Workflows

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ATCC

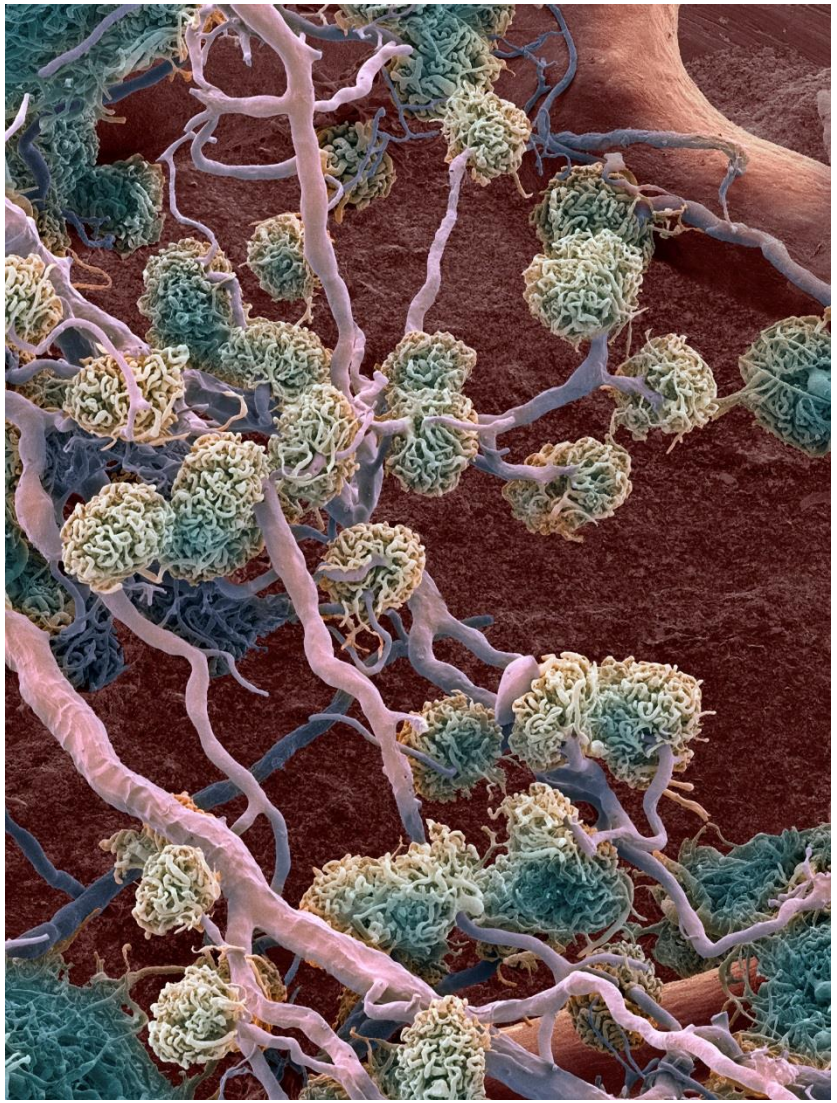
About Us

ATCC is a global leader in providing authenticated, high-quality biological resources and standards for industry, academia, and government.

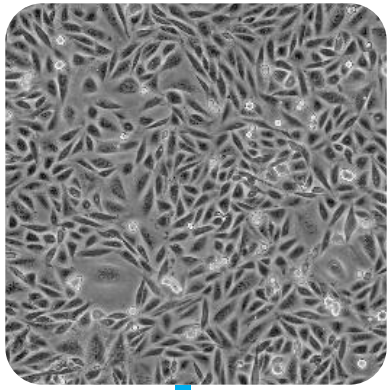
- Founded in 1925, ATCC is a private, nonprofit, global biological resource center and standards organization that provides scientists with the biomaterials and resources they need to conduct critical life science research.
- World's trusted, premier biological materials resource and standards development organization:
  - 4,000+ cell lines
  - 80,000+ microorganisms
  - Genomic and synthetic nucleic acids
  - Media, sera, and reagents
  - Advanced cell models
  - Standards

Agenda

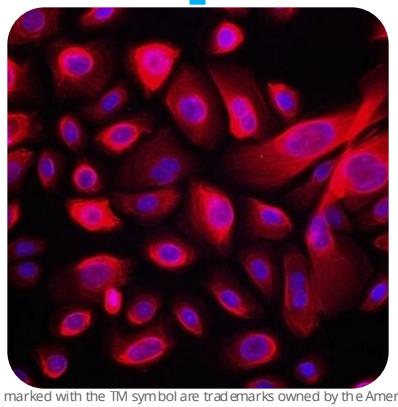
- ATCC mission and future directions
- Cell line tools to further toxicology research:
  - Hepatocytes
  - Immortalized cell lines (hTERTs)
    - Renal models
  - Peripheral blood mononuclear cells (PBMCs)
- Summary
- Questions



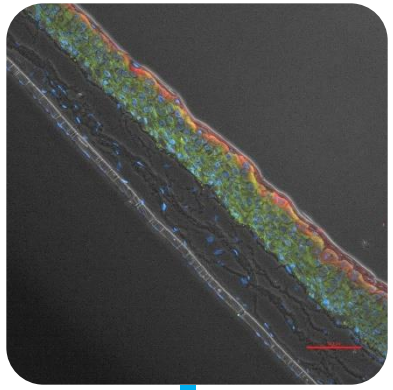
Evolution of In Vitro Cell Models



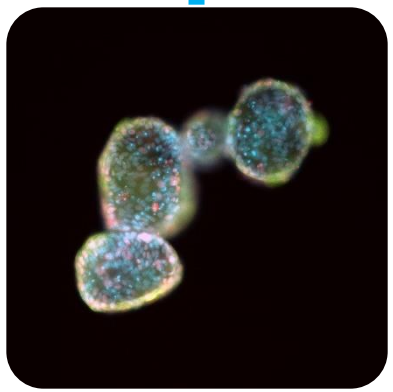
First generation
Continuous cell lines



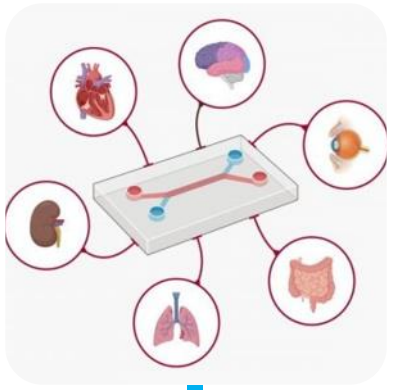
Second generation
Transfected cell lines
Reporter cell lines
Primary cells



Third generation
Immortalized primary cells
Gene-edited cell lines



Fourth generation
3-D models
Organoids

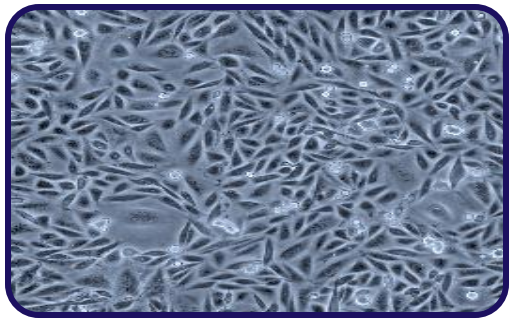


Fifth generation
Microphysiological systems
Organ-on-a-chip

Characteristics of Various Cell Models

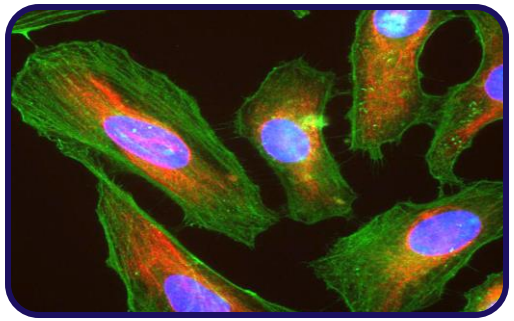
	Continuous (cancer) cell lines	Primary cells	hTERT-immortalized primary cells
Mimic in vivo characteristics	+	++++	+++
Proliferative capacity	+++	+	+++
Experimental reproducibility	+++	+	+++
Predictability in toxicological studies	+	+++	+++
Genomic stability	Aneuploid	Diploid	Diploid/near diploid
Supply	+++	+	+++
Ease of use	+++	+	++

ATCC Toxicology Portfolio



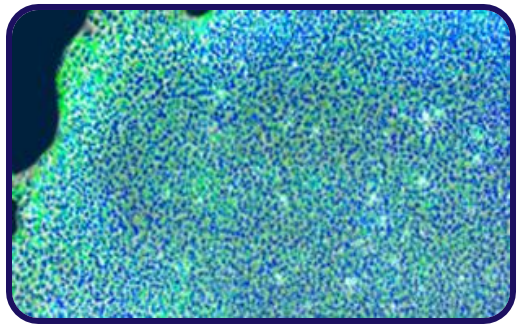
Primary Cells

- ✓Derived from multiple human tissues
- ✓High quality at low passages (Primary Cell Solutions™)
  - PBMCs
  - Hepatocytes (HepatoXcell™)
  - Dermal
  - Immune
  - Lung
  - Cardiovascular



Immortalized Primary Cells

- ✓>75 primary cell derived lines
- ✓Maintain primary cell function
  - Eye (hTERT-RPE)
  - Renal (RPTEC/TERT1)
  - Cardio-vascular (HUVER/TERT)



Stem Cells

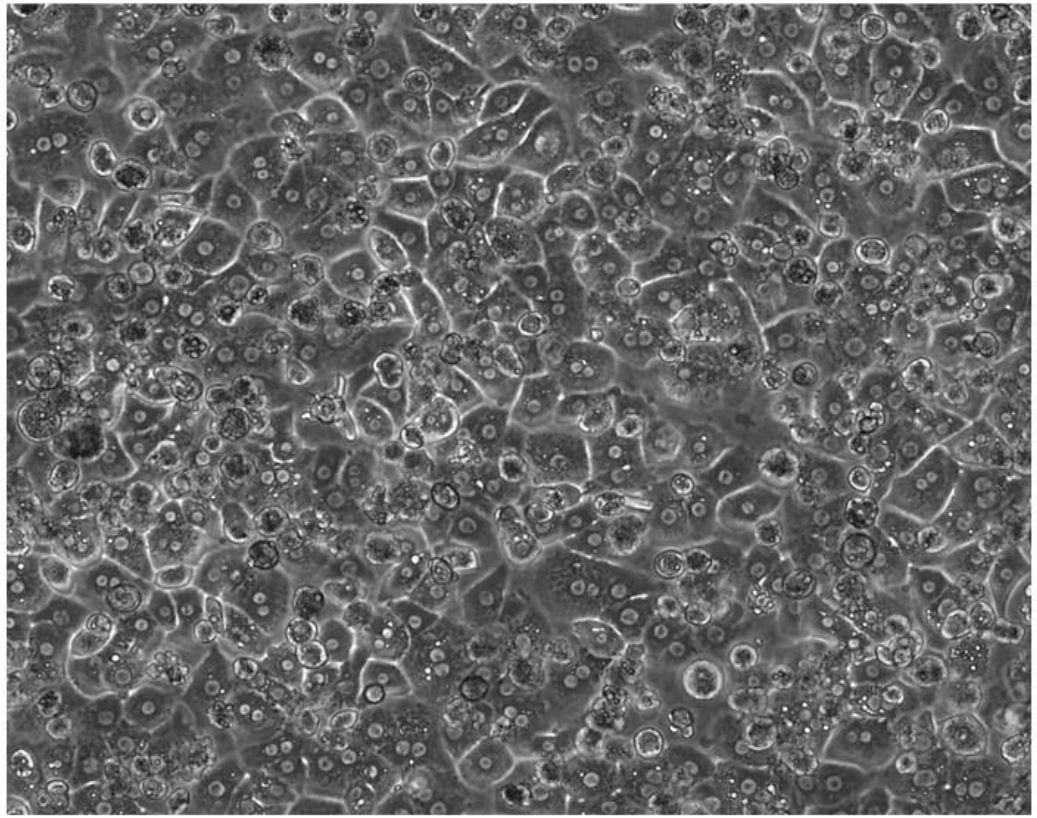
- ✓iPSC Lines
- ✓iPSC-derived NPCs
- ✓iPSC-derived immune cells

Specialty Cell Culture Media

- ✓Companion growth media & supplements for
  - Primary Cells
  - Immortalized Cells
  - Stem Cells

