

## Features

- Corneal Three Dimensional Structure with
- Tight Junctions
- Constructed with Normal Human Corneal
- Epithelial Cells
- Native Corneal Morphology, Physiology & Barrier
- Quantifiable, Objective Endpoints
- Topical Testing of Ophthalmics
- Cost-Effective Alternative to Animal Testing

## Ideal Applications:

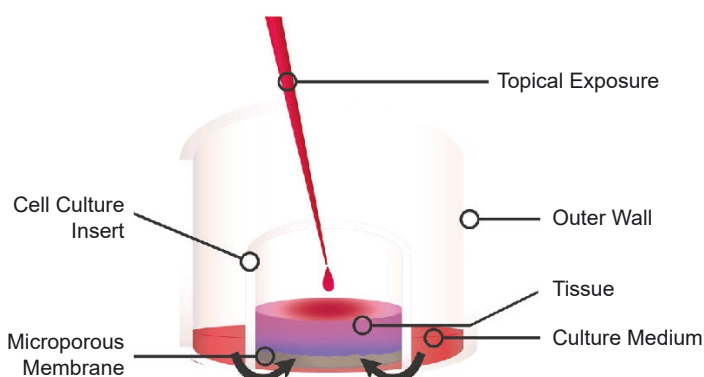
- Drug permeability
- Infection Studies
- Eye-related Bioavailability
- Assessment
- Testing of Ophthalmic Products

## The EpiCorneal Model

Mattek's EpiCorneal ocular tissue model consists of normal human Corneal Epithelial cells which have been cultured to form a stratified, squamous epithelium which closely parallels normal human corneal tissue. The corneal cells, which are cultured on specially prepared cell culture inserts using serum free medium, differentiate to form a multi-layered structure containing tight junctions and express cornea-specific drug transporters and enzymes. Water soluble, non-water soluble and neat test materials can be directly applied to EpiCorneal tissue model.

The EpiCorneal tissue model exhibits *in vivo*-like morphological and growth characteristics which are uniform and highly reproducible. EpiCorneal consists of highly organized basal cells which progressively flatten out as the apical surface of the tissue is approached, analogous to the normal *in vivo* corneal epithelium. EpiCorneal is mitotically and metabolically active and releases many of the pro-inflammatory agents (cytokines) known to be important in ocular irritation and inflammation.

Culture medium is fed through microporous membrane

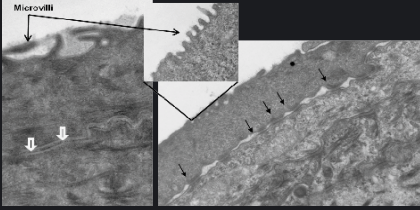


Dosing of the COR-100 tissue model grown in cell culture inserts at air liquid interface (topical tissue surface exposed to air).

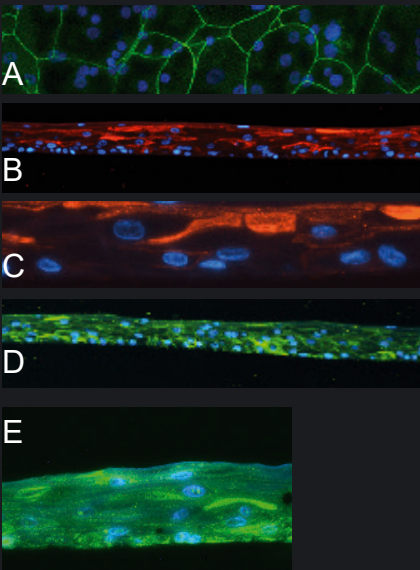
## Histology of EpiCorneal



Histological cross-sections of EpiCorneal tissue model. Formalin fixed, paraffin embedded, H&E stained cross-section of EpiCorneal tissue model. Tissue structure closely parallels human corneal epithelium.

