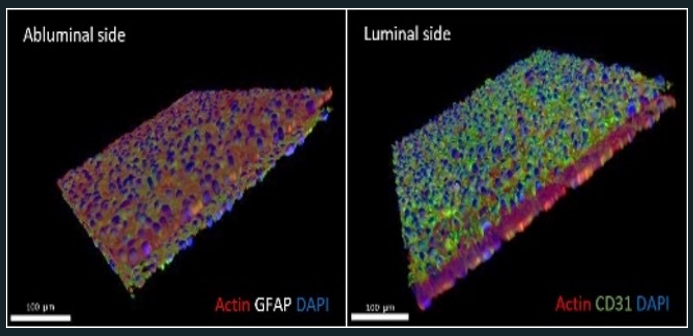
Blood-Brain barrier model

AKITA®
by Finnadvance

Drug permeability testing



Advantage of AKITA® plate & services

> Highest throughput

> Compatible with standard 96 / 384 well plate formats

> Flow & static cell culture

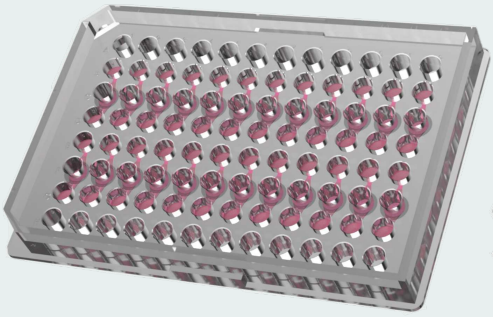
> Plate-only & CRO services

The AKITA® microfluidic plate

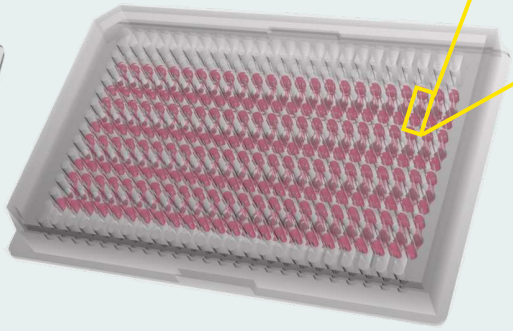
The AKITA® Plate is designed for plug & play workflows, thus ensuring ease of use, robust data collection, and time-saving. With an integrated microporous membrane to separate the apical and basal culture chambers, this platform allows both shear flow and static (co)culture simultaneously.

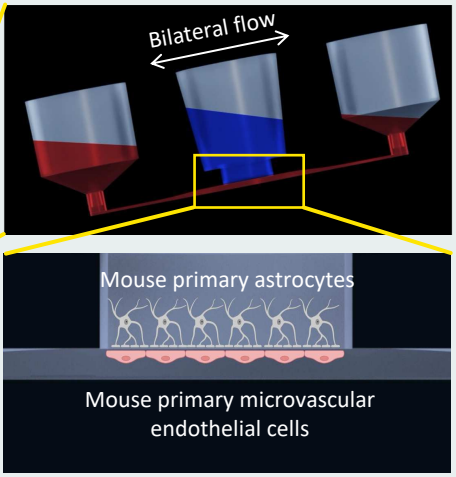
Hence, the AKITA® Plate has the ability to recapitulate the structural and functional complexity of multiple human organs, such as barrier models, air-liquid interface models, microtissue vascularization, and more.

96 well plate format (24 independent testing units)



384 well plate format (96 independent testing units)





The AKITA® microfluidic plates are compatible with standardized 96- and 384-well plate formats, yielding high throughput and easy-to-handle co-culture systems. Additionally, the gravity-driven flow by our AKITA® Wave rocker helps enhance the maturation, tightness, and biological relevance of our gut barrier model.

Blood-brain barrier-on-chip for drug permeability assay

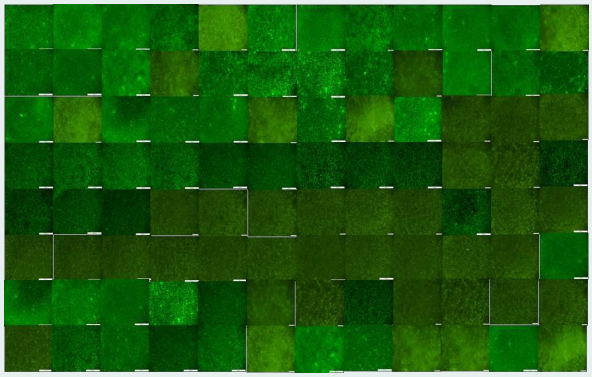
The blood-brain barrier regulates the entry of substances into the central nervous system. It plays a key role in brain homeostasis but may also block the entry of drug compounds thus inhibiting their therapeutic effect. Our engineered blood-brain barrier-on-chip provides a robust, high throughput biomimetic model for permeation studies or immunotherapy screening applications. We de-risk your drug development with a patient-relevant model.