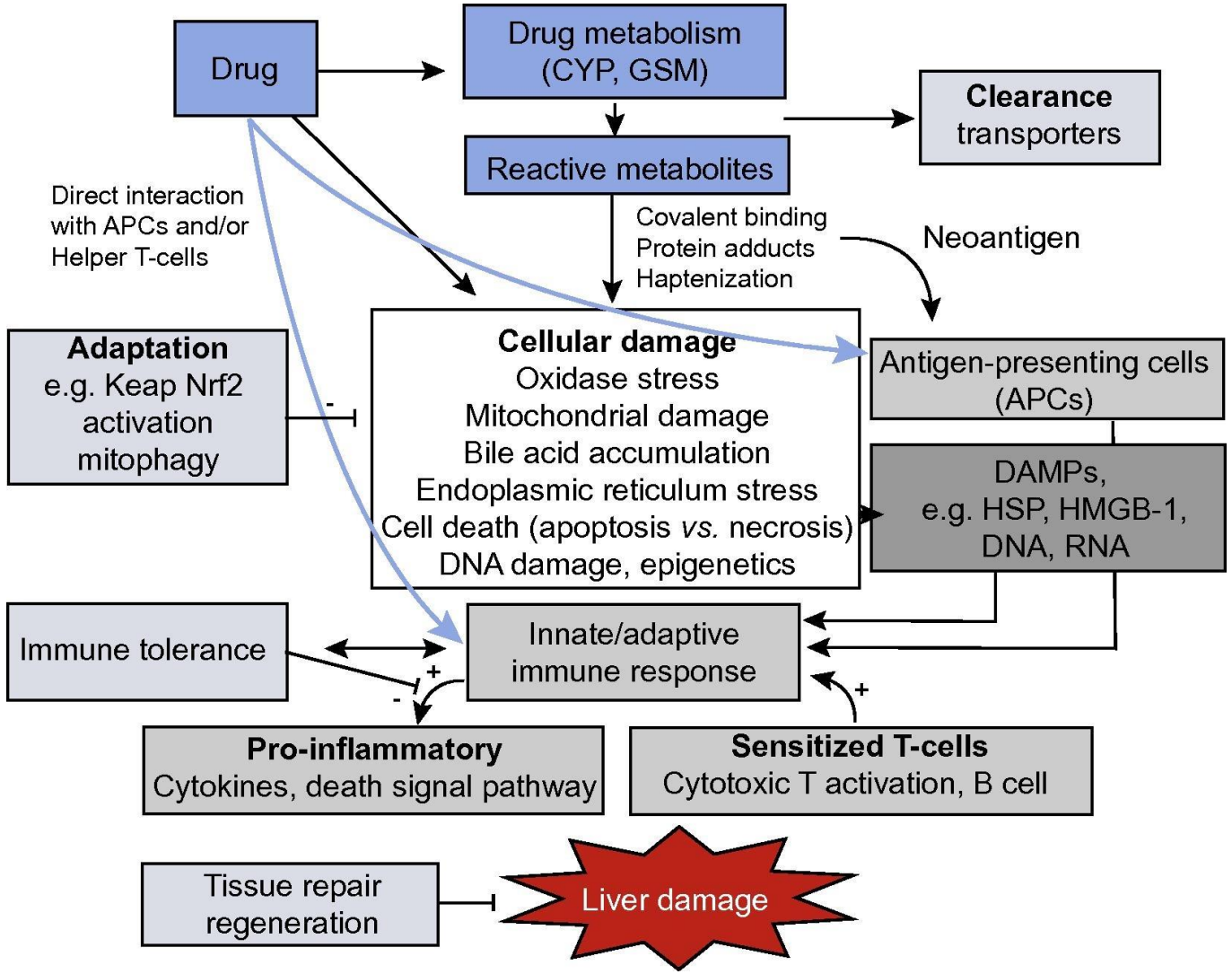
Hepatocytes – A Gold Standard

- Derived from human donor liver tissue
- Retain key drug-metabolizing enzymes
- More physiologically relevant than other models for toxicity
- Support a wide range from ADME studies



HepatoXcell™ Plus: Primary Human Hepatocytes (ATCC® PCS-450-010™), 2 days after plating, 20x magnification.

Why Use Primary Human Hepatocytes?



Chen M, et al. J Hepatol 63(2): 503-514. PubMed: 25912521

Primary Human Hepatocytes

Challenges and solutions

Challenge	ATCC Hepatocyte Solutions
Limited access to donor information	Access to donor information (age, gender, race, BMI) prior to purchasing
Lack of pre-qualification	All lots are pre-qualified
Limited model types	Wide range of model types to choose from
Limited availability	View available lots easily on our website
Loss of metabolic expression	Enzyme induction, profiling, and uptake transporter data available
Low viability	Minimum 70% viability, but often much higher
Limited genomic data availability	Omics data available

Hepatocyte Qualification by Application

ADME Assays

- Transporter → (7-day hepatocytes)
- Induction → (7-day hepatocytes)
- Metabolism → (3 - day, suspension hepatocytes)
- Clearance → (3 - day, suspension hepatocytes)
- Uptake → (3 - day, suspension hepatocytes)

In Vitro Toxicity Assays

- Short Term (3-day plateable)
- Long Term (7-day plateable, 3-D spheroid-qualified)

Advanced Cellular Modelling (Disease, Tox, MPS)

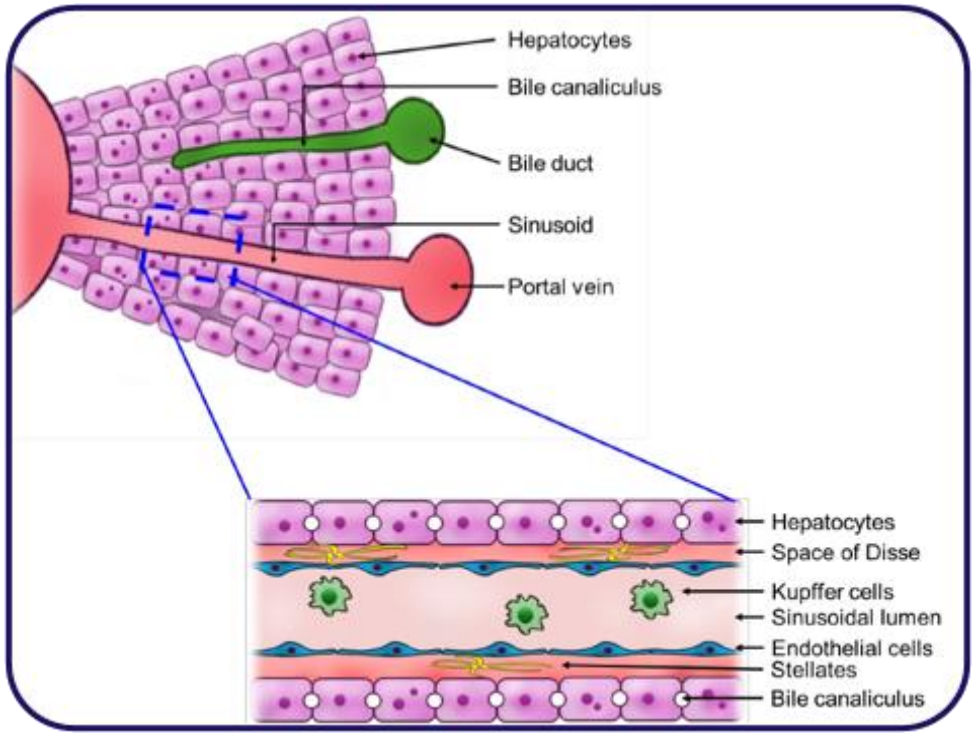
(7-day plateable, 3-D spheroid-qualified)

HepatoXcell™

Enzyme and transporter characterization

Enzyme Induction	Enzyme Profiling (Metabolic Activity)	Uptake Transporter Activity
CYP1A2, CYP2B6, CYP3A4	CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4, UGT, SULT	BSEP, NTCP, OATP1B1/1B3, OCT2

Liver Microphysiological Systems (MPS)



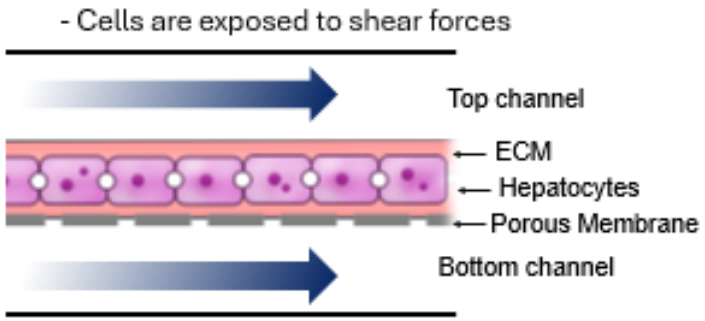
- **Human liver**: primary role is to metabolize drugs
- **Conventional human hepatocyte cultures**: often rapidly lose metabolic activity over time
- **Microphysiological systems:** integrate microfluidics to simulate the liver's dynamic microenvironment, enabling improved modeling of the human liver function over extended culture periods = **improved models of human liver toxicology**

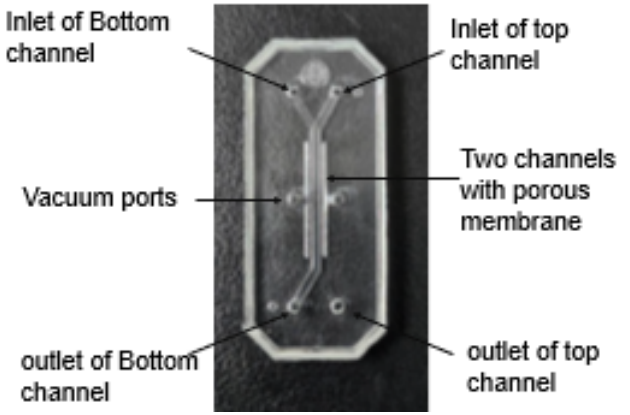
Regulatory agencies are requiring a shift from animal to human-based models
Ex: U.S. FDA's 'Roadmap for Reducing Animal Testing – New Approach Methodologies'

