





# Innovative Microphysiological Model Using HepatoXcell™ Primary Human Hepatocytes and Locsense Artemis

**Brian Shapiro, PhD** 

Marketing Segment Manager, ATCC

Sujoy Lahiri, PhD

Lead Scientist, R&D, ATCC

Susan Roelofs, PhD

CEO and Founder, Locsense



### ATCC®'s mission and future direction





### Brian Shapiro, PhD Marketing Segment Manager, Toxicology, ATCC

Dr. Brian Shapiro is a distinguished Marketing Segment Manager at ATCC, where he plays a pivotal role in bridging the gap between scientific innovation and the biomedical research community. With a robust background in oncology, toxicology, and metabolic diseases, Dr. Shapiro is dedicated to advancing research through the development and promotion of cutting-edge cell models and tools. Beyond his technical contributions, Dr. Shapiro is also the Executive Producer of ATCC's podcast, "Behind the Biology," where he communicates the latest scientific breakthroughs and insights to a broader audience.

# Agenda



- 1. ATCC's mission and future direction
- 2. HepatoXcell™ ATCC's new offering of primary human hepatocytes
- 3. Locsense Artemis
- 4. Constructing a gut-liver model
- 5. Conclusions



# 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
- Global supplier of authenticated cell lines and viral and microbial standards
- Sales and distribution in 150 countries,
   20 international distributors
- Talented team of 700+ employees, over one-third with advanced degrees









# Modernization of the ATCC® portfolio

Present



The R&D teams at ATCC are diligently working on new products to address the requirements of the scientific community.



ATCC is dedicating resources to key technologies to ensure its products and services remain leaders in biological research.



The ATCC cell and micro collections were historically deposited by academic and other research scientists

# **HepatoXcell™ Primary Human Hepatocytes**





Sujoy Lahiri, PhD Lead Scientist, ATCC

Sujoy Lahiri, PhD, is an R&D scientist in ATCC. He leads the primary cell division, working on advanced cellular models using primary cells as well as expansion of ATCC's immortalized primary cell portfolio. Dr. Lahiri has extensive knowledge in the field of toxicology and drug metabolism. Previously, Dr. Lahiri worked at National Institutes of Health, where his work focused on lipid biochemistry. Dr. Lahiri received his PhD from the Weizmann Institute of Science, where he studied sphingolipid biochemistry and metabolism.



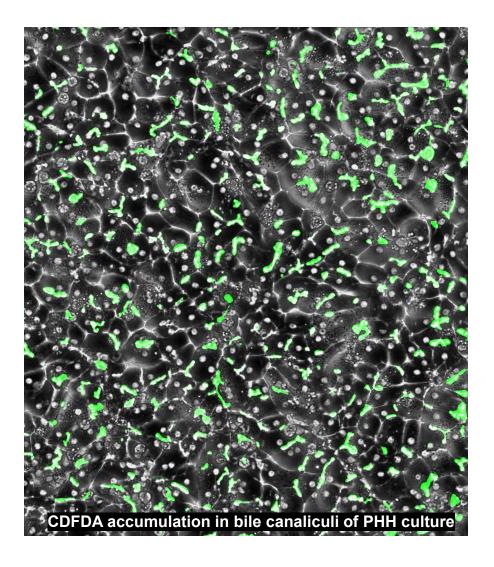
# Hepatoxcell by ATCC

Primary Human Hepatocytes

# **Challenges in ADME-Tox testing**



- Limited models for in vitro ADME-Tox testing
  - Over dependence on primary human hepatocytes (PHH)
  - Limited success with immortalized hepatic cell lines or iPSCderived hepatocytes
- Industry shortage of primary human hepatocytes for toxicological testing
  - Higher number of successful liver transplants
  - Difficult to acquire healthy liver tissue
- Choosing and ordering the right lot can be difficult
  - Access to donor information
  - Number of available vials per lot
- Characterization information of PHH offerings can be lacking
  - Lots not prequalified
  - Genomic data isn't available
- Prohibitive cost



