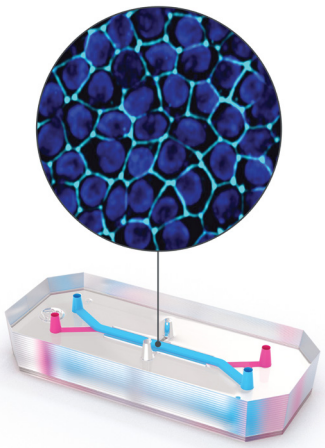
Proximal Tubule Kidney-Chip S1 BioKit

Evaluate drug candidate toxicity at clinically relevant dosing concentrations in a co-culture human kidney model



Overview

Predicting drug-induced kidney toxicity and drug-drug interactions continues to be a challenge in pharmaceutical research due to a reliance on models that do not translate to human response. These models, which include conditionally immortalized proximal tubule epithelial cell lines (ciPTEC) or transgenic mice, routinely fail to predict clinical toxicity as they lack key transporters and biomarkers that are essential for human relevance. The Kidney-Chip S1 recreates the proximal tubule-peritubular capillary interface, combining primary human cells in a dynamic microenvironment to encourage more human-relevant transporter expression and localization. Applications include preclinical toxicity testing of drug candidates across a diverse array of endpoints.

Model Configuration

To recreate the tissue-tissue interface of the proximal tubule, primary human renal proximal tubule epithelial cells (RPTECs) are seeded in the top channel, and primary human renal microvascular endothelial cells (RMVECs) isolated from the glomerulus are seeded in the bottom channel (see **Figure 1**). The model's two-channel structure allows distinct epithelial and endothelial media to be flowed through each channel, enabling physiological cell functionality and model stability for up to 14 days.

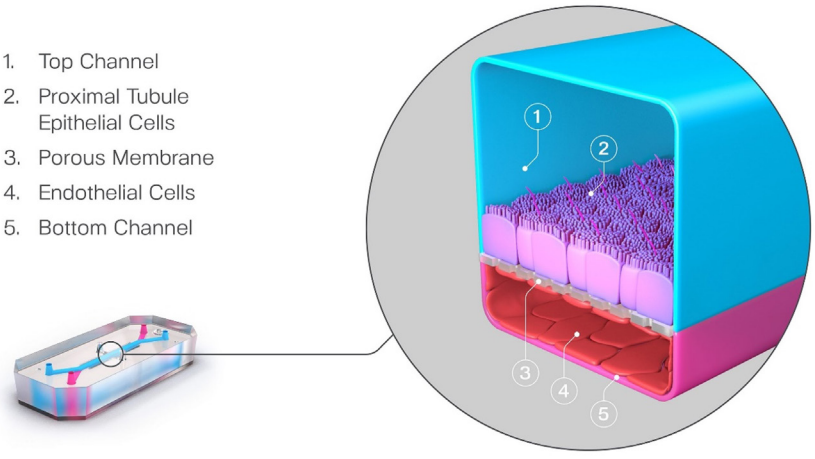


Figure 1: *Proximal Tubule Kidney-Chip S1 Cross Section.*

Model Characterization

Inside the Proximal Tubule Kidney-Chip S1, cells achieve an *in vivo*-like phenotype with high differentiation, functional transporter activity, and appropriate epithelial cell polarity and morphology (including kidney-specific marker expression and a well-defined brush border) (see **Figure 2**). This allows for more physiological analyses of healthy kidney function and drug candidates' safety risk. Long-term culture enables users to take multiple measurements for mechanistic studies, biomarker discovery, and nutrient metabolism.

- **Primary human model:** Avoids translational issues caused by species differences or unrepresentative immortalized cell lines.
- **Stable functionality:** Maintains albumin reabsorption and characteristic cell morphology for up to 14 days in culture.
- **Improved morphology:** Displays significantly improved epithelial cytoarchitecture over static cell culture, with more *in vivo*-like polarization, cell height, and cilia formation.
- **Enhanced transporter activity:** Unlike Transwell models, restores expression and functionality of key renal transporters, which are typically lost during cryopreservation (see **Figure 3**).

Learn more in the Proximal Tubule Kidney-Chip Characterization Note.