MPS Platforms

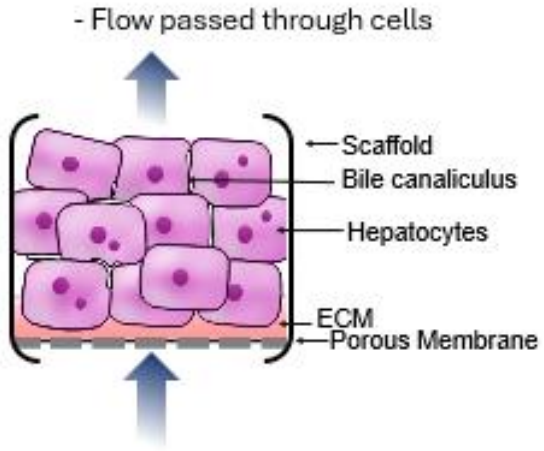
Emulate and CN Bio

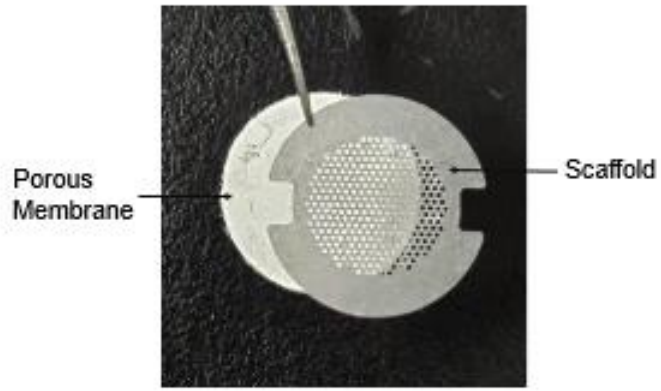
Emulate: **Flat-bed design**





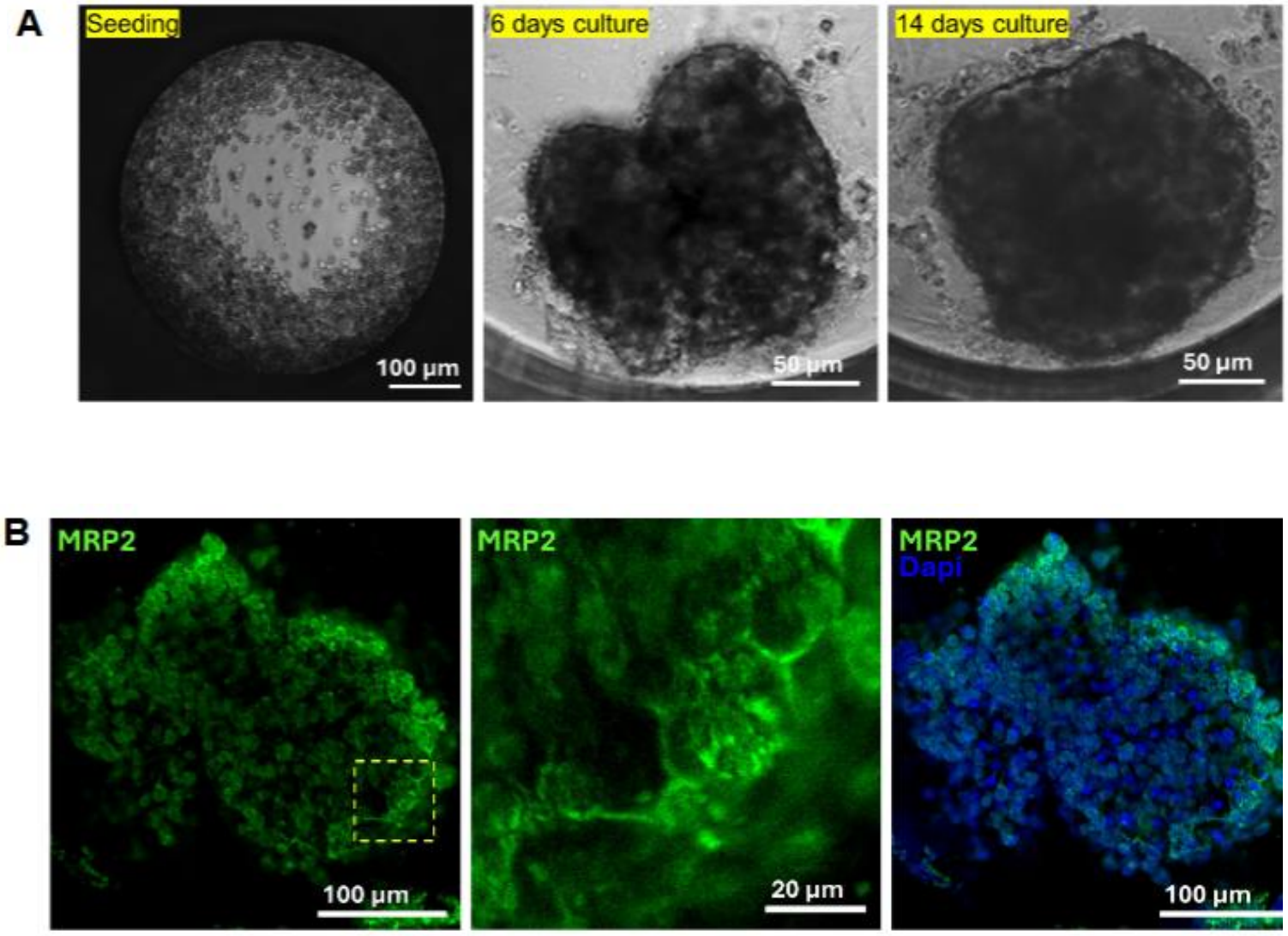
CN Bio: **3D Meshed-bed design**



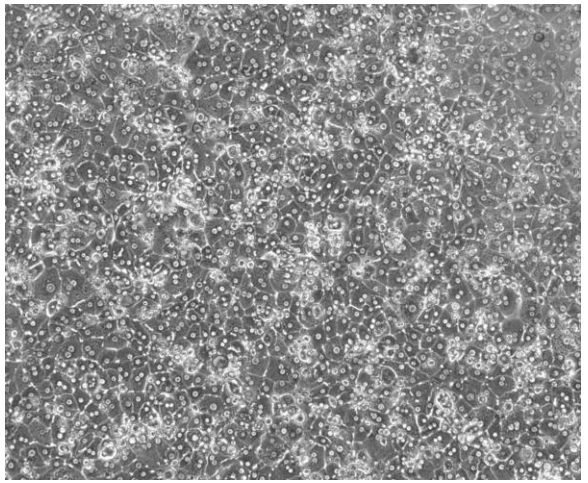


HepatoXcell™ MPS Applications

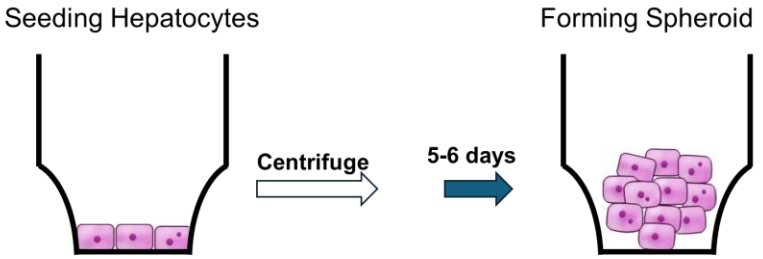
Spheroids



2-D Sandwich Culture



Schematic overview of spheroid cultures for 3-D hepatocytes

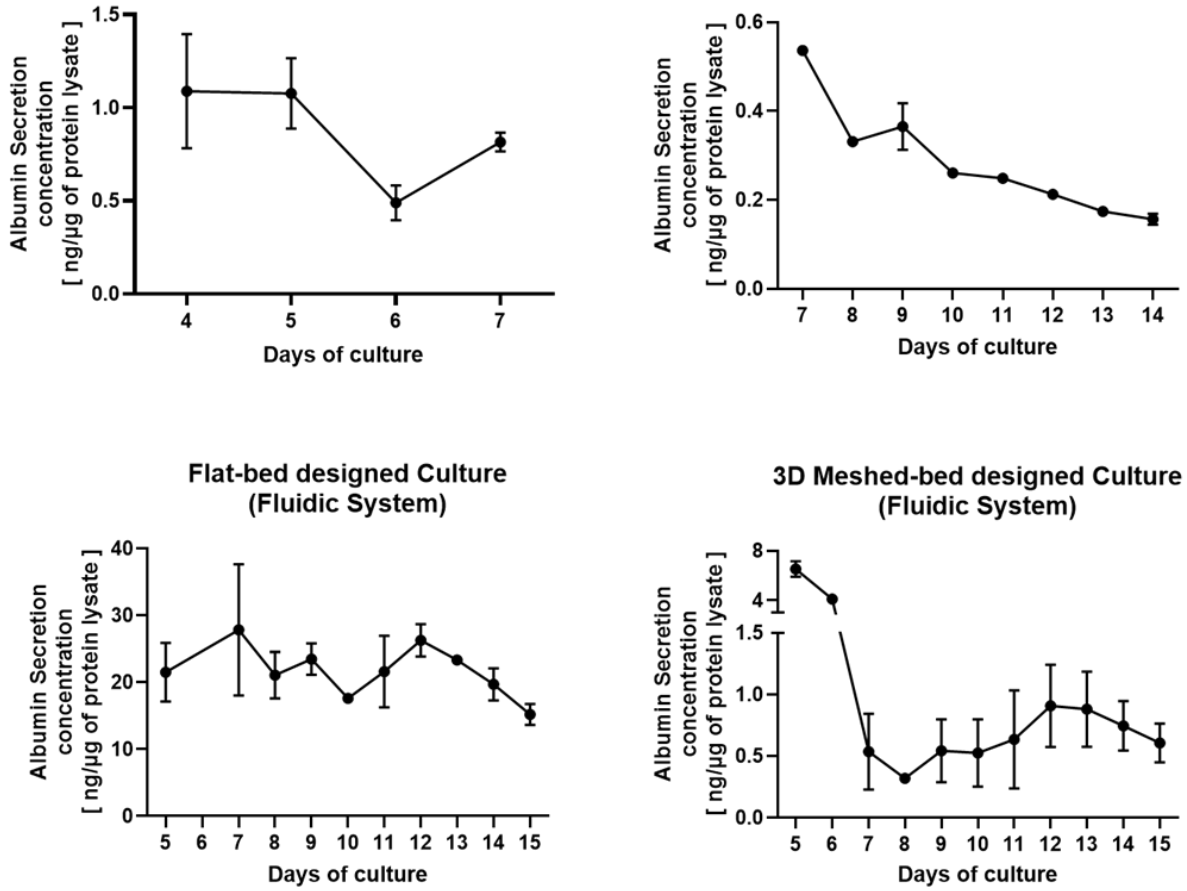


A and B: Spheroid-cultured HepatoXcell™ Pro in Akura 96 Spheroid Microplate (InSphero).