# HepatoXcell<sup>™</sup> hepatocytes and media



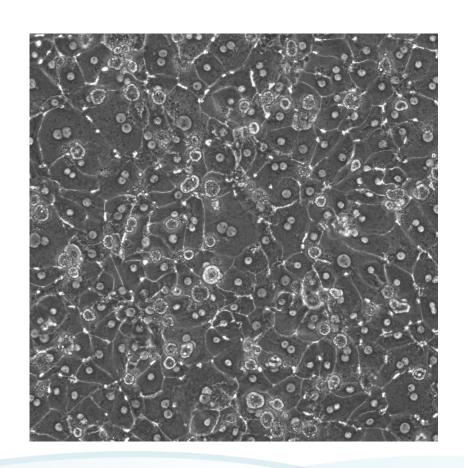
HepatoXcell™ Eco	ATCC <sup>®</sup> No. PCS-450-012™	Suspension	1 vial, ≥ 4 x 10 <sup>6</sup> cells/via
HepatoXcell™ Plus	PCS-450-010™	3-Day Plateable	1 vial, ≥ 4 x 10 <sup>6</sup> cells/via
HepatoXcell™ Pro	PCS-450-011™	7-Day Plateable	1 vial, ≥ 4 x 10 <sup>6</sup> cells/via
HepatoXcell™ Thawing Medium	PCS-450-032™	1 bottle	250 mL
HepatoXcell™ Maintenance Medium	PCS-450-034™	1 bottle	500 mL
HepatoXcell™ Plating Medium	PCS-450-038™	1 bottle	100 mL
HepatoXcell™ Plating Medium	PCS-450-038™	1 bottle	100 mL

## HepatoXcell™



#### ATCC's solution for your predictive drug development and toxicity testing

- HepatoXcell™ primary human hepatocytes come with ATCC's quality assurance
- Lot selection tool provides easy access to donor and lot information
- Lots are prequalified as per plate-ability or suspension viability
- CoA includes viability, metabolism, induction, and uptake data
- Access to transcriptome and whole-exome data for individual lots
- Competitive pricing



## Hepatocyte lot selection web tool



Home > Cell Products > Primary Cells > PCS-450-012

#### HepatoXcell™ Eco: Normal Human Hepatocytes

PCS-450-012 <sup>™</sup>

Hepato\*\*cell\*\*

HepatoXcell™ Eco are Primary Human Hepatocytes Suspension Cells, derived from normal, healthy, human liver tissues.

