

# 3D Blood-Brain Barrier Small Molecule Transport Assay

Human brain microvascular endothelial cells (HBMEC)

## OrganoService

- **Kickstart drug permeability studies in a physiologically relevant 3D human BBB model**  
Perform your BBB transport assay in a perfusable human brain microvascular endothelial model
- **Robust and reproducible assay**  
Automated workflow ensures consistent performance and data quality
- **Complement your BBB transport studies with additional toxicity studies**  
Assess the toxicity of your compounds and their effect on the HBMEC barrier with our OrganoService BBB toxicity assay
- **Sampling & data reporting in one go**  
Receive basal and apical samples, as well as post-assay barrier QC data
- **Membrane-free permeability**  
Transport assay executed without the obstruction of artificial membranes

# About OrganoService

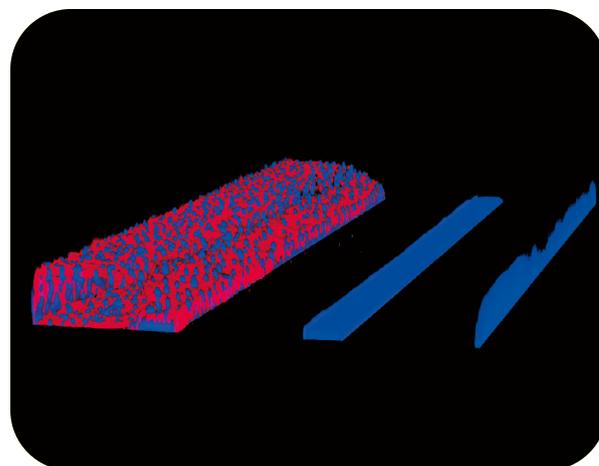
## Blood-Brain Barrier Small Molecule Transport Assay

**Profiling and screening of your compounds with a high-throughput Small Molecule Transport Assay on our established HBMEC blood-brain barrier model.**

### **The role of the blood- brain barrier in drug development**

The blood-brain barrier (BBB) ensures a homeostatic environment for the central nervous system (CNS) and is essential for healthy brain functioning. While the BBB protects the brain from harmful substances, its selectivity can also complicate drug delivery to the brain for CNS disorders, as many small-molecule pharmaceuticals are restricted from entering the brain in sufficient quantities to elicit a response. It is therefore necessary to develop therapeutic drugs that can be delivered to the CNS in a non-invasive manner, without disruption of the BBB. An essential step to achieving this is assessing small molecule transport across the human BBB, where human brain microvascular endothelial cells (HBMEC) are widely used to model the BBB. Therefore, Assessing BBB drug permeability in vitro in a sensitive and reliable manner has been challenging.

Until now, either traditional 2D in vitro models that do not recapitulate key aspects of the BBB, or resource intense, low- throughput animal studies have been used.



*Robust HBMEC BBB model in the OrganoPlate®*

### **Blood-Brain Barrier Small Molecule Transport Assay OrganoService**

To study small molecule transport and penetration kinetics across the BBB in a high-throughput manner, we developed a robust HBMEC BBB model combined with a validated small molecule transport assay. The controls include Digoxin (low/none-crossing) and Propranolol (high-crossing), and each compound is also assessed with 4 cell-free controls. Furthermore, each screen is quality controlled with pre-assay TEER measurements to ensure all HBMEC tubules are leak-tight, as well as with post-assay Barrier Integrity (BI) measurements with sodium fluorescein to confirm barrier maintenance.

### What will you get:

- Screening of your compounds in a validated, physiologically-relevant BBB model
- Screening of up to 6 compounds in one concentration per OrganoPlate
- 4 technical replicates and 4 cell-free controls per compound
- Digoxin and Propranolol used as low and high permeability control compounds
- Basal and apical samples shared, including post-assay QC barrier integrity data
- Extend the compound screen with more plates, in case a larger screen is desired

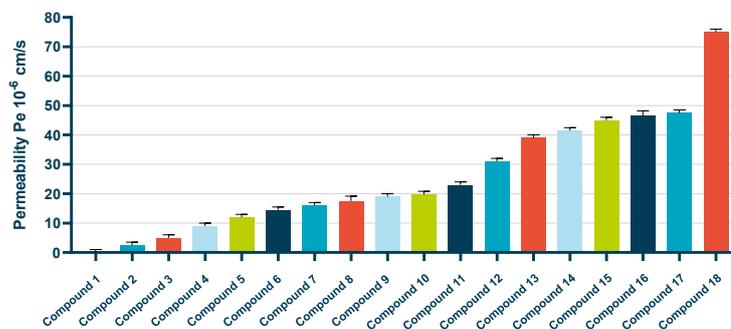
# Results

## Blood-Brain Barrier Small Molecule Transport Assay

### Small Molecule Permeability

- Small molecules were added to the apical side of the HBMEC model
- Samples were collected from the basal side after 1-3 hours
- Basal compound concentrations were measured with mass spectrometry and used to determine the compounds' permeability
- The assay can differentiate between low-, moderate- and high-crossing compounds and shows low variation within tested conditions

BBB permeability values following exposure. Control compounds match expectations based on in-vivo data.



## Service details

### Compound testing

Total compounds per plate

6

Number of concentrations/compound

1

Exposure

Apical

Number of technical replicates

4

Number of controls (own controls also permitted)

2 (Digoxin, Propanol) + cell-free control per compounds (n=4)

Analysis method

Mass spectrometry by customer

Medium samples shared

3 per compound: t=0 working solution, t=2h apical & basal samples

Assay time

2h

Time points

0h, 2h

Data delivery

Basal and apical samples shared, and post-assay barrier QC data

Data points/compound

12

Test article volume requirement

50  $\mu$ L of 1,000X stock solution

Test article solvent

DMSO, PBS, Water

Turn-around time

6-8 weeks