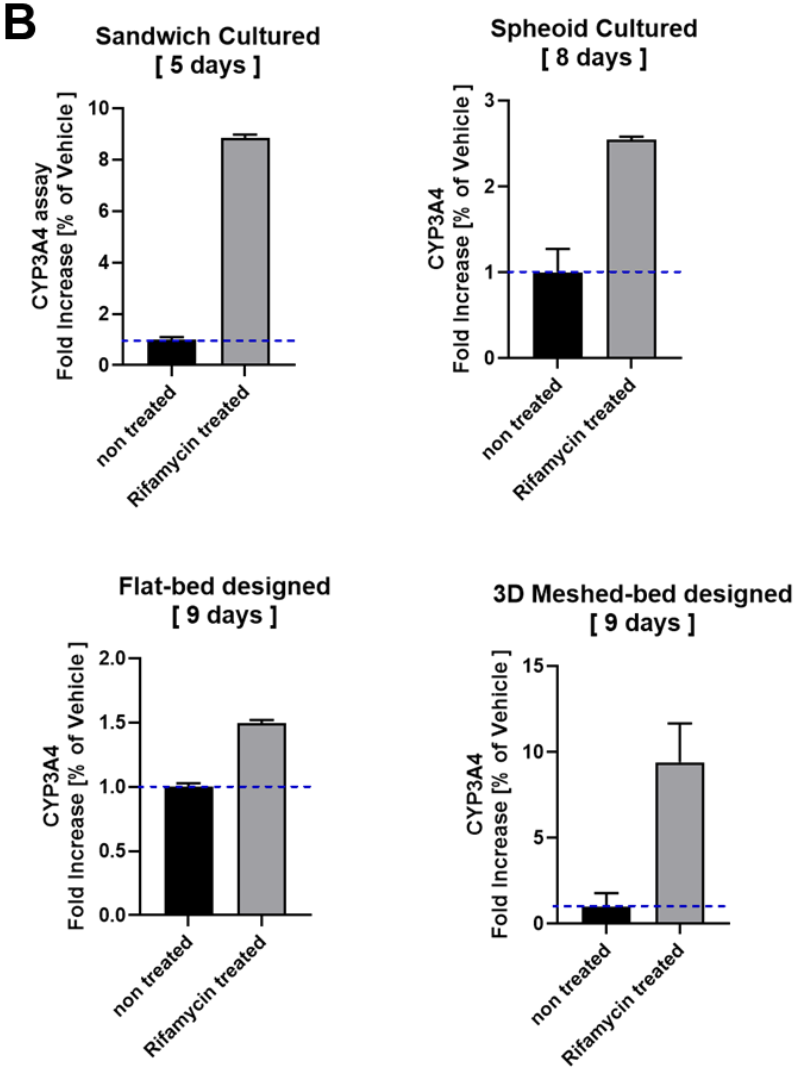
HepatoXcell™ Applications

MPS comparisons

A



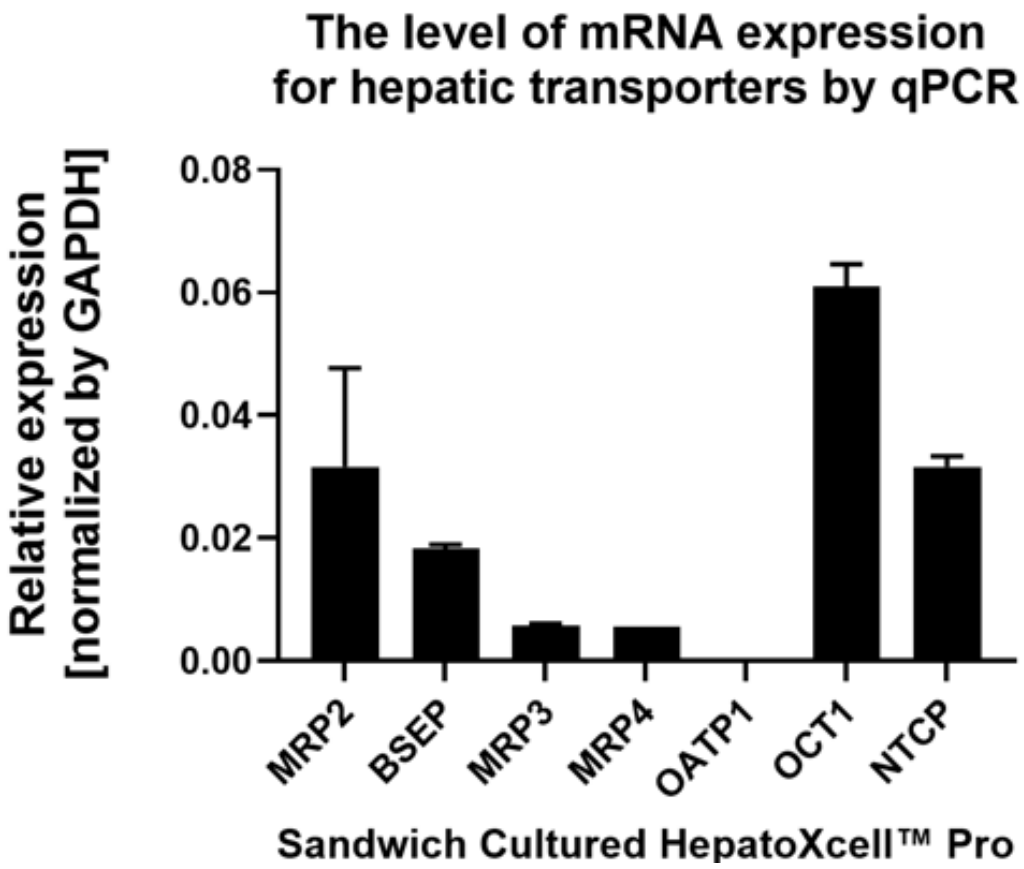
B



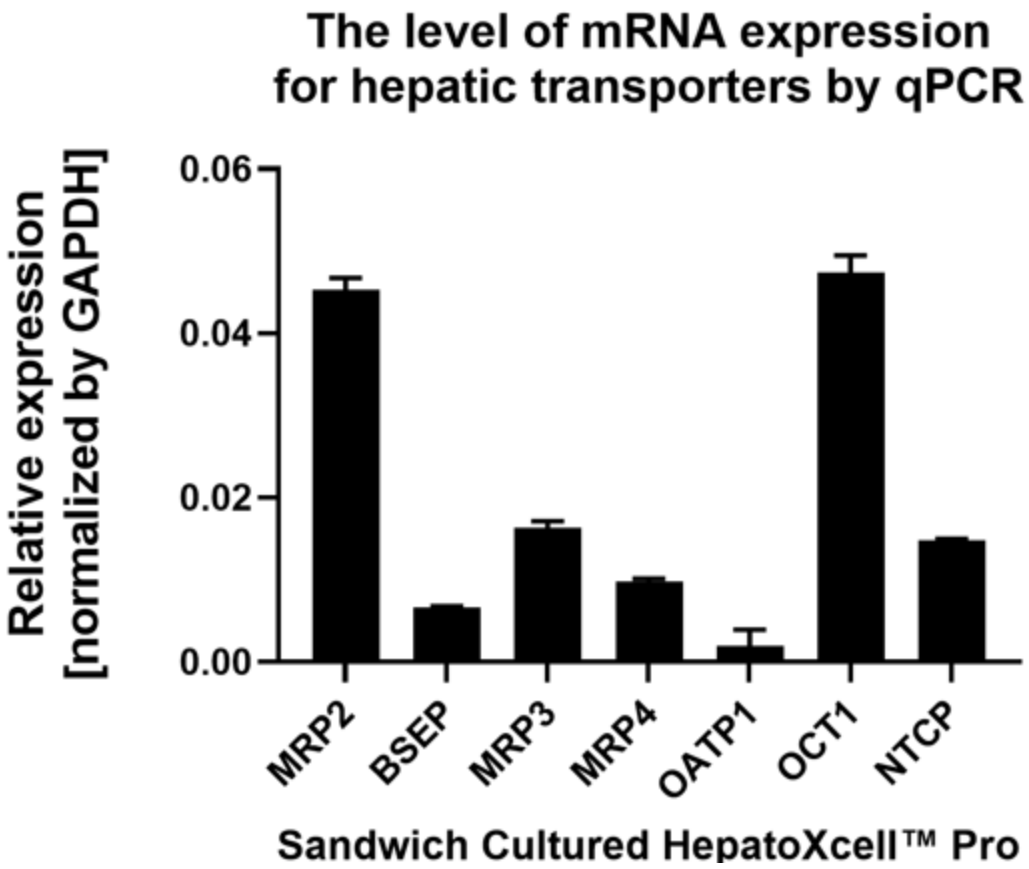
HepatoXcell™ MPS Applications

Transporter mRNA expression

Flat-bed (Emulate) System



Meshed-bed (CN Bio) System

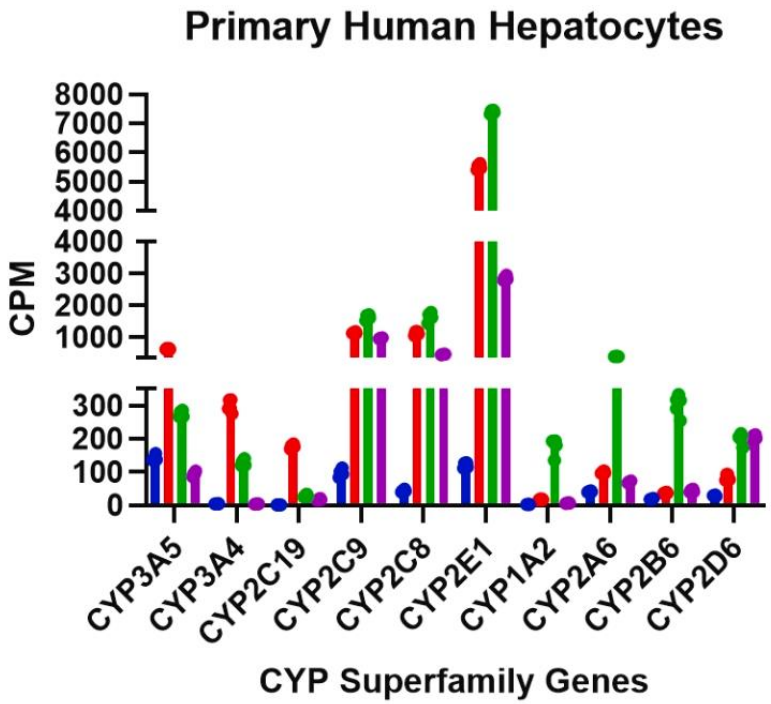


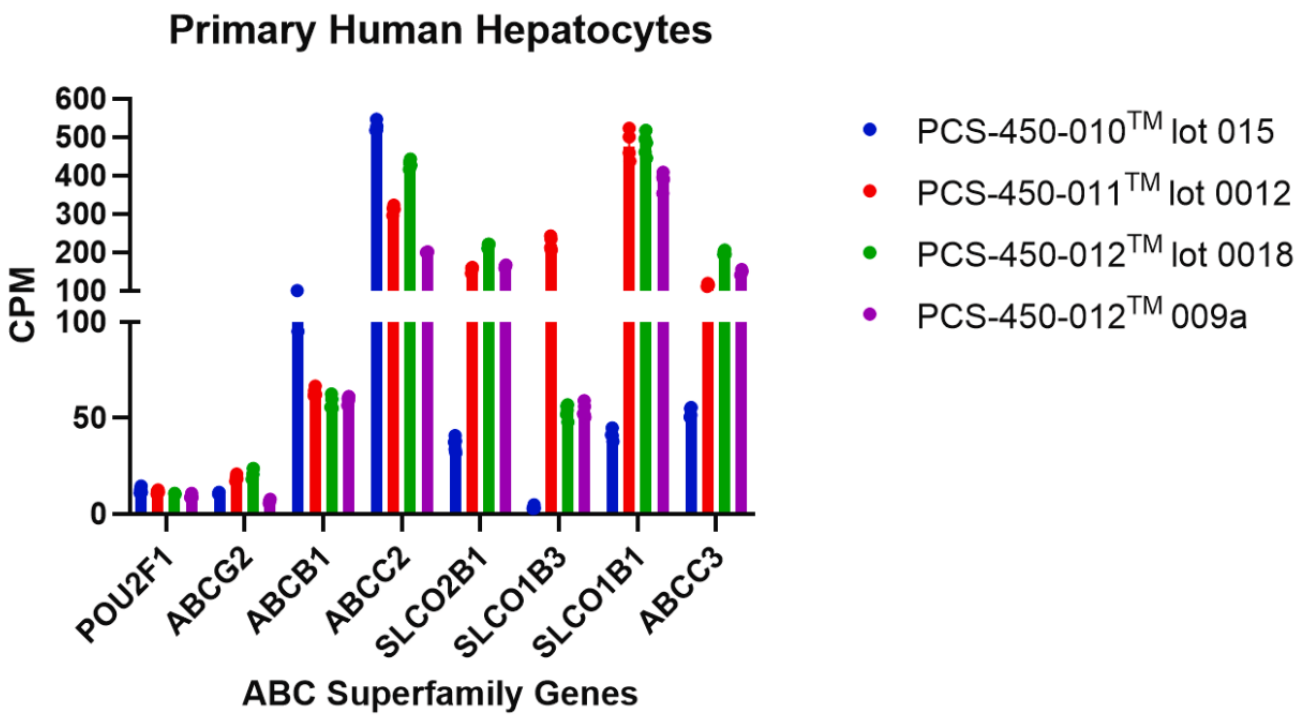
HepatoXcell™ Applications

Transcriptomic, proteomic, and activity Data

- Collaboration with bioinformatics team and Precision Quantomics
- Transcriptome and exome data available for each lot

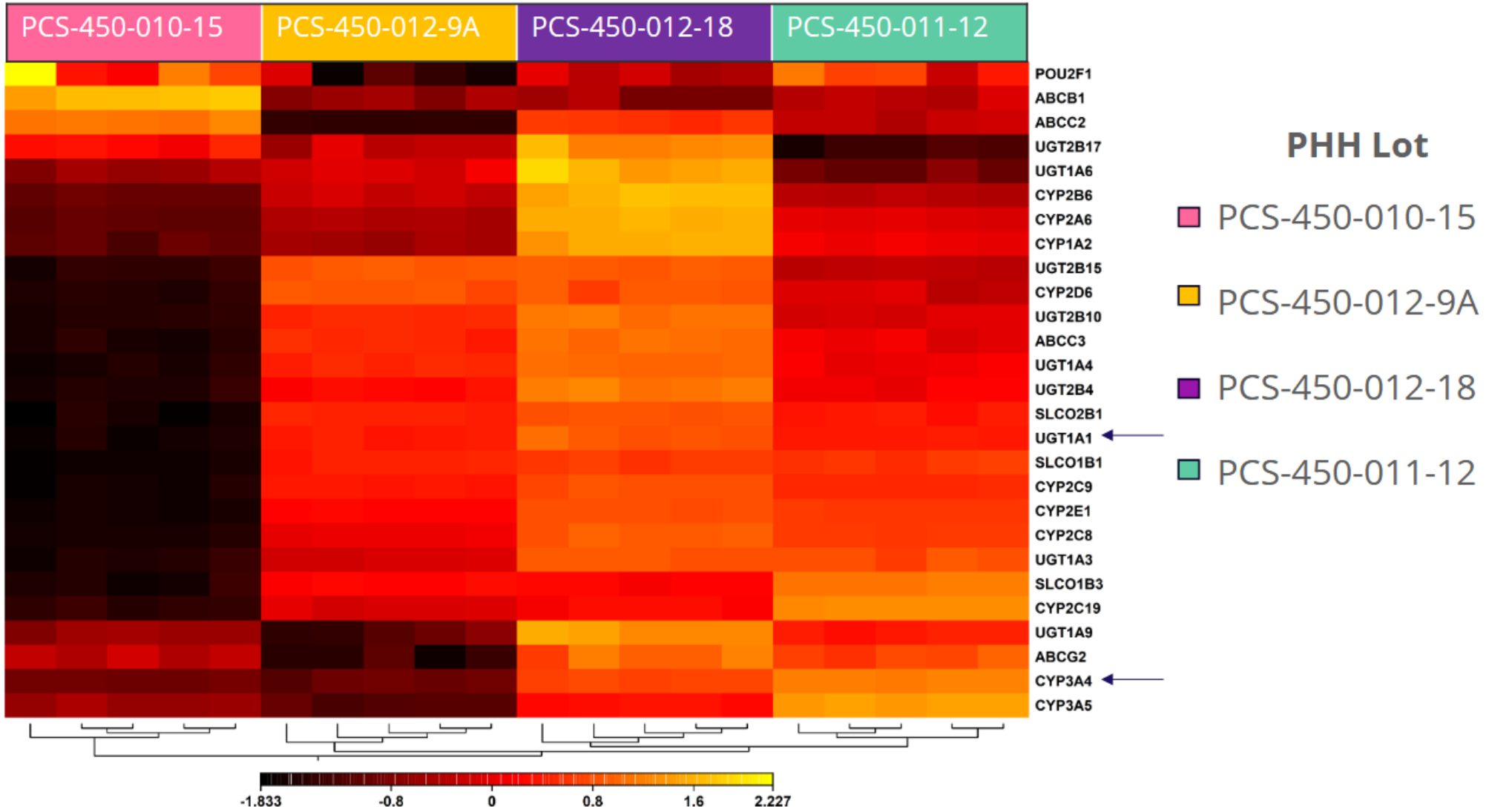
Gene expression profiling of key cytochrome P450 enzymes and transporters across hepatocyte lots