 Product category
 Human cells

 Product type
 Primary cell

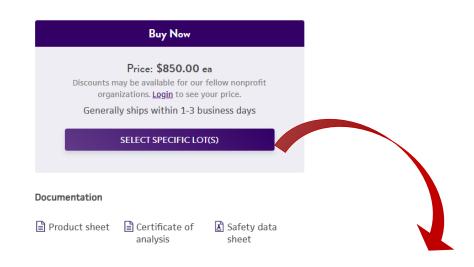
 Organism
 Homo sapiens, human

 Morphology
 round and often in clusters while in suspension

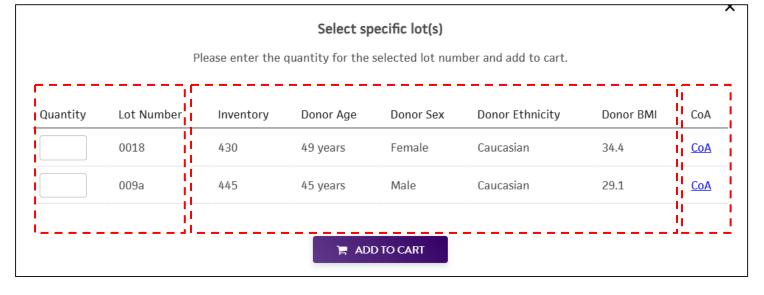
 Tissue
 Liver

 Applications
 Toxicology Cancer research

- Select a specific lot
- Add to your shopping cart



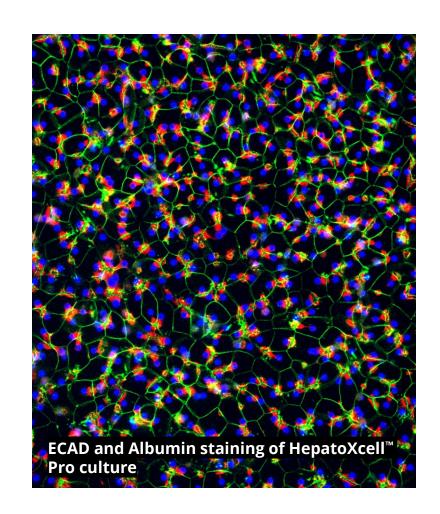
SHARE



# Why choose our primary human hepatocytes?



- High viability and functionality:
  - HepatoXcell<sup>™</sup> exhibit excellent viability and retain key liver functions
  - This makes them ideal for drug metabolism, toxicity studies, and liver disease research.
- Comprehensive characterization:
  - Each batch undergoes rigorous testing to ensure consistency and reliability
  - Testing includes assessments of enzyme activity, protein expression, and metabolic function.
- Genetic diversity:
  - Sourced from multiple donors, reflecting the genetic variability found in the human population.
  - Allows for comprehensive studies on how different genetic backgrounds can influence liver function and drug response



# **ATCC®** premium hepatocyte offering



	Hepatocyte Premium Offering	<b>HepatoXcell™ Pro</b> : 7-day plateable hepatocytes
<u>\$</u>	Application	Toxicology testing, ADME, drug development, disease research, advanced cellular modeling, co-culture, microphysiological system
	Assays	Metabolism, hepatotoxicity, TEER, induction of CYP mRNA, transporter efflux, transporter uptake, metabolite formation, compound stability, inhibition, gene expression, clearance assay

# **ATCC®** hepatocyte offering



	Hepatocyte Plateable Offering	<b>HepatoXcell</b> <sup>™</sup> <b>Plus</b> : 3-day plateable hepatocytes
5	Application	Toxicology testing, ADME, drug development
	Assays	Metabolism, hepatotoxicity, transporter uptake, clearance assay
	Suspension Hepatocyte Offering	<b>HepatoXcell™ Eco</b> : Suspension hepatocytes
	Hepatocyte	HepatoXcell™ Eco: Suspension hepatocytes  ADME, Drug development

# **ATCC®** upcoming hepatic offerings



- Pooled primary human hepatocytes
- Spheroid/3-D qualified hepatocytes appropriate for MPS
- Non-parenchymal cells (NPC)
- Subcellular fractions S9 microsomes and cytosol
- MPS application data using multiple platforms



## Early access program - HepatoXcell™



- 3 vials of Hepatocytes at a 20% discount
- Hepatocyte Media at a 15% discount
- Free domestic shipping (no dewar charge)



Ask me for a quote!

Michelle Touloumes

Strategic Account Manager, ATCC
mtouloumes@atcc.org



### **Locsense Artemis**







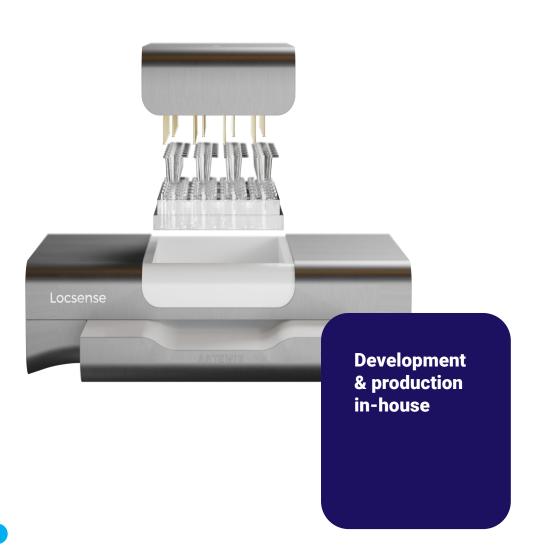
# Susan H. Roelofs, PhD CEO and Founder, Locsense

Dr. Susan Roelofs is the CEO and founder of Locsense B.V., a pioneering laboratory equipment company situated in Enschede, Netherlands. There, she is responsible for strategy and operations. Dr. Roelofs obtained her MSc degree in Applied Physics from the University of Twente with a specialization in Biophysical Engineering. She completed her PhD in Lab-on-Chip technology at the University of Twente in 2015.

Locsense focuses on the development of in-vitro sensing equipment. Currently Locsense' team consists of 10 persons. Since 2019, Locsense has successfully launched new products, including their flagship device, the Artemis Impedance spectrometer / TEER detector.