High throughput readout capacity

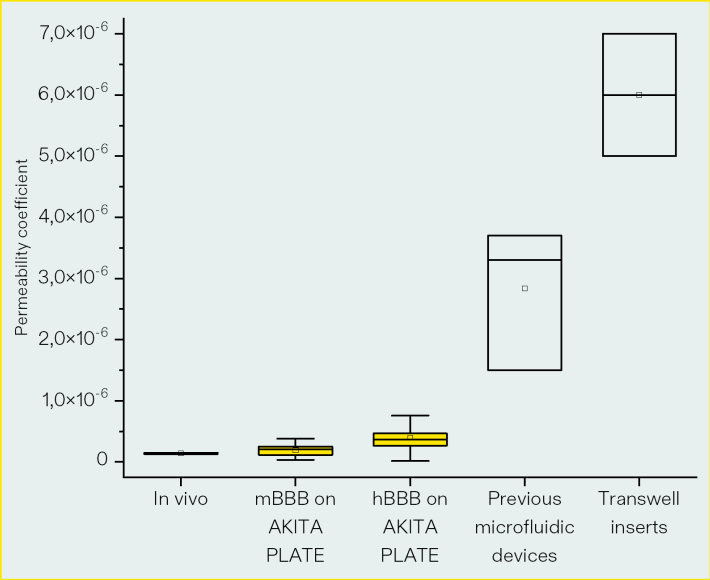
Our microfluidic blood-brain barrier-on-chip platform design includes the static condition of the brain side. In parallel, the dynamic flow condition of the brain microvasculature mimics *in-vivo* conditions.

Our current blood-brain barrier model is established using a co-culture of mouse primary cells: brain microvascular endothelial cells and astrocytes are cultured on opposing sides of a semipermeable membrane.

Live cell analysis is made easy as the AKITA® Plate is compatible with standard microscopes. On the right panel, the barrier integrity was evaluated with calcein staining.



High-throughput semi-automatized live cell imaging of mouse blood brain barrier performed in our 384 well plate (96 independent testing units).



In vivo - like blood-brain barrier permeability with AKITA® Plate

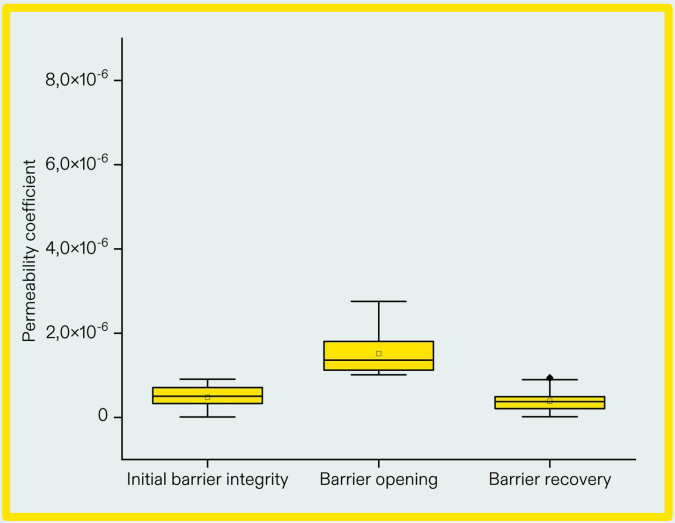
Both mouse (mBBB) and human (hBBB) blood-brain barrier-on-chip are formed after 7 days under flow conditions. The barriers achieve permeability coefficient (Papp) of 1,7E-7 cm/s for 70 kDa dextran, close to the *in-vivo* Papp of 1,5E-7 cm/s (left panel).

The human blood-brain barrier is formed by seeding the human cerebral microvascular endothelial cell line (hCMEC/D3) to the microchannel, this model is currently under development.

Reversible barrier opening assay on AKITA® Plate

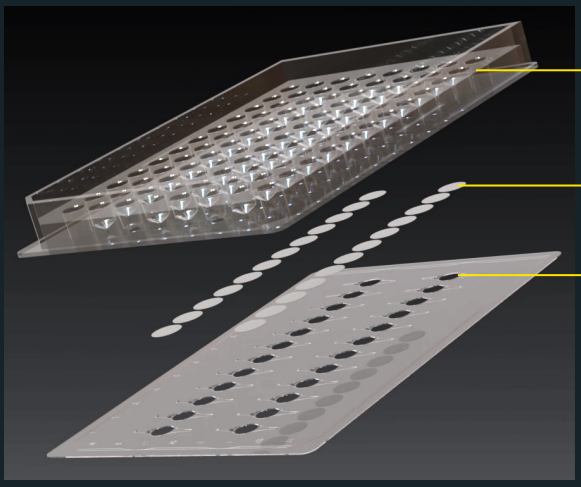
For barrier leakage assays, complex compound or particle permeation studies, blood-brain-barrier permeability can be altered to simulate a leaking barrier.

Barrier opening with a hypertonic solution is reversible as the barrier is recovering the opening after the osmotic shock.