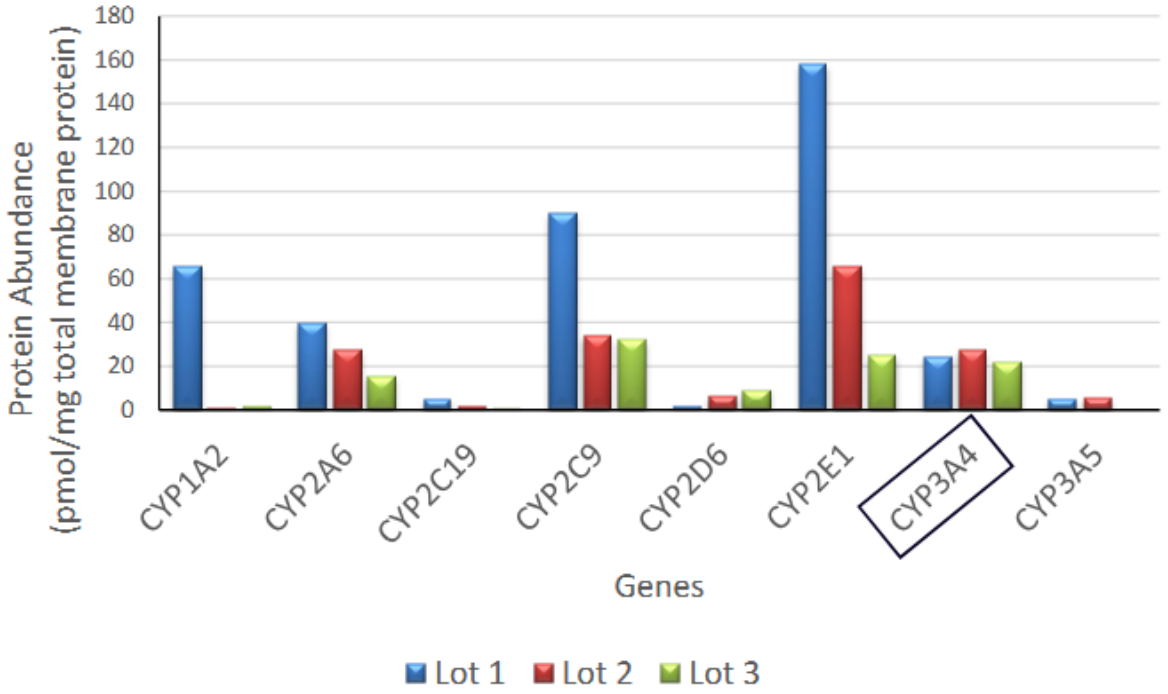
HepatoXcell™ Applications

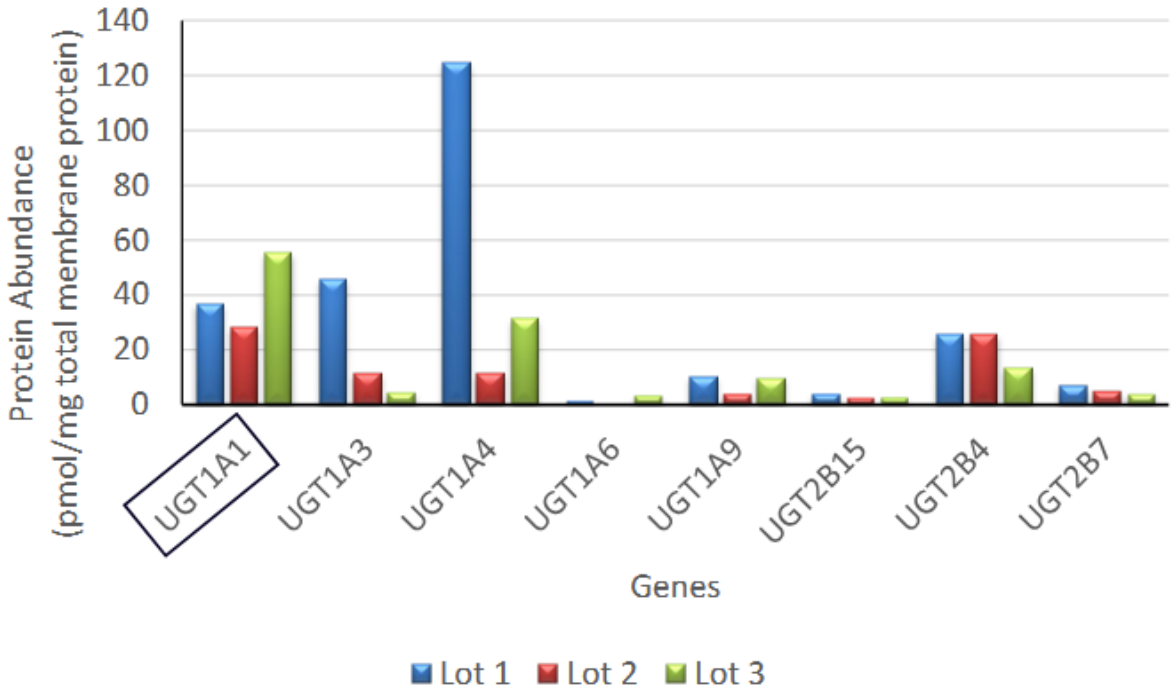
Cross-donor comparison of key gene expression



HepatoXcell™ Applications

Donor-specific differences in metabolizing enzyme abundance



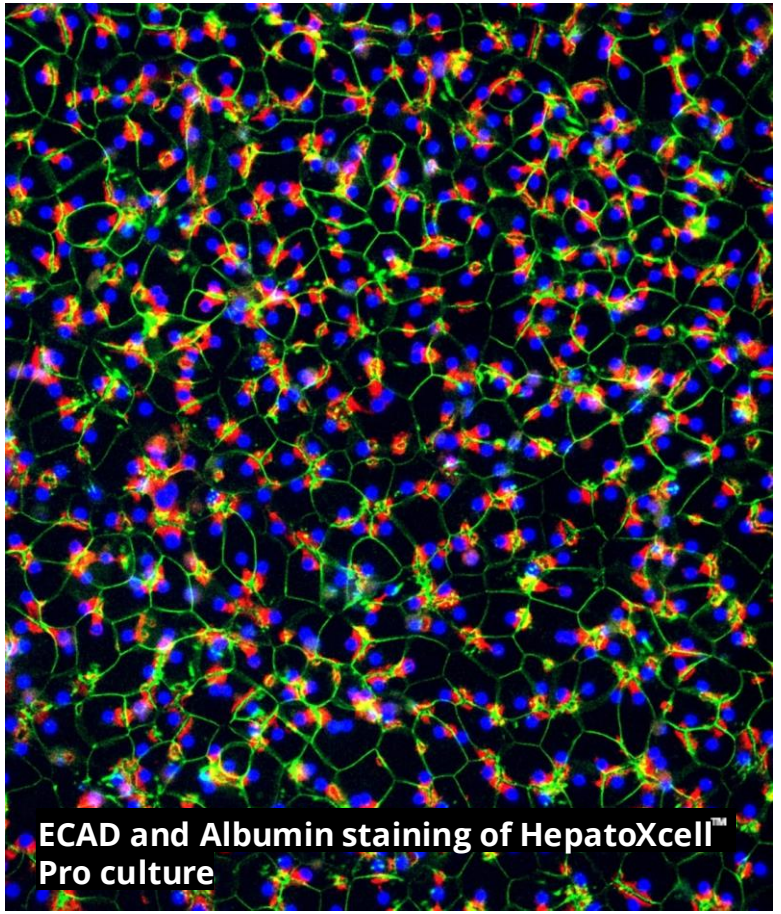


HepatoXcell™ Catalog #	Lot #
PCS-450-011-0012	1
PCS-450-011-0027	2
PCS-450-011-0037	3

ATCC Primary Human Hepatocytes

Summary

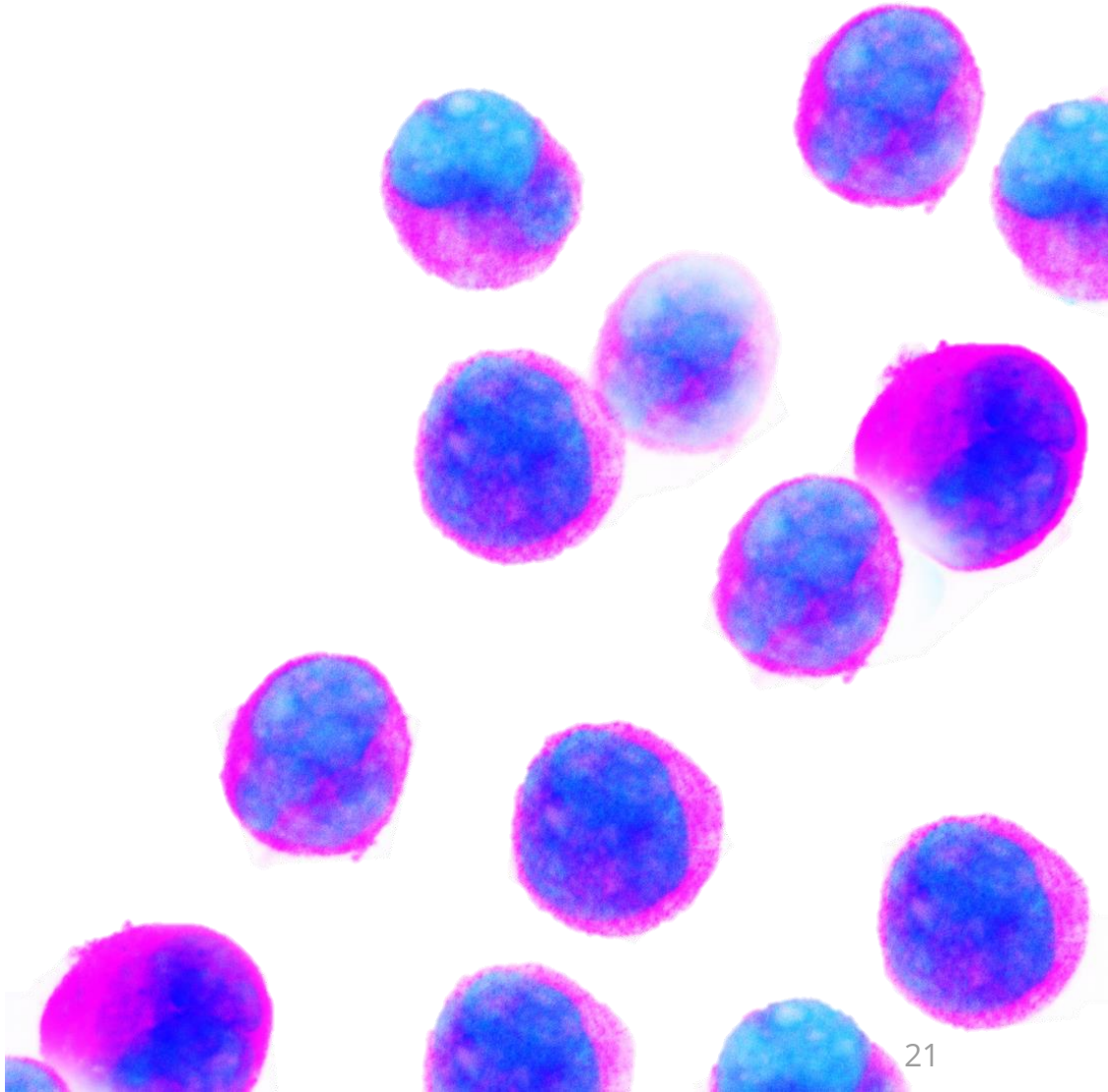
- Gold standard for human liver toxicity
- Characterized lots reduce variability and improve reproducibility
- Microphysiological systems maintain function over time
- Transcriptomic and proteomic data support mechanistic insight
- Integrated approaches using various methodologies enhances predictive toxicology



ECAD and Albumin staining of HepatoXcell™ Pro culture

Peripheral Blood Mononuclear Cells

- Peripheral blood mononuclear cells (PBMCs) are widely used in toxicology research to identify immunotoxicity
- Comprise a variety of immune cells to give access to a human immune response
- PBMCs add a critical immune safety dimension to in vitro toxicology workflows



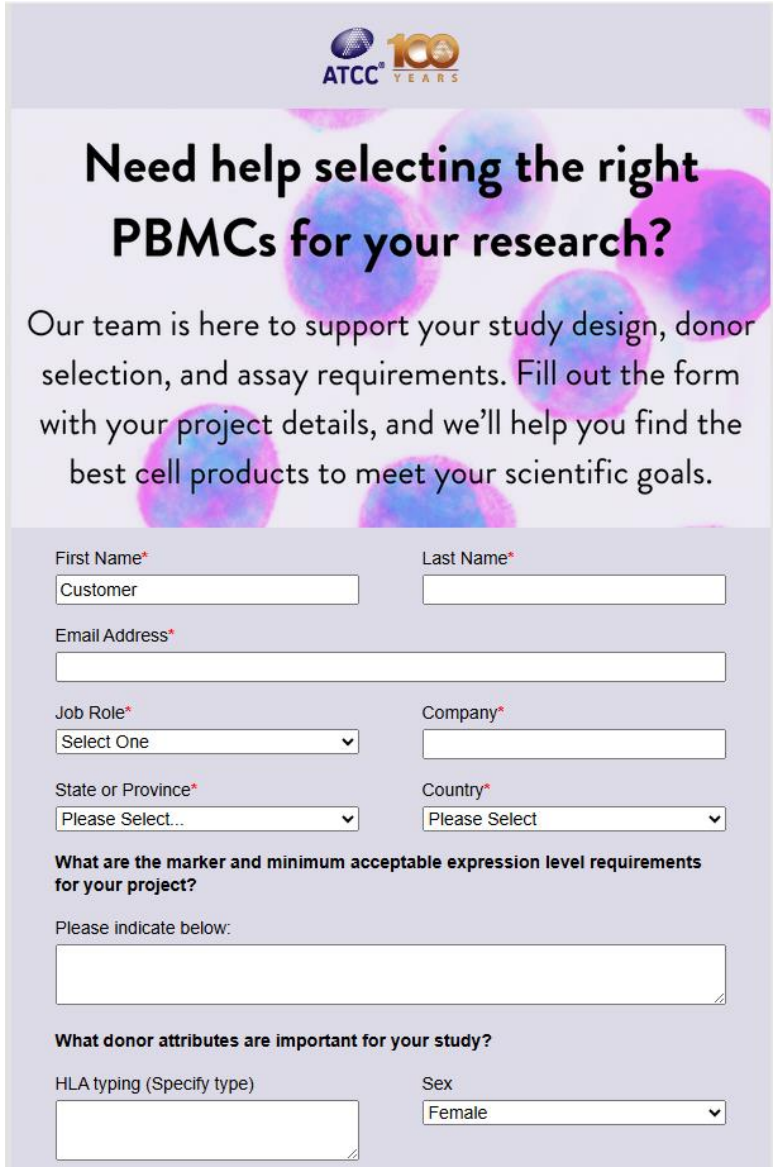
PBMC Applications

PBMCs Use Cases	
Immunological Research	Toxicology and Drug Screening
Cancer Research and Immunotherapy	Cellular Therapy & Regenerative Medicine
Autoimmune Disease Research	Infectious Disease Research
Vaccine Development and Testing	Stem Cell Research