Model Morphology

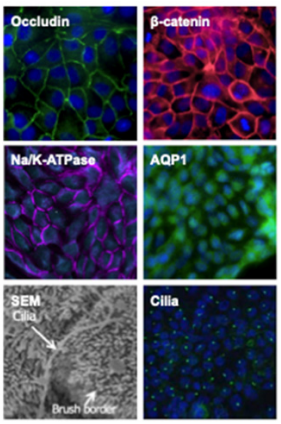


Figure 2: *Immunofluorescent staining and SEM imaging demonstrates expression of kidney-specific markers as well as presence of cilia and a brush border membrane.*

Renal Transporter Gene Expression

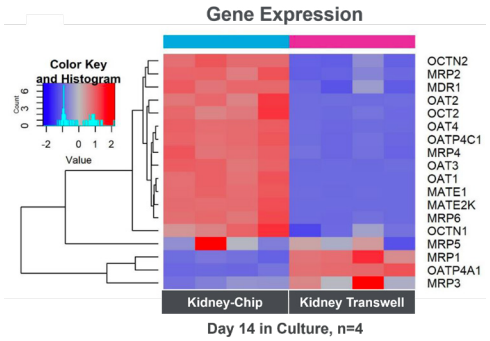


Figure 3: *Kidney-Chip S1 displays enhanced expression of uptake and efflux transporters that are critical for renal clearance.*

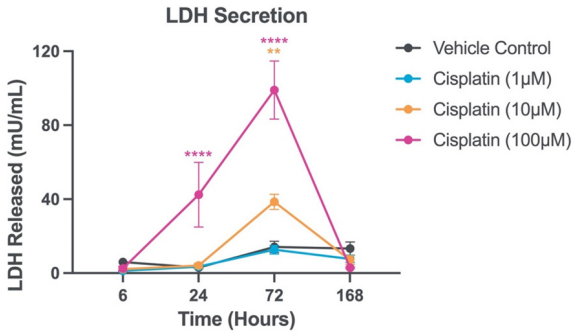
SUPPORTED APPLICATION

Toxicology

Unlike conventional *in vitro* models, the Proximal Tubule Kidney-Chip S1 can model mechanisms of drug-induced nephrotoxicity at clinically relevant drug concentrations. Side-by-side studies demonstrate the Kidney-Chip S1 has improved concentration-dependent responses compared to static epithelial monoculture models. A diverse array of endpoints can be measured in a time-dependent manner, including:

- **Morphological damage**
- **Cell death:** LDH, ALP, Caspase 3/7 (See **Figure 4**)
- **Oxidative stress:** Reactive oxygen species
- **Kidney injury panel:** KIM-1, clusterin, TFF3, VEGF

LDH Release



2-way ANOVA, Uncorrected Fisher's LSD Test (n=3). **p<0.01, ****p<0.0001, in comparison to vehicle control at that timepoint. Error bars mean ± SEM.

Figure 4: *Cisplatin exposure demonstrates a concentration- and time-dependent release of LDH from Proximal Tubule Kidney-Chip S1 epithelial channel effluent.*

Compatible with Zoë Culture Module®

The Proximal Tubule Kidney-Chip S1 is designed to be cultured using a Zoë Culture Module, a complete Organ-on-a-Chip platform that provides the dynamic conditions needed to culture up to 12 Organ-Chips per Zoë.

Proximal Tubule Kidney-Chip S1 Specifications

Specification	Details
Validated applications	Toxicology
Storage conditions	• Cells: Store in liquid nitrogen • ER-1® Reagent: -20°C • ER-2® Reagent: 2–8°C • Other kit components: Ambient temperature (15–25°C)
Shelf life	• Cells: Guaranteed for 6 months from date of shipment • Organ-Chip consumables: 2 years from date of manufacture • ER-1 & ER-2: 1 year from date of manufacture
Cell types	Emulate-qualified primary renal proximal tubule epithelial cells (RPTECs) and primary human renal microvascular endothelial cells (RMVECs), isolated from glomerulus
Characterization endpoints	• Transcriptomic analysis demonstrating expression of key gene signatures • qPCR of SGLT2, Aquaporin-1, and NA+/K+ ATPase • Immunofluorescent staining of tight junction proteins and kidney-specific markers (β-catenin, AQP-1, occludin and Na+/K+ ATPase) • Functional albumin reabsorption

Ordering Information

Every Proximal Tubule Kidney-Chip S1 BioKit includes the essential components needed to create the Proximal Tubule Kidney-Chip S1—including Emulate-qualified cells—and is available in multiple sizes to meet various study needs.

To learn more, visit emulatebio.com/kidney-chip

Product Name	Primary Human Cells	Chips per Kit	Catalog Number
Proximal Tubule Kidney-Chip S1 BioKit	Chip-S1® Stretchable Chips, Pod® Portable Modules, ER-1® / ER-2® Chip Activation Reagents, Steriflip® Filter, Emulate-qualified human cells: Primary renal proximal tubule epithelial cells (RPTECs) and primary human renal microvascular endothelial cells (RMVECs), isolated from glomerulus	12	BIO-KH-C012
		24	BIO-KH-C024