

August 2018

Value Proposition

Altis Biosystems has developed a patent-pending stem cell technology which recreates the human intestinal epithelium for compound screening and microbiome research.

Our goal is to make drug discovery faster, cheaper, safer and reduce the need for animal testing.

Mission Statement

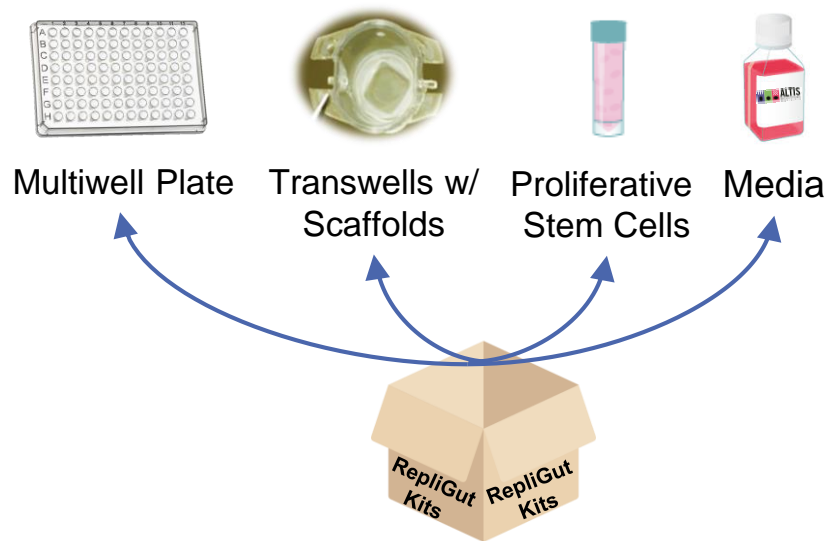
Our mission is to develop, manufacture, and sell innovative research tools and services to accelerate drug development.

Altis is a Contract Research Organization

Altis provides services

- Permeability
- ELISA
- Toxicology
- Transport
- Gene Expression
- Immunohistochemistry
- Custom cell isolation

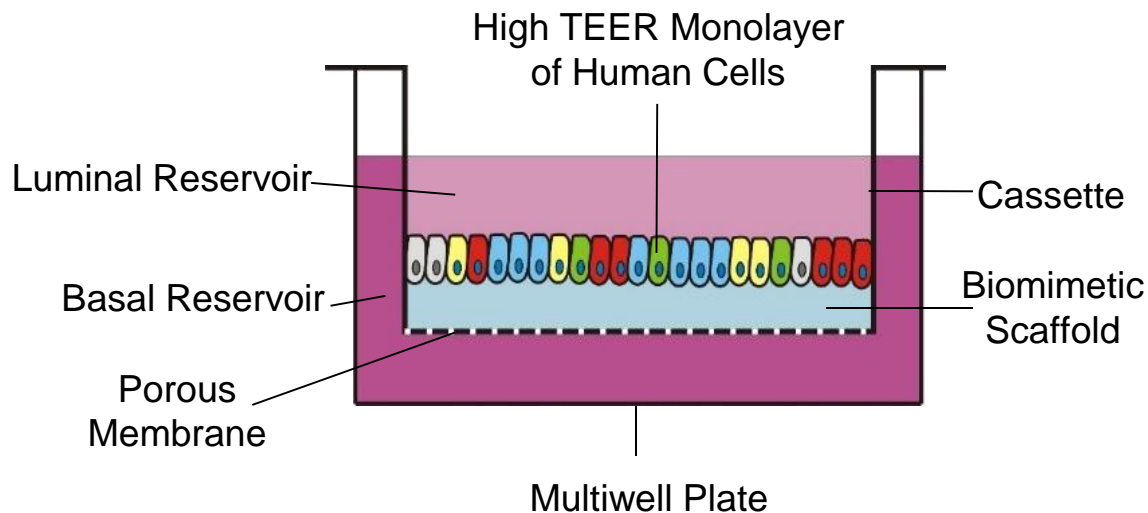
Altis sells RepliGut Kits



RepliGut is available in 6, 12, 24 or 96 well plates

RepliGut Planar

An Individual Tissue Sample



Altis' technology:

- Monolayer of human intestinal stem and differentiated cells
- Either of the small or large intestine
- Uses **proprietary** biomimetic scaffolds on a porous membrane

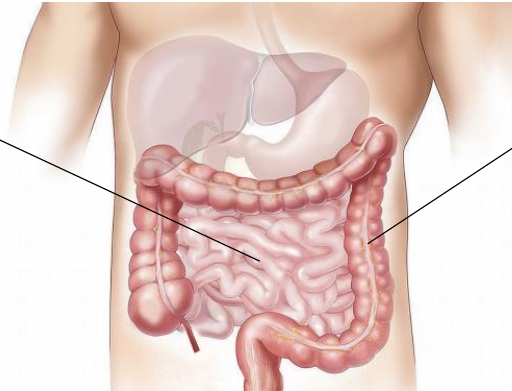
Intestinal Epithelium Biobank

For Each Donor

- Epithelial cells from all regions of transplant-grade intestine
- Demographic information available
- Storage at low passage numbers
- Test on the same donor and region over time