PBMCs – Challenges and Solutions

Challenge	ATCC PBMC Solution
Limited access to donor information	Access to donor information (age, gender, race, blood type)
Lack of cell population characterization	$CD45^+$, $CD3^+$, $CD4^+$, $CD8^+$, $CD14^+$, $CD19^+$, $CD56^+$ characterization
Failure in predict human immune responses	Predictive, high-fidelity models for physiological relevance
Regulatory risks from inconsistent sources	Ethically-sourced from IRB-consented donors and rigorously tested for reproducibility and traceability
Limited access to HLA data	HLA data available upon request
Scalability and workflow constraints	Available in 25M cells/vial, cryopreserved for long-term, compatible with high-throughput platforms and GMP-adjacent environments
Matching lots to your needs	Lot selection tool on our website

ATCC Provides Support for PBMC Lot Selection



ATCC 100 YEARS

Need help selecting the right PBMCs for your research?

Our team is here to support your study design, donor selection, and assay requirements. Fill out the form with your project details, and we'll help you find the best cell products to meet your scientific goals.

First Name* Customer

Last Name*

Email Address*

Job Role* Select One

Company*

State or Province* Please Select...

Country* Please Select

What are the marker and minimum acceptable expression level requirements for your project?

Please indicate below:

What donor attributes are important for your study?

HLA typing (Specify type)

Sex Female

Ethnicity

Repeat donor availability for longitudinal studies

Cell quantity and packaging

Desired total cell quantity per donor per billion

Preferred vial size 25 million cells/vial

If other vial sizes are needed, please indicate the vial size below:

Number of vials per lot

Application Area

What is the intended use of the PBMCs?

- Immunology research
- Vaccine development
- CAR-T development
- Toxicity testing
- Cell therapy
- Other

If other, please indicate the usage below:

Lot selection preferences

Please indicate your lot preference Reserve entire lot for exclusive use

Shipping and logistics

Preferred delivery timeline < 8 Weeks

Shipping

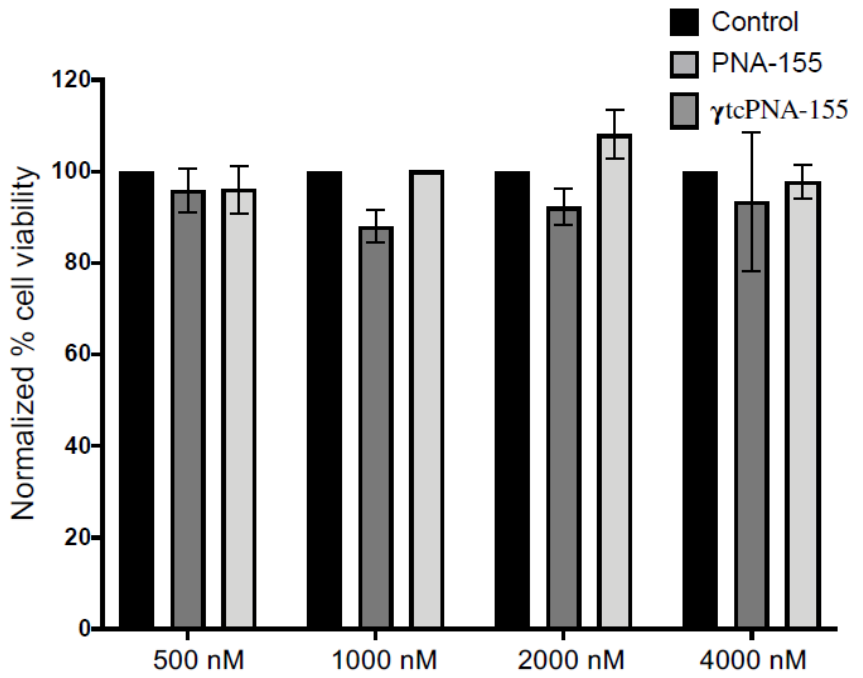
- Bulk Shipment
- Batch Shipment

Additional comments or requirements

Submit

ATCC PBMCs in Cancer Therapeutic Testing

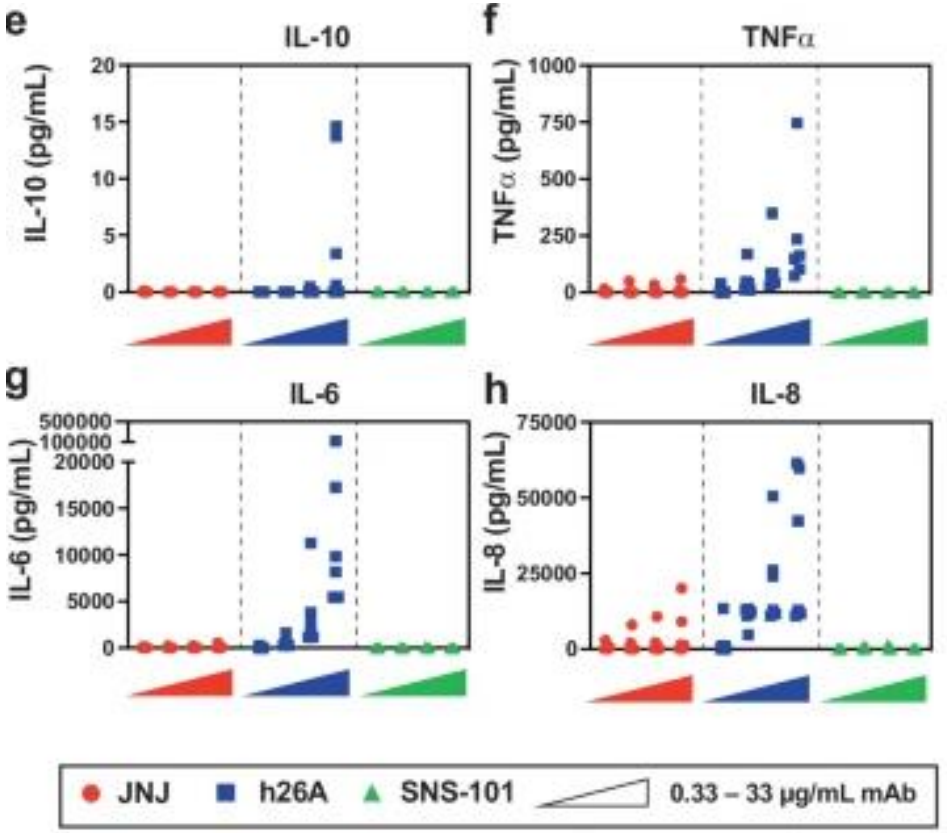
- Therapeutic potential of chemically modified, synthetic, triplex peptide nucleic acid-based oncomiR inhibitors for cancer therapy
- microRNA-155 (miR-155) is an overexpressed oncomiR in many types of lymphomas and leukemias
  - Attractive target for oncomiR inhibitors
- Tested the cytotoxicity of potential cancer therapeutics on PBMCs by measuring cell viability



Dhuri et al., Cancer Res 81(22): 5613-5624, 2021. PubMed: 34548334

ATCC PBMCs in Cancer Therapeutic Testing

- VISTA checkpoint inhibition by pH-selective antibody SNS-101 with optimized safety and pharmacokinetic profiles enhances PD-1 response
  - JNJ and h26A: non-pH selective antibodies
- Co-cultured PBMCs with human umbilical vein endothelial cells (HUVECs) to assess cytokine release when treated with a promising cancer therapeutic

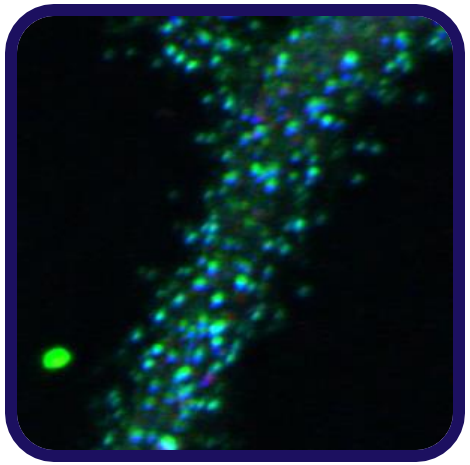


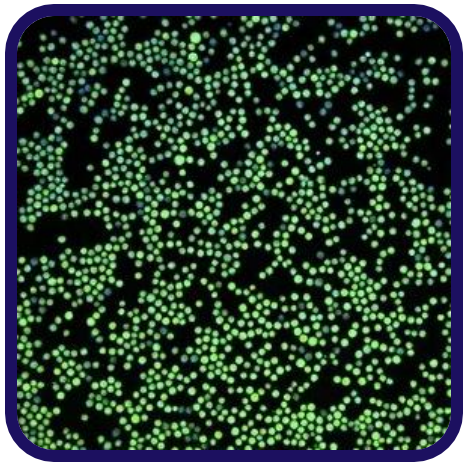
Thisted et al., Nature Comm 15(1): 2917, 2024. PubMed: 38575562

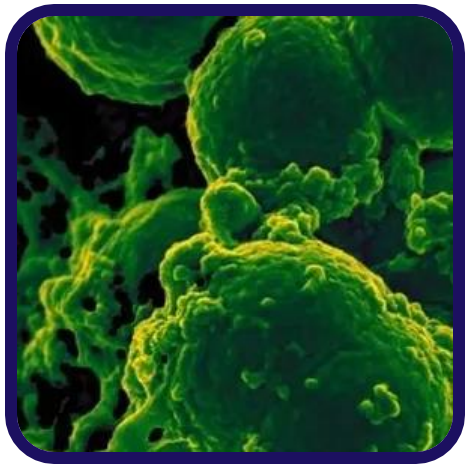
PBMCs

Summary

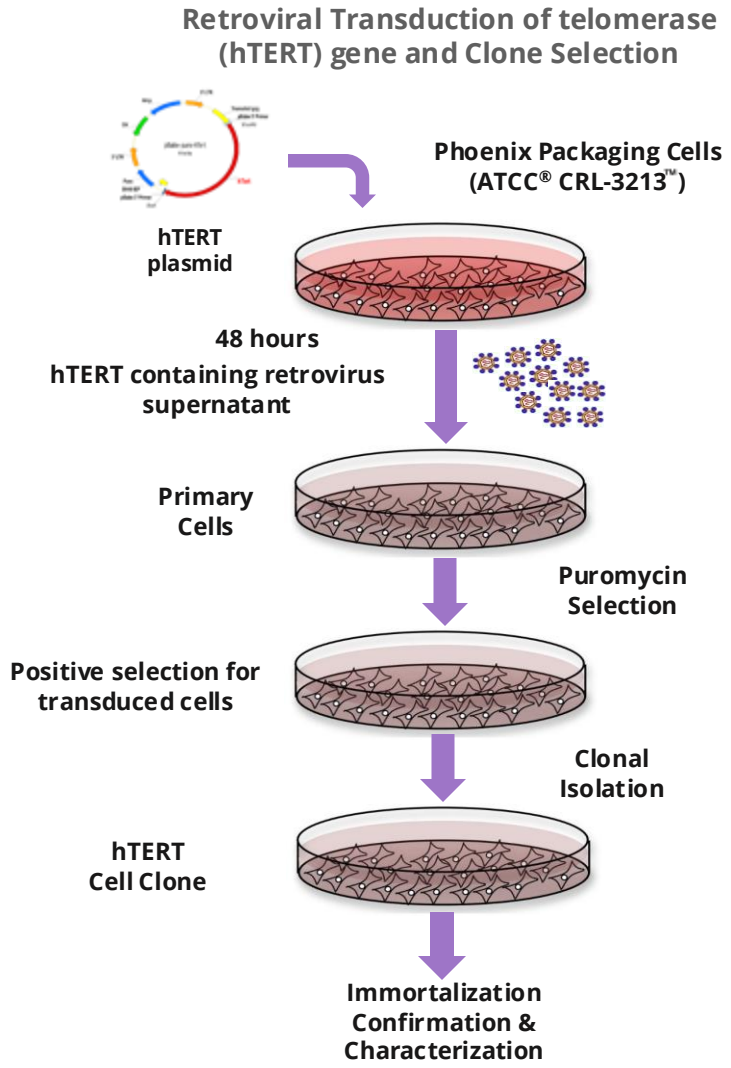
- Predict human immune responses that animal models miss—cytokine release, hypersensitivity, immunosuppression
- Donor demographic availability captures population variability for robust risk assessment
    - Ability to select lots with the cell populations that match research and application needs
- Quality-controlled cells that are well-characterized for related immune cell subpopulations
- Integrates with metabolic assessment—test hepatocyte-generated metabolites for immune effects