# Artemis ST impedance spectrometer

**02** Broad spectrum analysis

Frequency range from 10Hz - 100kHz.

Monitor the barrier function over time while

**Time lapse** 

cells are situated inside the incubator

**03** Easily cleanable

Autoclavable parts in contact with cells

**04** Incubator compatible

Smartlid including cells can be placed inside the incubator





# Applications of barrier integrity monitoring

#### Quality

Cell culture growth, barrier formation

#### **Disease modelling**

Using gene editing, e.g., COPD or atopic dermatitis

#### **Drug effectiveness**

Compound testing



#### **Treatment strategies**

Concentration and duration therapeutics

#### **Toxicology**

Testing of chemicals, e.g., cosmetics

# Aim



# Developing of a highly representative in vitro gutliver model using:

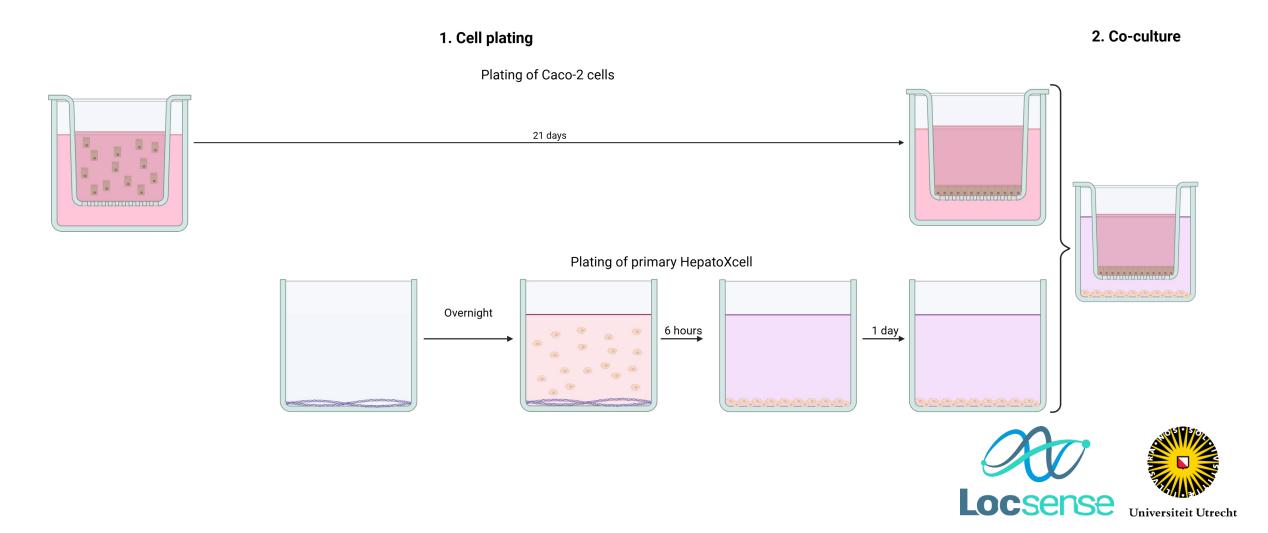
- Caco-2 (ATCC® HTB-37™) gut epithelial cells
- HepatoXcell<sup>™</sup> Pro (ATCC<sup>®</sup> PCS-450-011<sup>™</sup>) primary human hepatocytes