Small Intestine

Duodenum
Jejunum
Ileum



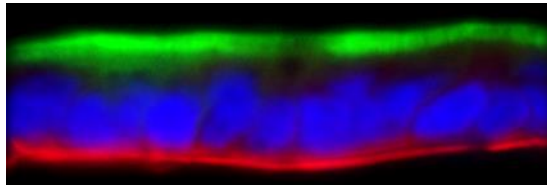
Colon

Ascending Colon
Transverse Colon
Descending Colon

RepliGut Planar Epithelium

Possesses key *in vivo* properties, including:

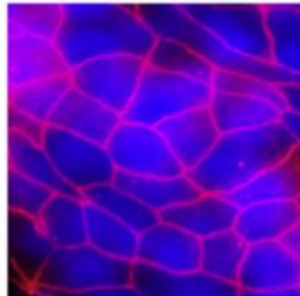
1. Polarized Monolayer



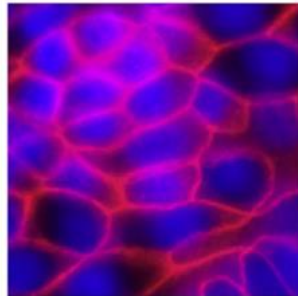
Monolayer in Cross-section:
Apical (Actin)
DNA
Basal (Integrin-β4)

2. Tight Junction Proteins

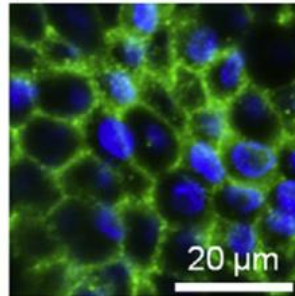
ZO-1/DNA



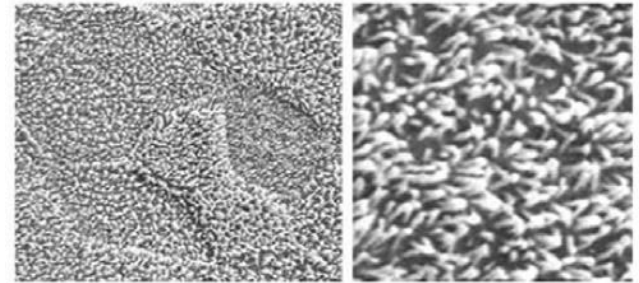
Occludin/DNA



E-cadherin/DNA



3. Microvilli



— 5 μm

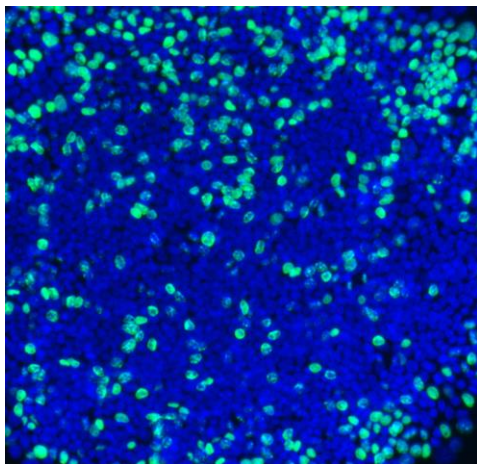
— 1 μm

RepliGut Planar Epithelium

Possesses key *in vivo* properties, including:

4. Proliferative & Differentiated Cell Types

Expansion Media

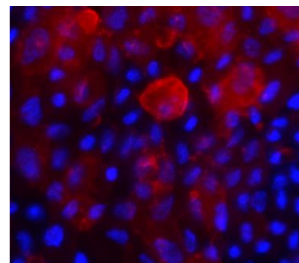


3-hour EdU Pulse

EdU+ Cells
Nuclei

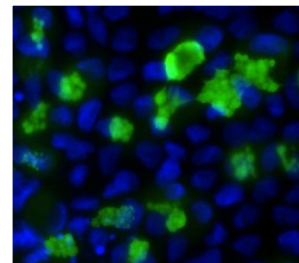
Differentiation Media

Enterocytes



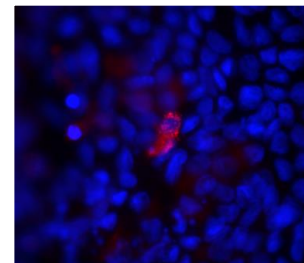
ALP
Nuclei

Goblet Cells



MUC2
Nuclei

Enteroendocrine Cells

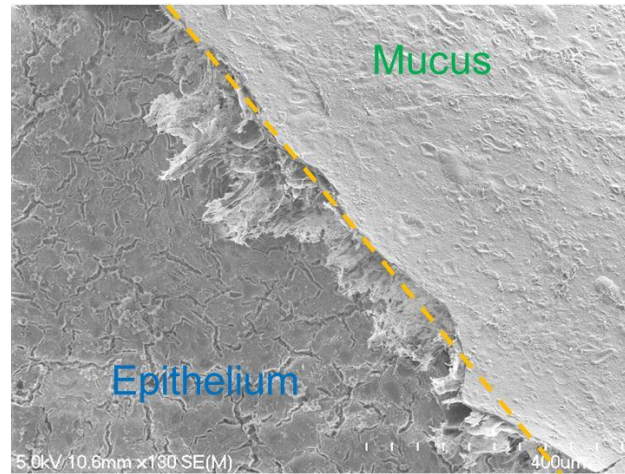
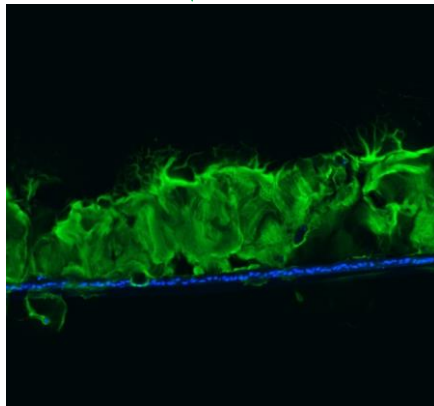
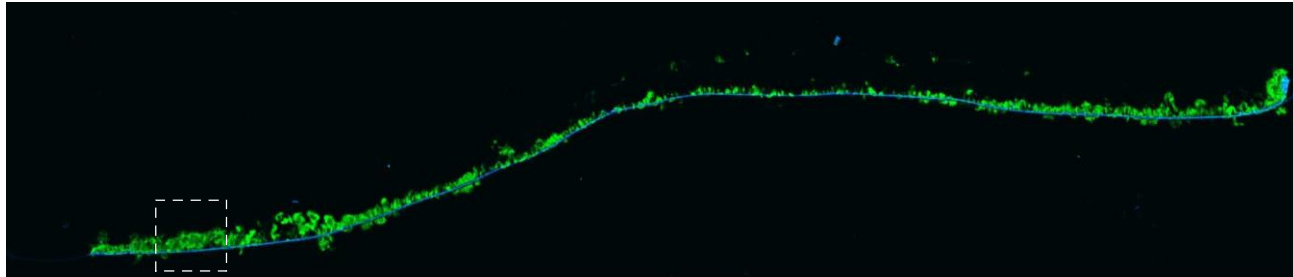


CHGA
Nuclei

RepliGut Planar Epithelium

5. Active Mucus Production

Mucus (Muc2)
Nuclei

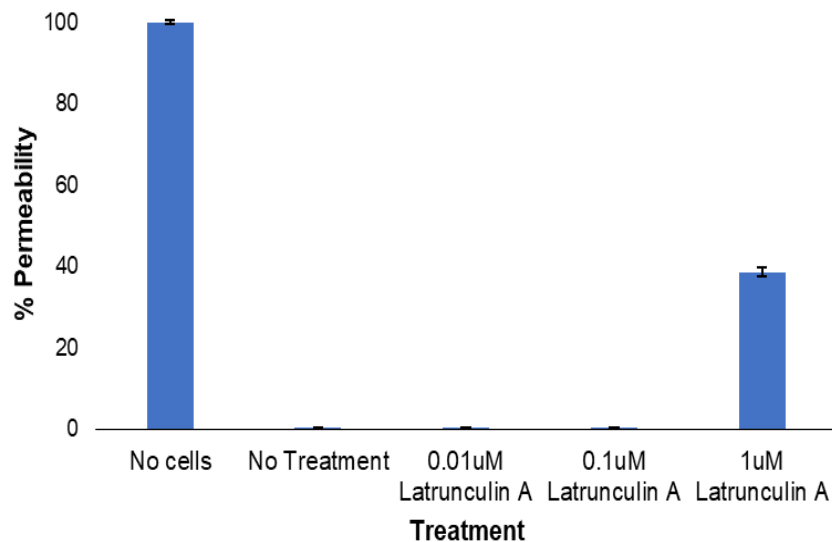


RepliGut Planar Epithelium

Possesses key *in vivo* properties, including:

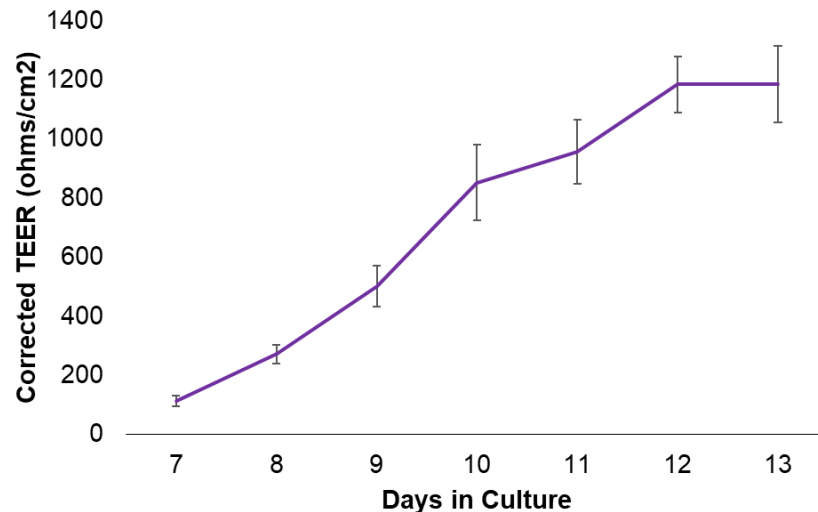
Low permeability and High TEER

Colon Permeability



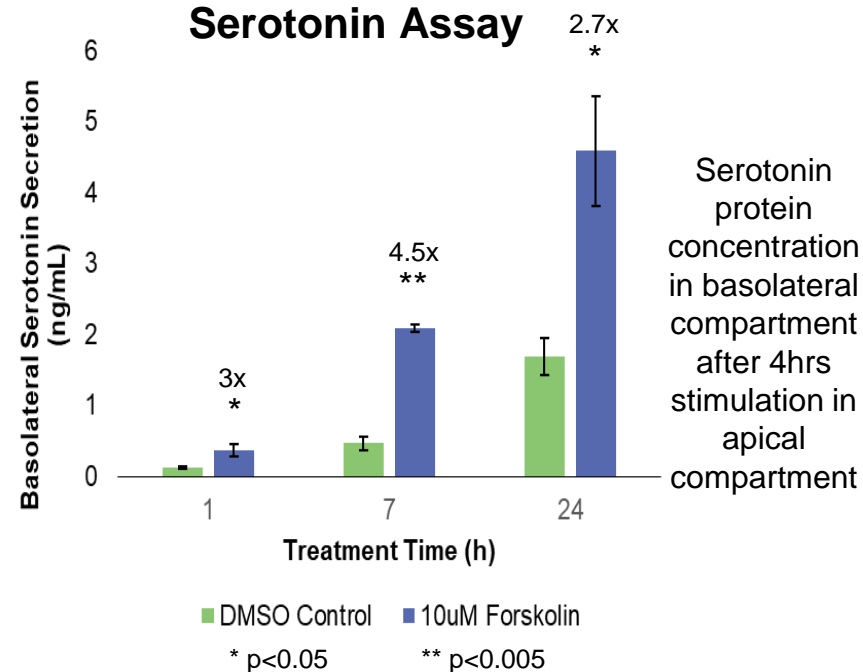
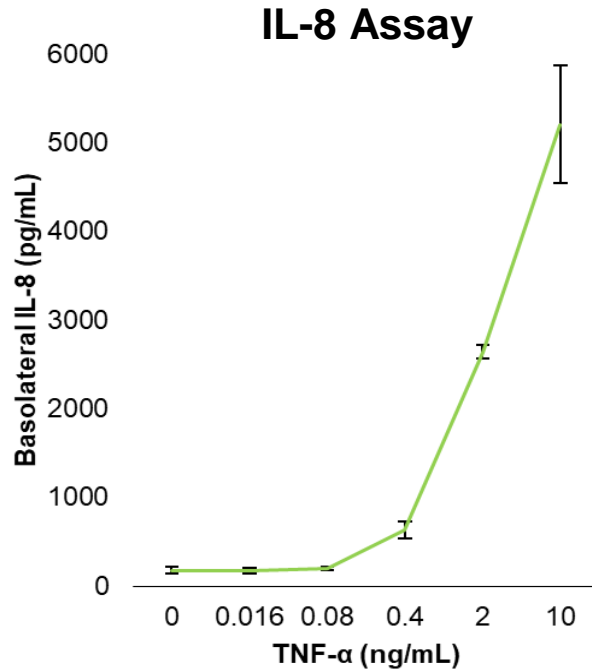
Permeability of FITC-dextran (MW=40,000)

Small Intestine TEER Measurements



RepliGut Planar Epithelium in 96-well transwell

Cytokine and Neurotransmitter Assays



IL-8 protein concentration in basolateral compartment after 4hrs stimulation with TNF- α in basolateral compartment

Protein Expression in RepliGut - Small Intestine

Transporter Proteins

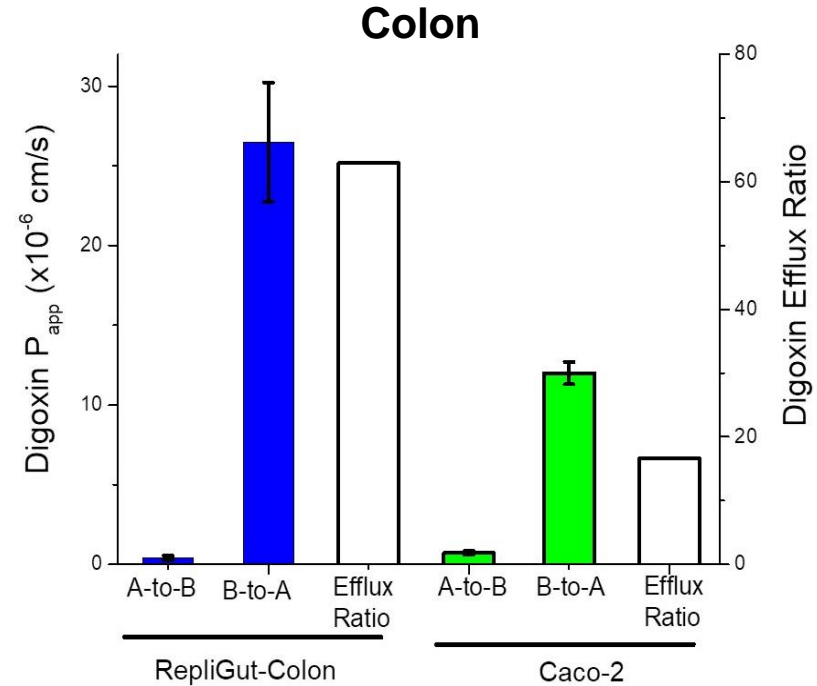
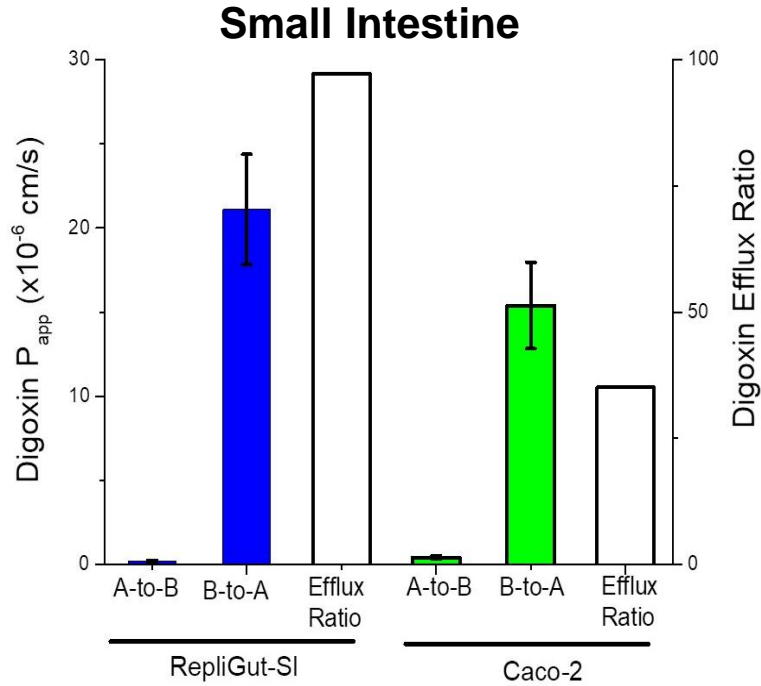
Transporter	Protein Expression	
	RepliGut monolayer	Fresh Tissue
P-gp	+++	+++
BCRP	++	++
MRP1	+	++
MRP2	++	++
MRP3	+	+
MRP6	+	+
OCT3	+	++
NaK ATPase	+++	+++
gamma GTP	+++	+++