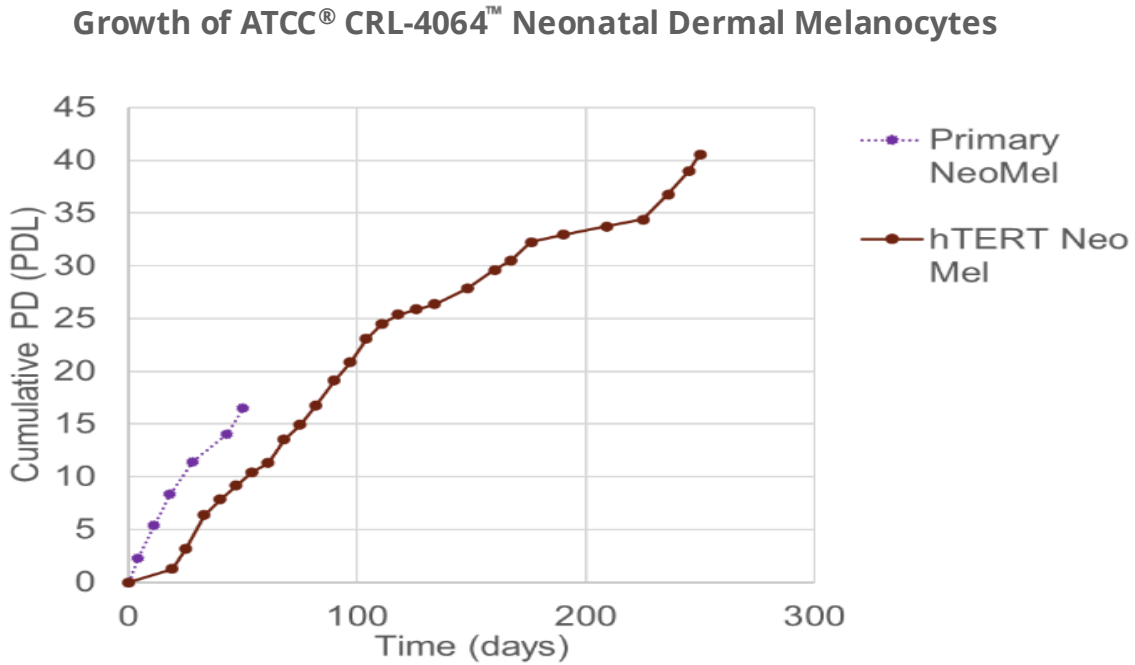






hTERT-Immortalized Cells





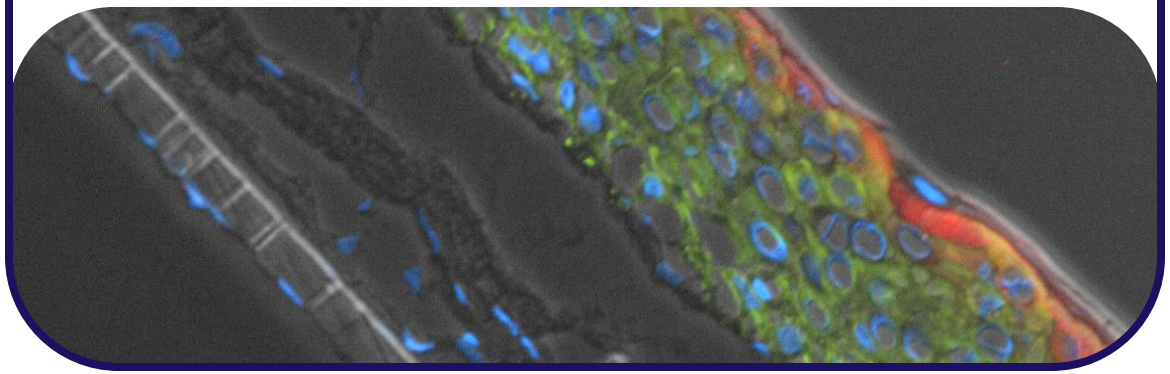
Properties of ATCC hTERT-Immortalized Cells

Characteristics

- Retain expression of phenotypic markers
- Have a stable karyotype
- Nonmalignant
- Normal cell cycle controls, functional p53 pRB checkpoints
- Contact inhibited
- Anchorage dependent
- Retain normal growth responses to serum and mitogens
- Require growth factors and proliferation
- Possess a normal karyotype
- Do not show changes associated with transformation such as tumorigenesis

Applications

- Long-term studies of biochemical and physiological aspects of cell growth
- In vitro model for differentiation and carcinogenesis
- Cancer research and studies of oncogenes
- Cell-based drug screening and toxicity studies
- Tissue engineering
- Genetic engineering
- Biological functions of hTERT



hTERT-Immortalized Cells

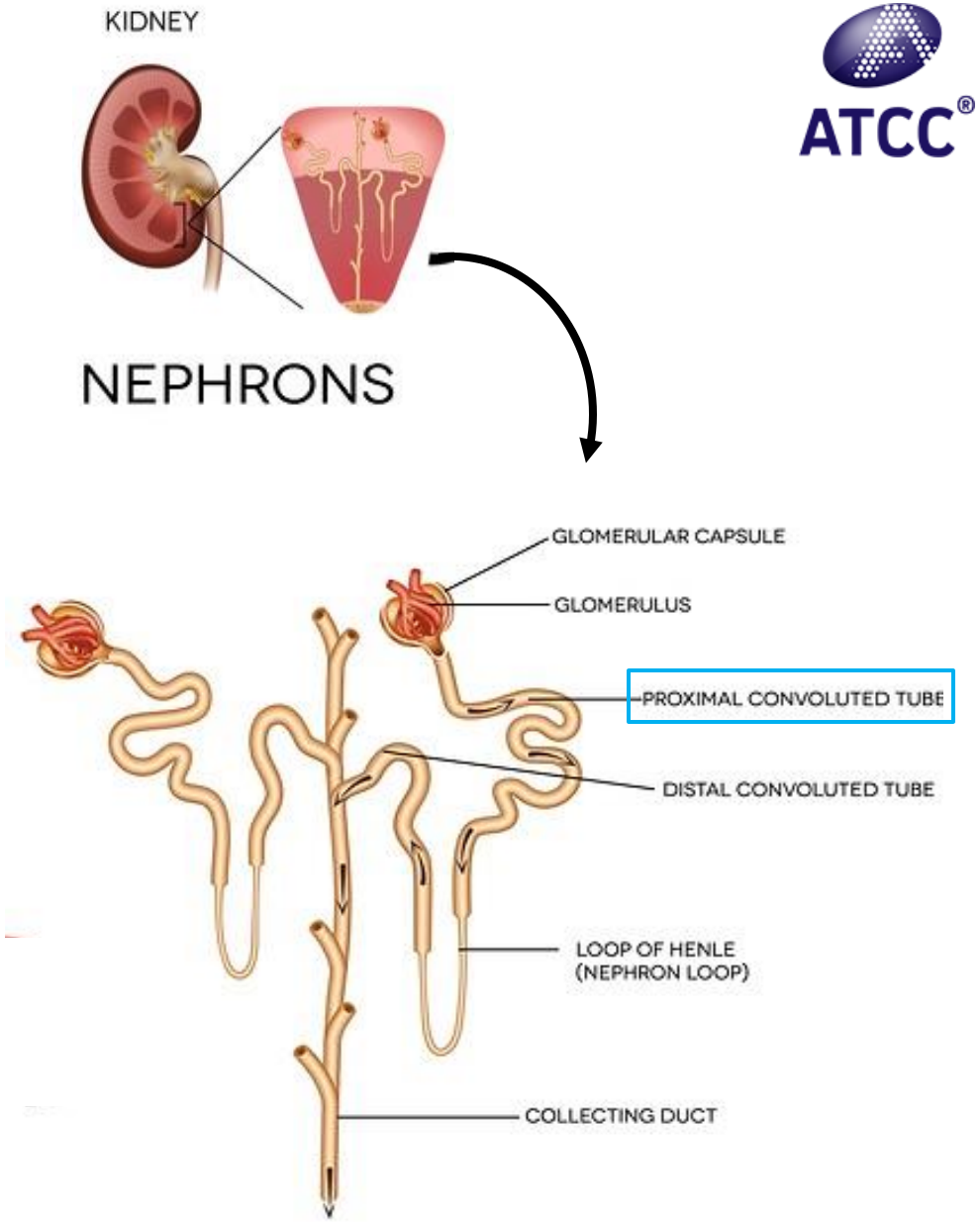
Challenges and solutions

Challenges With Other Models	ATCC hTERT Solution
Limited lifespan of primary cells	Continuous proliferative capacity, excellent for chronic exposure studies
Non-physiological relevance in continuous models	Maintain normal cellular characteristics
Loss of phenotypes over time	Maintain tissue-specific functions
Reproducibility across workflows	Consistent and well-characterized
Changes in metabolic enzyme expression over time	Maintain stable enzyme expression

Renal Function and Toxicity

- The kidney is one of the major target organs for drug-induced toxicity
  - Large functional reserve of the kidney
  - Nephrotoxic effects become obvious only after regulatory approval

- Renal proximal tubule (PT, blue box) is a major target for drug-induced toxicity due to its role in:
  - Glomerular filtrate concentration
  - Transport of drugs and organic compounds

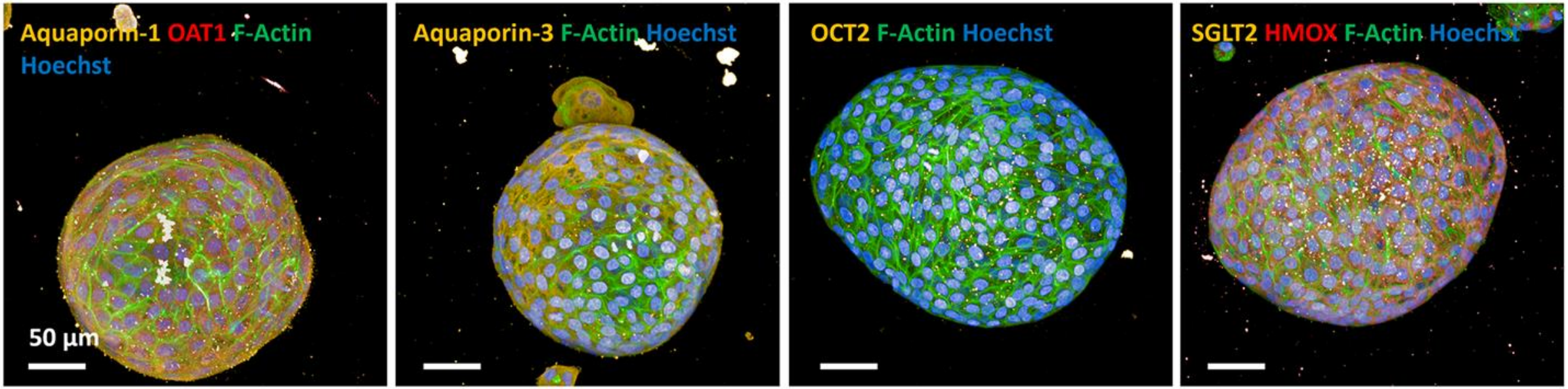


MedlinePlus. Renal hypouricemia. Accessed online March 2026 from https://medlineplus.gov/genetics/condition/renal-hypouricemia/.