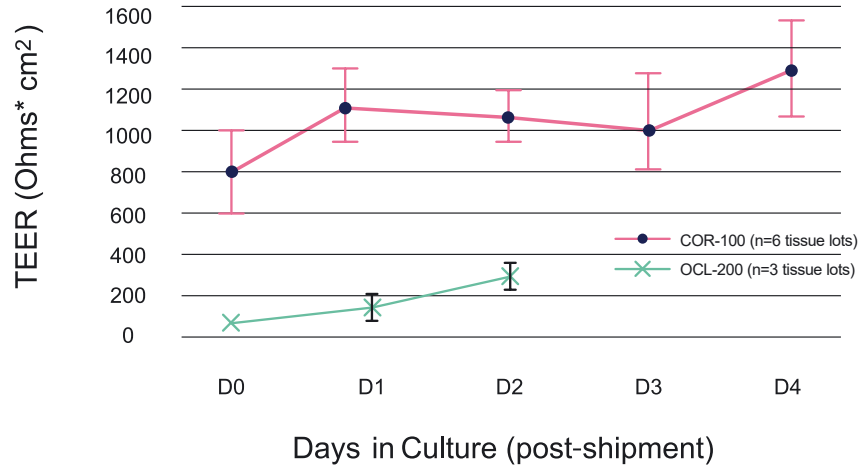


Ultrastructural features of COR-100 tissue. Apical cell layer of reconstructed tissue. Open arrows point to microvilli on the surface of the tissue. Tight junctions (white arrows) and desmosomes (closed arrow) are observed at the junction of adjacent epithelial cells.



Expression of cornea-specific markers by EpiCorneal tissue model (COR-100). Immunohistochemical staining for: A. Tight junction protein ZO-1 (green), 20X. B and C. D and E. Aldehyde Dehydrogenase-3 (ALDH-3A1) (green, D. 10x and E. 40x). A. Confocal microscopy (top view) and B-E. Fluorescent microscopy (tissue sections). Blue - DAPI counter-staining of nuclei.

## Transepithelial Electrical Resistance of COR-100 and OCL-200



Transepithelial Electrical Resistance (TEER) of EpiCorneal (COR-100, comprised of corneal epithelial cells) and EpiOcular (OCL-200, comprised of keratinocytes) tissue models. Note high TEER of COR-100 (avg. > 600  $\Omega \cdot \text{cm}^2$ ) when compared to OCL-200 (~200  $\Omega \cdot \text{cm}^2$ ). Culture area is 0.6  $\text{cm}^2$ .

Target	Mean Ct		Average Fold Increase in gene expression for COR-100 compare to OCL-200
	COR-100	OCL-200	
ABCB1	35.00 ( $\pm 3.14$ )	37.01 ( $\pm 2.11$ )	19.67
ABCC1	27.50 ( $\pm 3.50$ )	26.14 ( $\pm 0.50$ )	1.88
ALDH3A1	23.48 ( $\pm 3.49$ )	26.54 ( $\pm 0.64$ )	40.89
TXNRD1	26.76 ( $\pm 3.56$ )	25.94 ( $\pm 0.42$ )	2.77
MUC4	33.47 ( $\pm 2.58$ )	32.43 ( $\pm 1.28$ )	2.37
GAPDH	21.01 ( $\pm 3.17$ )	18.72 ( $\pm 1.63$ )	1.00
n (tissue lots) =	6	3	

Expression of drug transporters and cornea-specific markers in EpiCorneal tissue model. qPCR data shows expression of ABCB1 (p-gp) and ABCC1 (CFTR/MRP) - ATP-binding cassette, efflux transporters, multidrug resistance proteins with important role in drug disposition and distribution. Aldehyde Dehydrogenase 3 (ALDH3-A1) promotes resistance to UV and 4-hydroxy-2-nonenal-induced oxidative damage in the cornea. Pyridine nucleotide oxidoreductase (TXNRD1 or TrxR1) protects against oxidative stress. MUC4 - Mucin 4 is found predominantly in the most superficial cell layers in stratified corneal epithelium.