# Plating of Caco-2 cells and HepatoXcell™



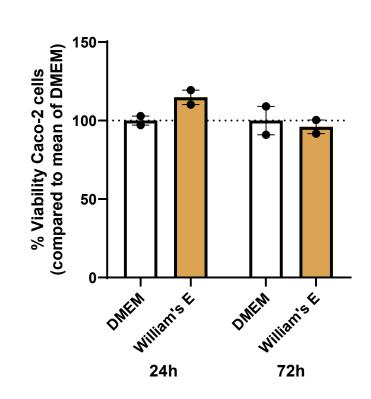


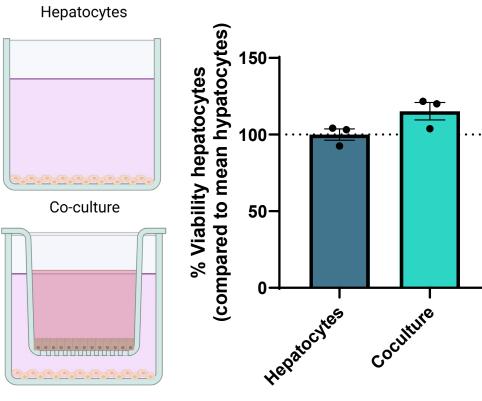
### Viability of the co-culture



DMEM

Williams-E





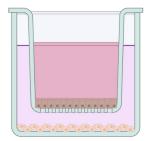




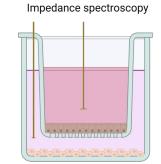
# **Analyzing the co-culture characteristics**