Metabolizing Enzyme Proteins

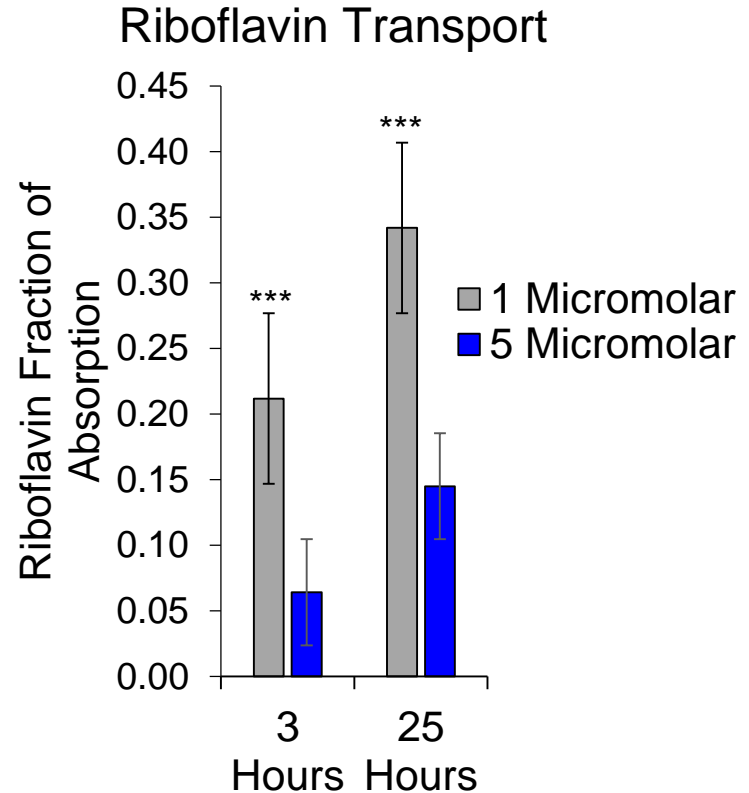
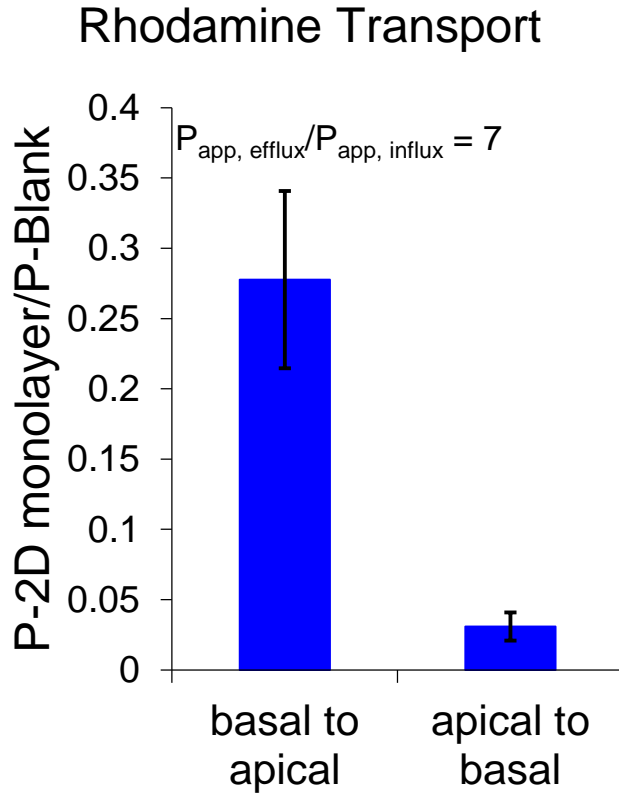
Metabolic Enzyme	Protein Expression	
	RepliGut monolayer	Fresh Tissue
CYP3A4	+	+
UGTB17	+	+
UGTB7	+	+
UGT1A10	+	+
UGT1A1	+	+
UGT2A3	+	-
CES1	+	+