Benefits of using hTERT RPTEC vs. Primary and Continuous Lines

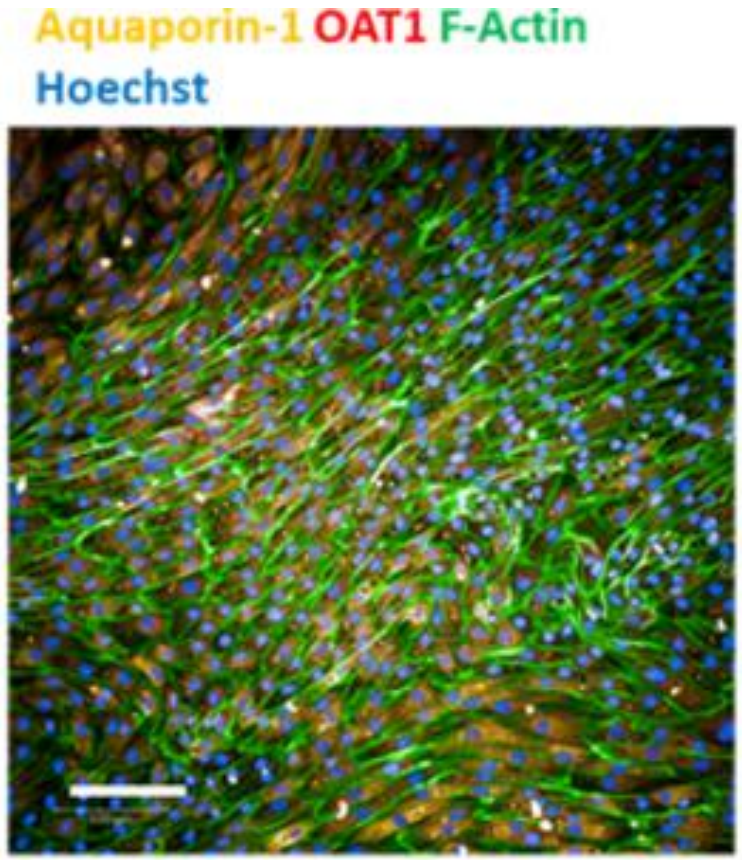
	Primary	Continuous	hTERT
Tissue origin	Human kidney-derived	Non-human or non-renal (cancerous)	Human renal proximal tubule epithelium
Transporter expression	Lost over time	Lack native transporters	Maintains endogenous transporters
Culture longevity	Limited	Continuous	Continuous without loss of key traits
Predictability	Moderate	Low	High
Physiological relevance	High initially	Low	High, retains in vivo characteristics

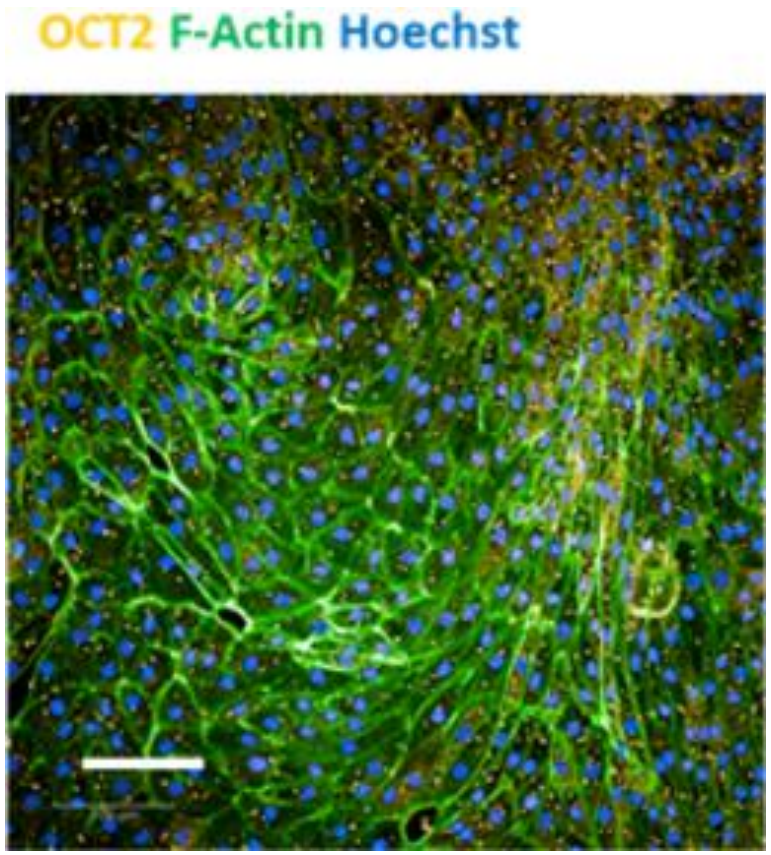
hTERT RPTEC “Tubuloids” for Nephrotoxicity Evaluation – Transporter Expression



Vidal Yucha SE, et al. PLoS One 17(11): e0277937, 2022. PMID: 36409750

hTERT RPTEC “Tubuloids” for Nephrotoxicity Evaluation



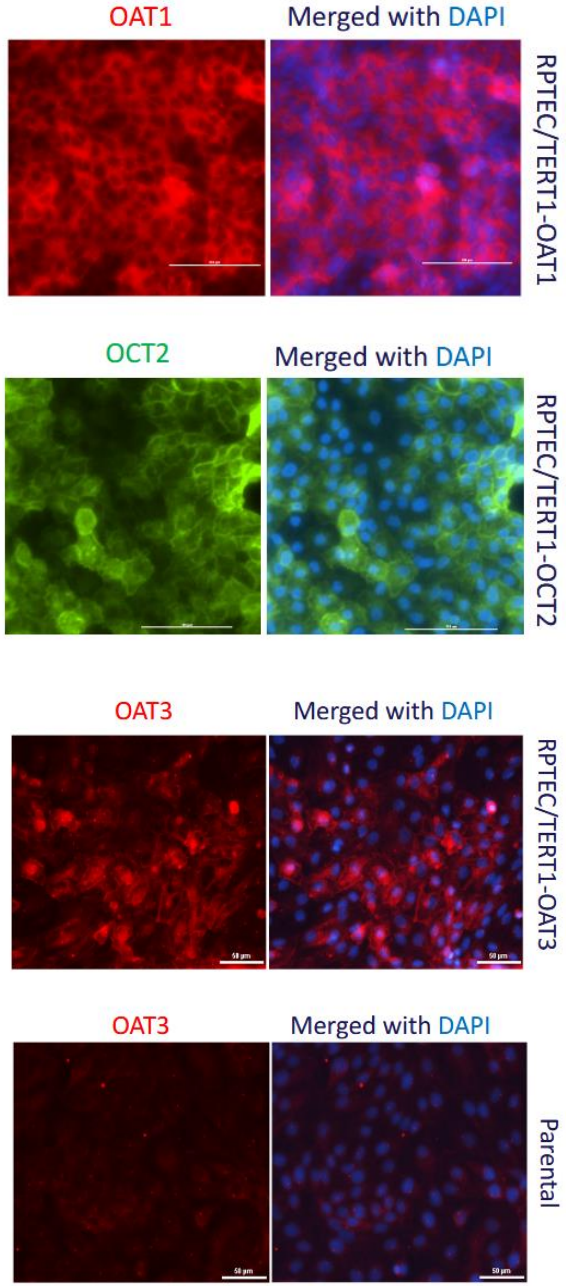


Vidal Yucha SE, et al. PLoS One 17(11): e0277937, 2022. PMID: 36409750

ATCC hTERT Cell Lines

Summary

- hTERT immortalized primary cells provide primary cell functionality with continuous cell line longevity
- Stable and reproducible models for toxicity across many passages and experiments
- Suitable for long-term and repeat-dose studies
- Ideal complement to hepatocytes and PBMCs when engaging in ADME testing



hTERT RPTEC SLC-overexpression

Summary

ATCC offers a variety of cell lines to fit your toxicology needs

Primary human hepatocytes

- Gold standard for ADME testing
- Clinically relevant metabolism and strong regulatory acceptance

PBMCs

- Robust immune populations for immunotoxicity testing and more

Immortalized primary cells (hTERTs)

- Authenticated for immortalization and karyotype stability
- Excellent for long term, reproducible, high-throughput research and workflows
- hTERT cells alone or in combination with other cells are a user-friendly solution for building reliable cell models for toxicity studies

Integrated approaches combine these tools to improve predictability across ADME, tissue toxicity, and immune safety

www.atcc.org/tox

Resources

HepatoXcell	hTERTs	PBMCs
• HepatoXcell Website	• hTERT Website	• PBMC Website

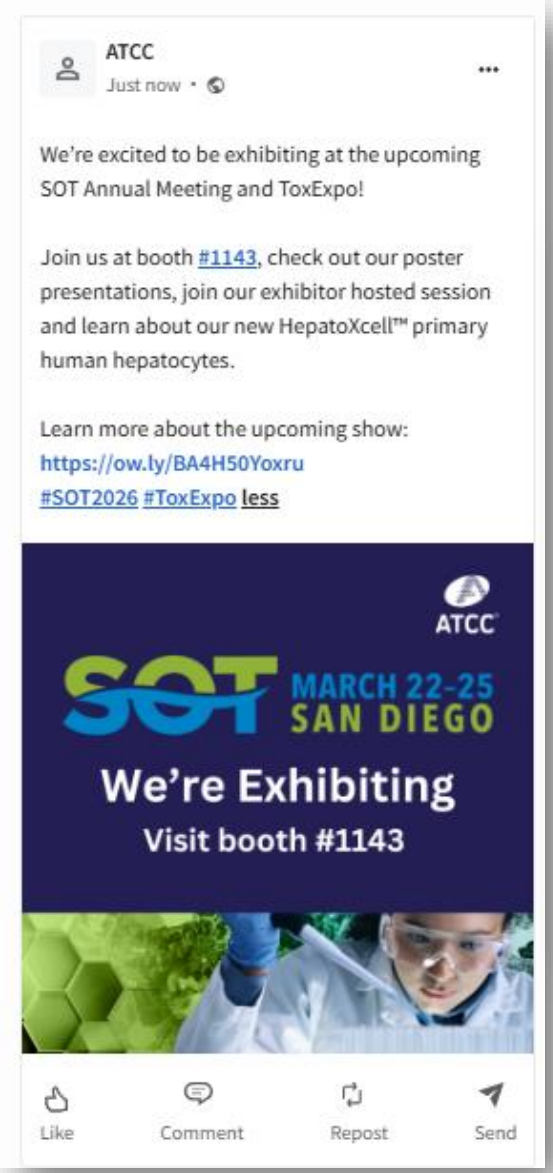
• Brochure:
  • HepatoXcell Catalog
	• Brochure:
	  • hTERT Catalog
		• Brochure:
		  • PBMC and Immune Cells Catalog

• Top 10 Application of Primary Human Hepatocytes • MPS World Summit 2025 Poster		• Applications of PBMCs

• Presentations:
  • Reproducible Models for Toxicity Studies
  • Innovative Microphysiological Model Using HepatoXcell Primary Human Hepatocytes and Locsense Artemis
  • From Cryopreservation to Functionality: HepatoXcell in Dynamic Liver-chip Environments
	• Presentations:
	  • Primary and hTERT-immortalized Cells: Physiologically Relevant Cell Models for Toxicological Assays
	  • The Development of a Standard In Vitro Model for Studying Metabolic Diseases
		• Presentations:
		  • Cell-based Models for the Discovery and Development of Cancer Therapeutics
		  • Model Immune and Cardiovascular Systems
		  • Accelerate Cancer Immunotherapy Drug Screening with Immune Checkpoint Reporter Cell Lines

• Videos:
  • How to Use Dry Shipper
  • Features and benefits
  • Plating in sandwich culture
	• Videos:
	  • Webinar: hTERT-immortalized Primary Epidermal Cells: Key Components in Complex Toxicological Models
		• Videos:
		  • Webinar: Functionally Characterized Human PBMCs: An Improved In Vitro Model of Human Immune Response

Upcoming Presentations at SOT & ToxExpo



Check out our Poster Presentations

Generation of a Novel Immortalized Human Corneal Epithelial Cell Line for Reliable In Vitro Ocular Toxicity Studies
Presenter: Xiangshan Zhao, PhD, Senior Scientist, ATCC
Date & time: Tuesday, March 24, 2026, from 9:15–11:45 AM
Location: ToxExpo, Hall B
Poster Board Number: M839
Abstract Number: 4340

ATCC's Human-Relevant Cancer Models for Mechanism-Based Toxicity and Drug Response Profiling
Presenter: Ajeet Singh, PhD, Senior Scientist, ATCC
Date & time: Tuesday, March 24, 2026, from 9:15–11:45 AM
Location: ToxExpo, Hall B
Poster Board Number: H622
Abstract Number: 4140

Human Liver-on-a-Chip Systems for Enhanced Mechanism-Based Toxicity Screening
Presenter: Carolina Lucchesi, PhD, Principal Scientist, ATCC
Date & time: Tuesday, March 24, 2026, from 9:15–11:45 AM
Location: ToxExpo, Hall B
Poster Board Number: H618
Abstract Number: 4136

Attend our presentations

Don't miss our Exhibitor-Hosted Session

Shaping the Future of Predictive Toxicology with HepatoXcell for Advanced MPS Platforms

Tuesday, March 24 | 10:45–11:45 AM | Room 23C

*This session is an Exhibitor-Hosted Session. Although not an official part of the SOT Annual Meeting scientific program, its presentation is permitted by the Society.

Join our Tiny Tox Talk

Mini Organs, Major Insights—Toxicology goes 3-D

Wednesday, March 25 | 11:20–11:40 AM | Tiny Tox Talks Theater

Presenter:
Carolina Lucchesi, PhD, Principal Scientist, ATCC

Join us at booth #1143

ATCC®

CREDIBLE LEADS TO INCREDIBLE

Thank You