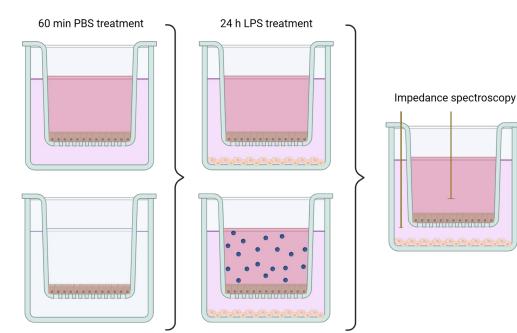
#### 2. Co-culture



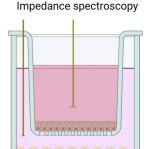
3. Barrier analysis



4. Induce stress on Caco-2 with PBS and/or LPS and barrier analysis



5. Barrier analysis and viability



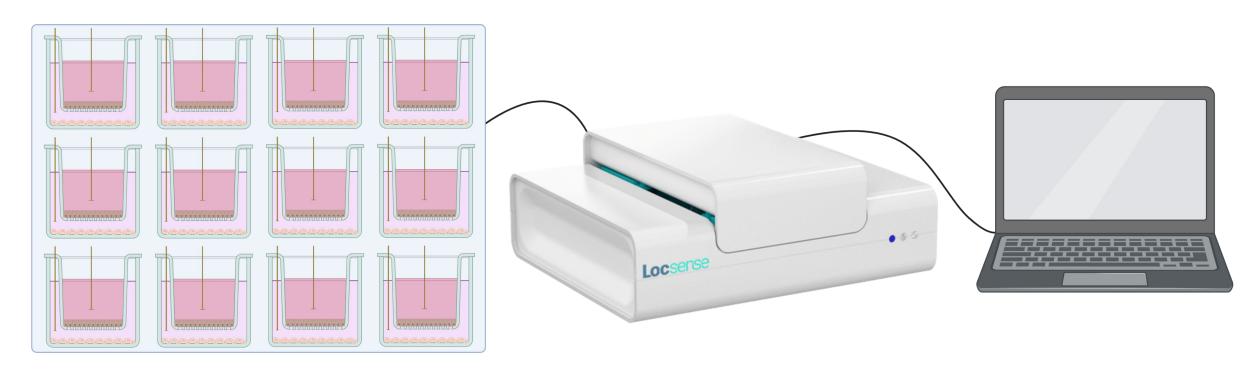






# **Locsense Artemis ST set-up**

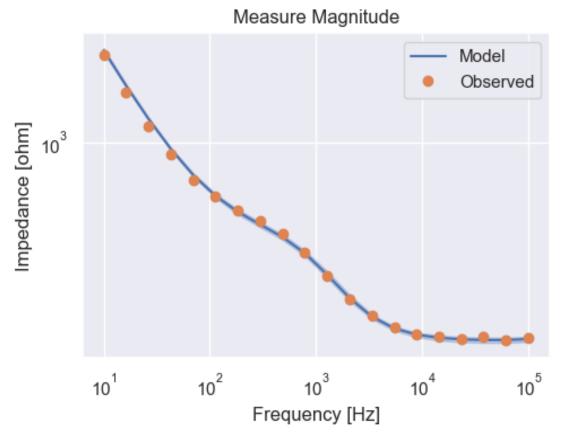


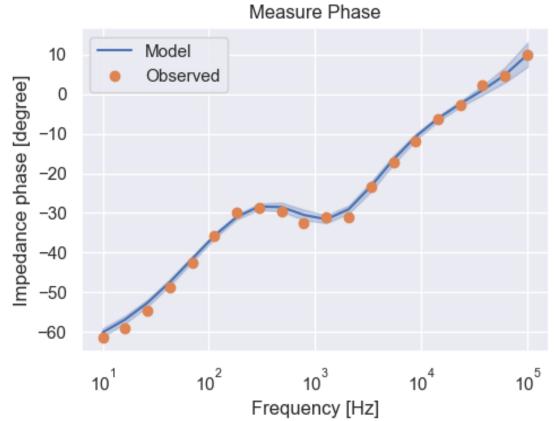




# Circuit model fitting





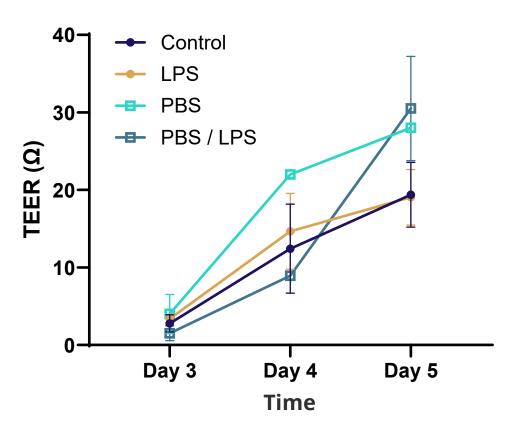


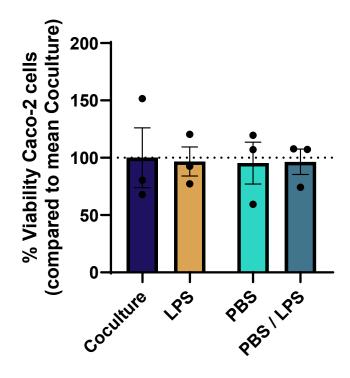


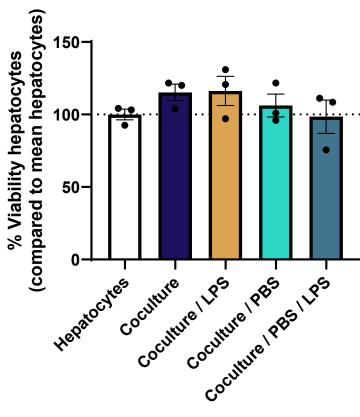


## **Co-culture response to stress**









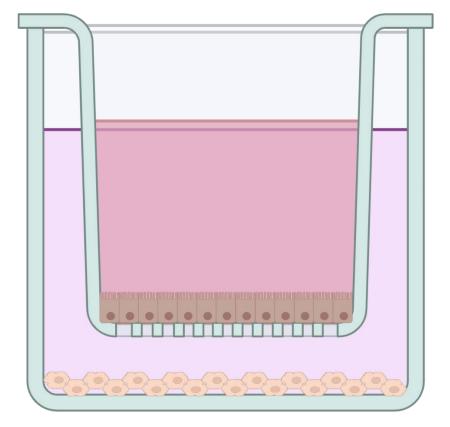




# Conclusions and take-home message



- We have developed a highly representative gut-liver axis model utilizing ATCC's HepatoXcell™ Pro Primary Human Hepatocytes and Caco-2 intestinal cell lines.
- The Artemis ST by Locsense is an effective tool to measure electrical impedance and membrane barrier function.
- The Caco-2 transwell intestinal barrier demonstrates substantial resistance to LPSinduced chemical stress, resulting in the preservation of hepatic culture integrity.





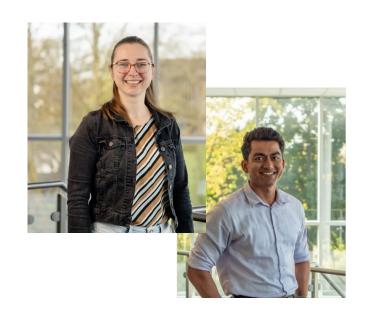
# Acknowledgement







Eline K. Geervliet, PhD Parth Patel





**Utrecht University** 

Marit Zuurveld, PhD



**ATCC** 

Sopheap Sun Ruby E. Thamert Emma Todd Carolina Lucchesi, PhD











# Questions