Pgp Transport in RepliGut vs Caco-2

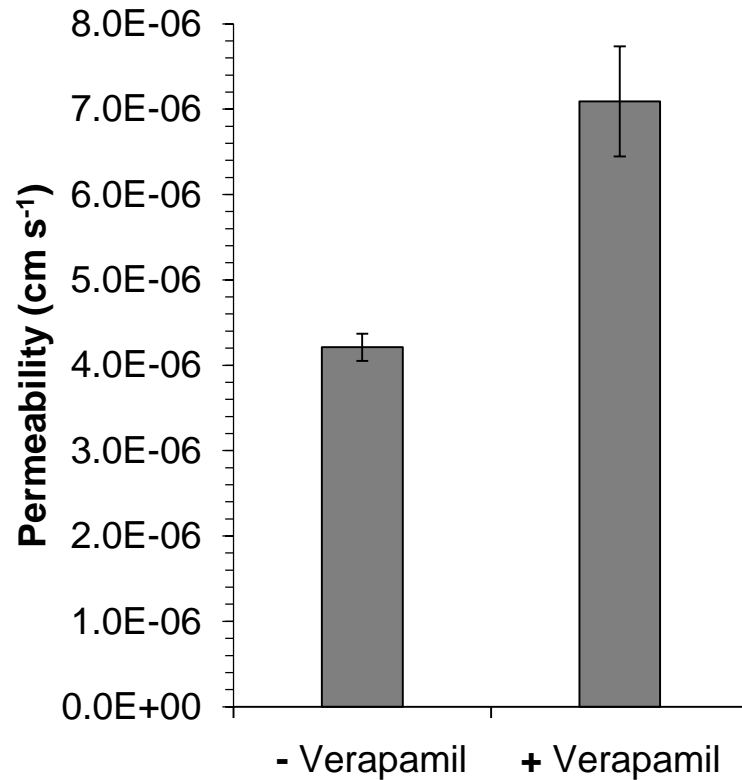
Active Transporters



P-glycoprotein and SLC52A3 Mediated Transport

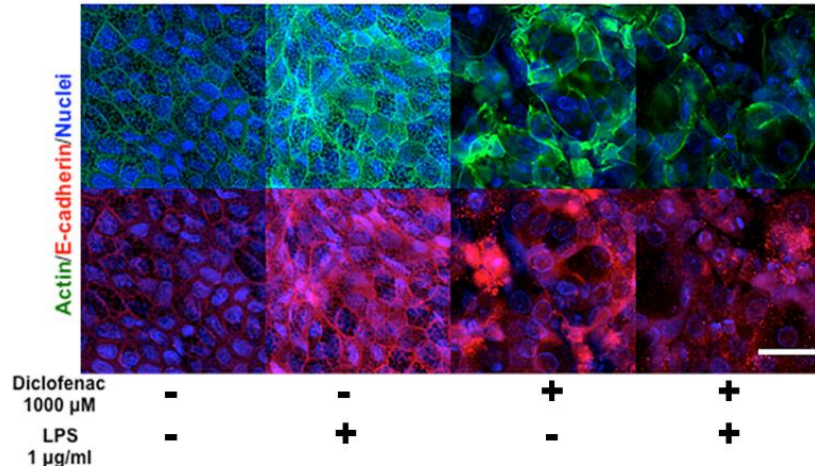


Drug-Drug Interaction Study - Digoxin and Verapamil

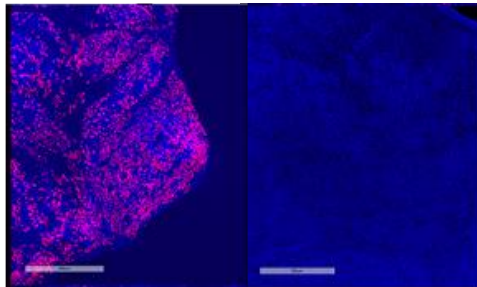


Verapamil blocks digoxin export by P-glycoprotein

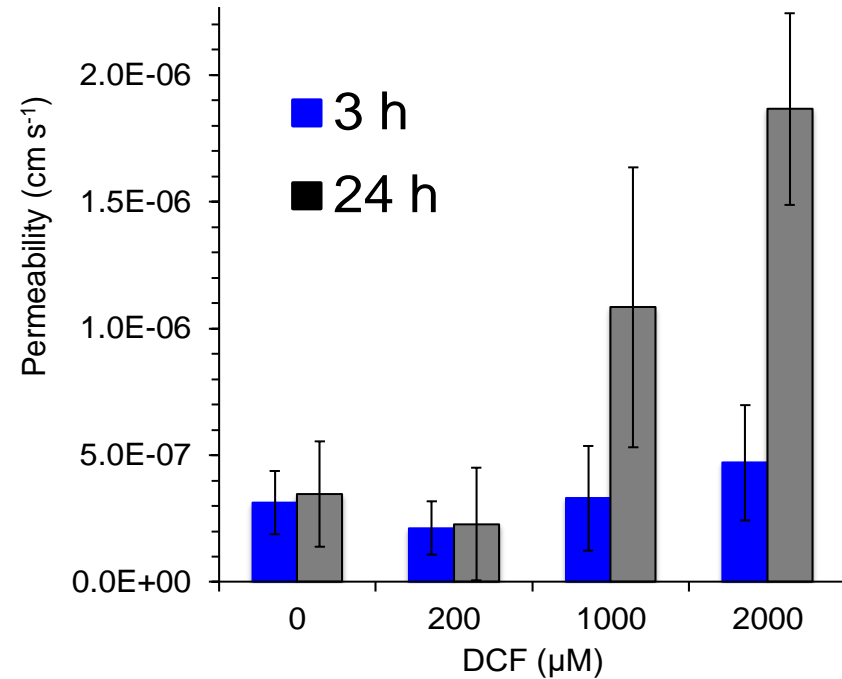
Diclofenac Toxicity on Small Intestine



Diclofenac (μM)
