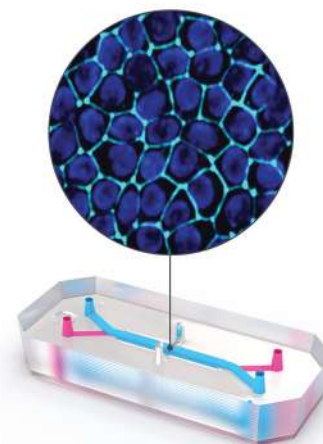


# Emulate Human Proximal Tubule Kidney Bio-Kit

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

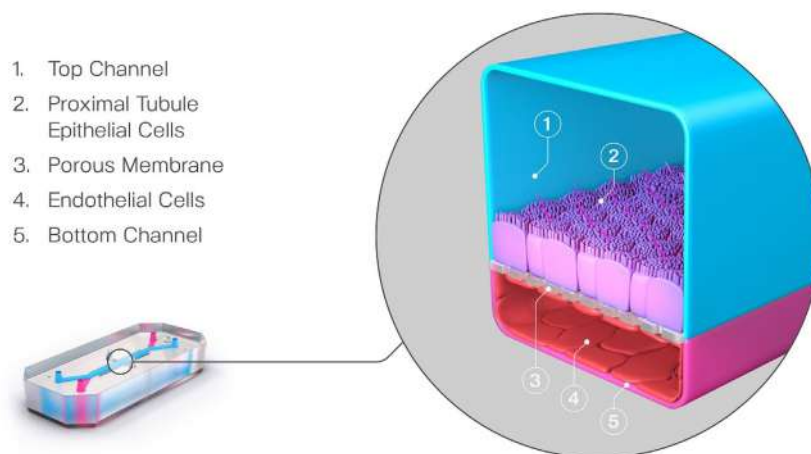


## Overview

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 Emulate Kidney-Chip 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 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 Cross Section.

## Model Characterization

Inside the Proximal Tubule Kidney-Chip, 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.

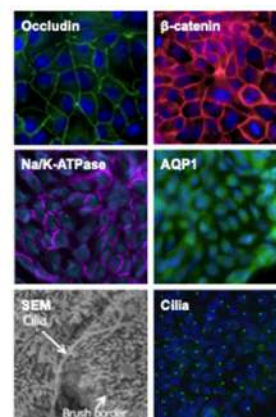
### SUPPORTED APPLICATION

## Toxicology

Unlike conventional *in vitro* models, the Proximal Tubule Kidney-Chip can model mechanisms of drug-induced nephrotoxicity at clinically relevant drug concentrations. Side-by-side studies demonstrate the Kidney-Chip 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:

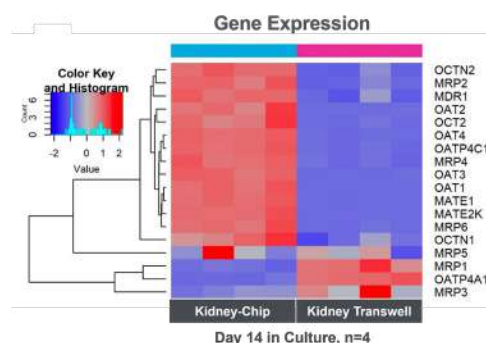
- **Morphological damage**
- **Cell death:** LDH, ALP, Caspase 3/7 (See **Figure 4**)
- **Oxidative stress:** Reactive oxygen species
- **Kidney injury panel:** KIM-1, clusterin, TFF3, VEGF

### Model Morphology



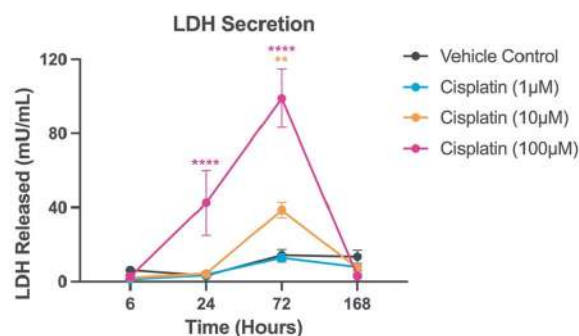
**Figure 2:** Immunofluorescent staining and SEM imaging demonstrates expression of kidney-specific markers as well as presence of cilia and brush border.

### Renal Transporter Gene Expression



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

### 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 epithelial channel effluent.

## Part of the Human Emulation System®

The Proximal Tubule Kidney-Chip is designed to be cultured using the Human Emulation System, a complete Organ-on-a-Chip solution that includes instruments, consumables, and software, providing the dynamic conditions needed to culture up to 12 Organ-Chips.



## Proximal Tubule Kidney-Chip Specifications

| Specification                     | Details                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Validated applications</b>     | Toxicology                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>Storage conditions</b>         | <ul style="list-style-type: none"> <li>Cells: Store in liquid nitrogen</li> <li>ER-1® Reagent: -20°C</li> <li>ER-2® Reagent: 2-8°C</li> <li>Other kit components: Ambient temperature (15-25°C)</li> </ul>                                                                                                                                                                                                                                                                       |
| <b>Shelf life</b>                 | 1 year from date of manufacture                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Cell types</b>                 | Emulate-qualified primary renal proximal tubule epithelial cells (RPTECs) and primary human renal microvascular endothelial cells (RMVECs), isolated from glomerulus                                                                                                                                                                                                                                                                                                             |
| <b>Characterization endpoints</b> | <ul style="list-style-type: none"> <li>Transcriptomic analysis demonstrating expression of key gene signatures</li> <li>qPCR of SGLT2, Aquaporin-1, and Na<sup>+</sup>/K<sup>+</sup> ATPase</li> <li>Immunofluorescent staining of tight junction proteins and kidney-specific markers (b-catenin, AQP-1, occludin and Na<sup>+</sup>/K<sup>+</sup> ATPase)</li> <li>Scanning electron microscopy of cilia and brush borders</li> <li>Functional albumin reabsorption</li> </ul> |

## Ordering Information

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

To learn more, visit [emulatebio.com/kidney-chip](https://emulatebio.com/kidney-chip)

| Product Name                   | Primary Human Cells                                                                                                                                                                                                                                                                             | Chips per Kit | Catalog Number |
|--------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|----------------|
| Proximal Tubule Kidney Bio-Kit | 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    |