0 1000



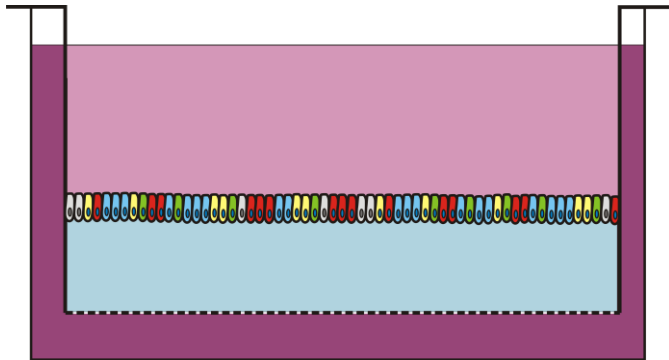
EdU/Nuclei



Two RepliGut Formats

RepliGut Planar

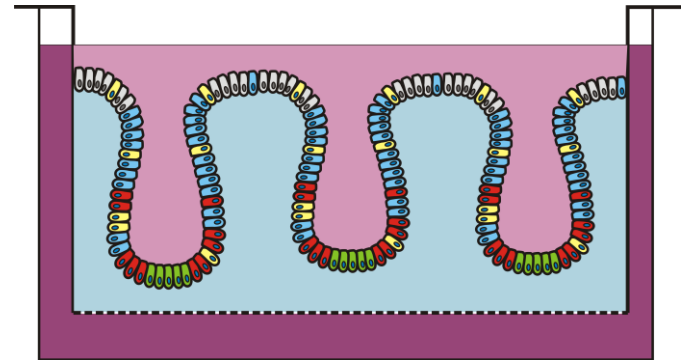
Produces a flat layer of primary cells



Available Now

RepliGut Crypt

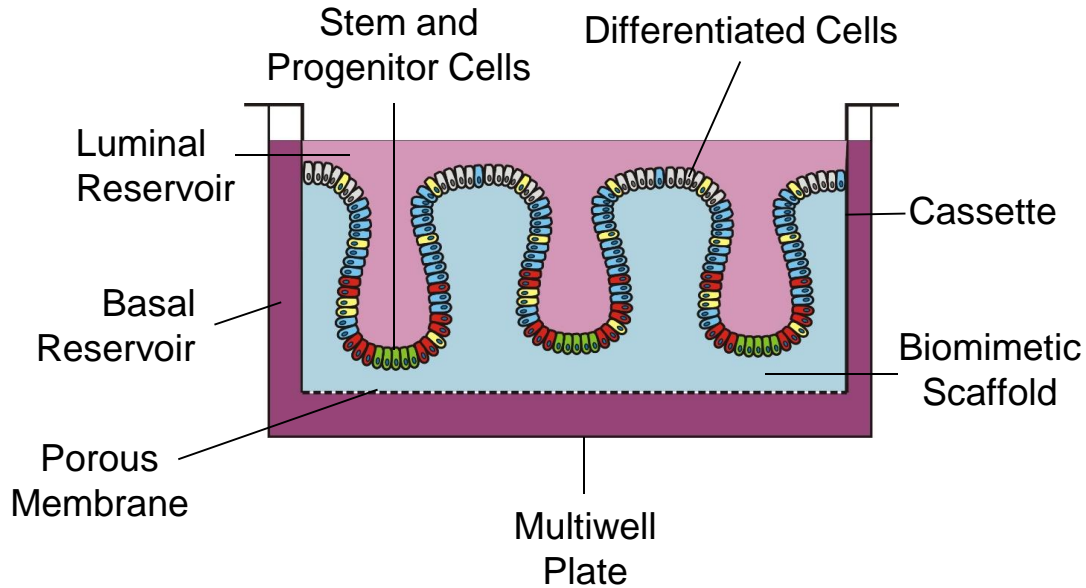
Mimics crypt architecture and polarization



Available 12-18 months

RepliGut Crypt

An Individual Tissue Sample



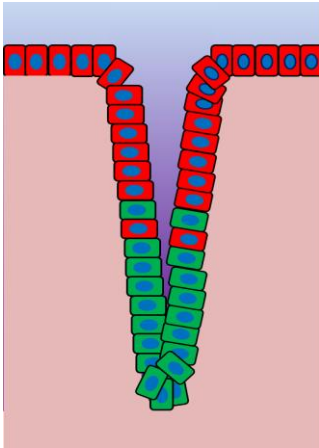
Altis' technology:

- Stem and differentiated cells mimic crypt architecture and polarization
- Either of the small or large intestine
- Uses **proprietary** biomimetic scaffolds on a porous membrane

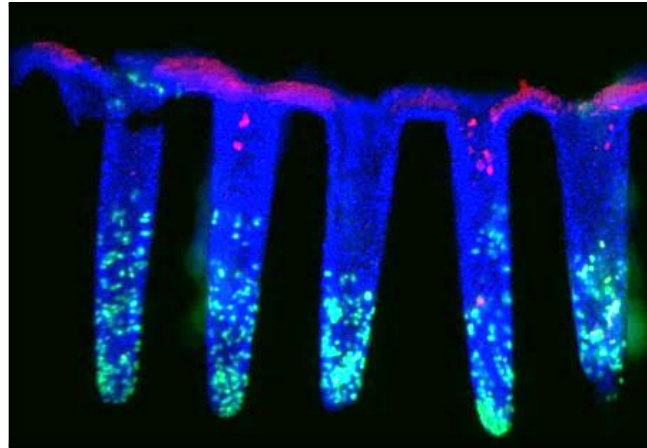
RepliGut Crypt Epithelium

Possesses key *in vivo* properties, including:

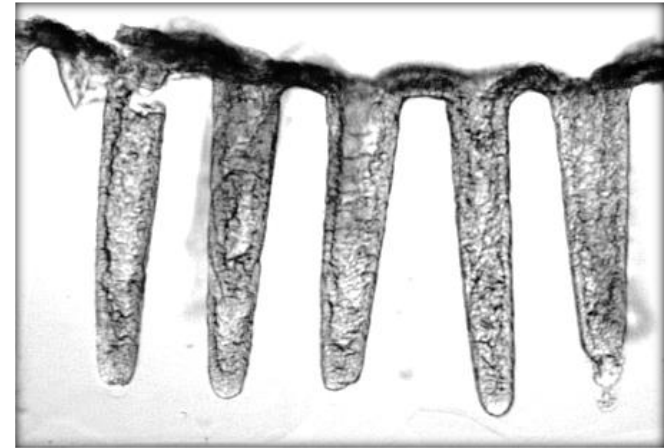
1. Physiologic cell compartmentalization along the crypt axis



Colon Crypt
Schematic



Immunohistochemistry
Differentiated Enterocytes (ALP)
Nuclei
Proliferative cells (EdU)

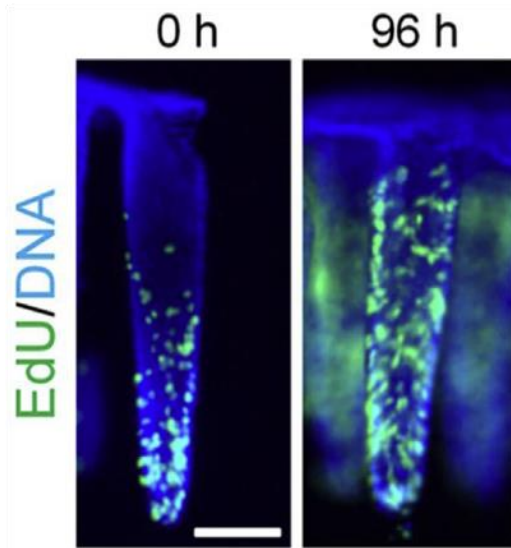


Brightfield

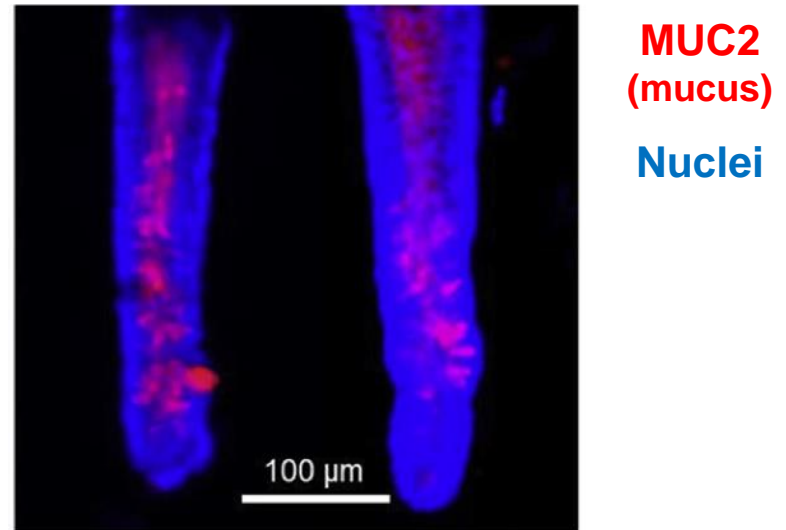
RepliGut Crypt Epithelium

Possesses key *in vivo* properties, including:

2. Cell migration up the crypt



3. Mucus secretion into crypt lumen



Images taken after 24-hour EdU Pulse

The Altis Advantage: Unique Technology

Enables numerous assays: Cytokine secretion, transport, permeability, toxicity, etc.

Transwell format allows for easy access to apical and basolateral compartments

High throughput format allows for multiple treatments per plate

Donor biobank allows for regional specificity with different demographics

Partnerships



Altis is currently interested in working with pharmaceutical and biotech companies to further validate and commercialize its technologies.

Contact Us

Please contact us for additional information

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Go With Your Gut