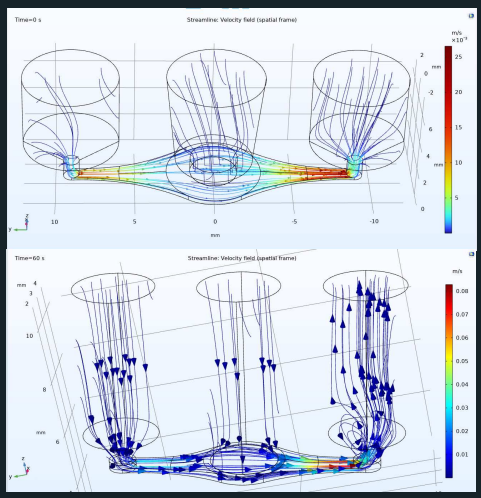


Visualization of the blood-brain barrier markers states about the in vivo-likeness of the blood-brain barrier-on-chip model. The dynamic flow has been noticed to increase the *in vivo* functionality of the model.

The immunofluorescent staining of tight junction marker CD31 highlights the tight junctions formed by the endothelial cells, while the astrocytic GFAP marker shows uniform distribution of astrocytes. These observations support our results from the permeability assays (see page 4 immunostainings).

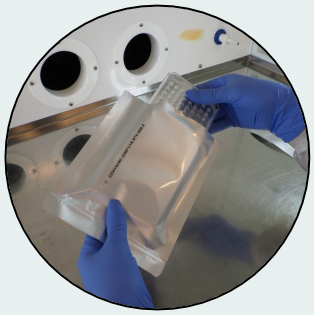


Consistent flow profiles

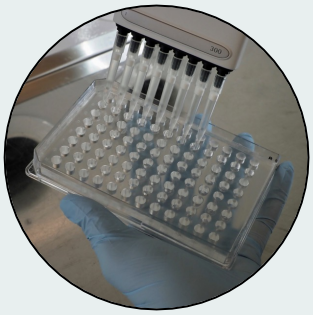


Workflow

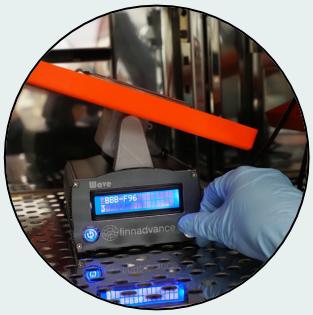
Simplified workflow indicating the main steps, for the detailed procedure please check for model-specific protocols.



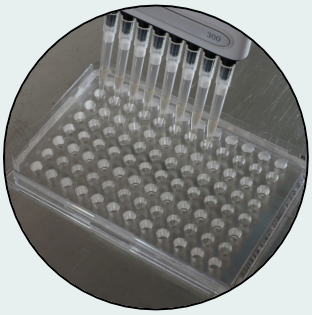
1. Unpack the AKITA® Plate



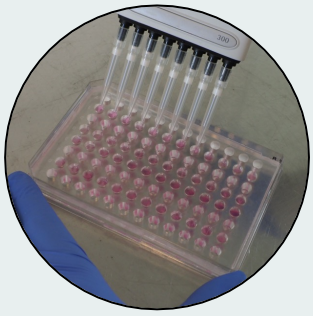
2. Coat with ECM solution



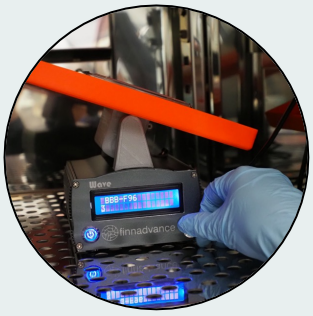
3. Incubate at 37 °C for 2 to 4 hours on the AKITA® Wave rocker



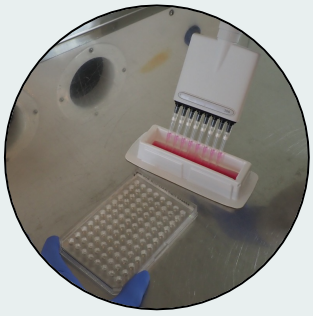
4. Rinse with PBS and then replace with warm culture media



5. Load the cells



6. Incubate at 37 °C on the AKITA® Wave rocker with model-specific settings



7. Change media every 24 hours

Fix the cells for endpoint analysis

8. Fix and store at 4°C

Readouts

One-touch TEER measurement

High content screening and imaging

Live fluorescent and confocal microscopy

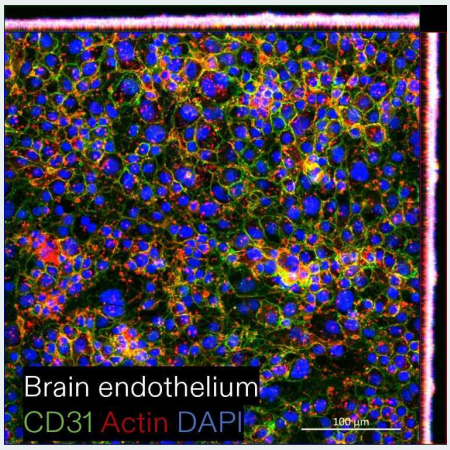
Timepoint/Endpoint analysis with medium sample collection

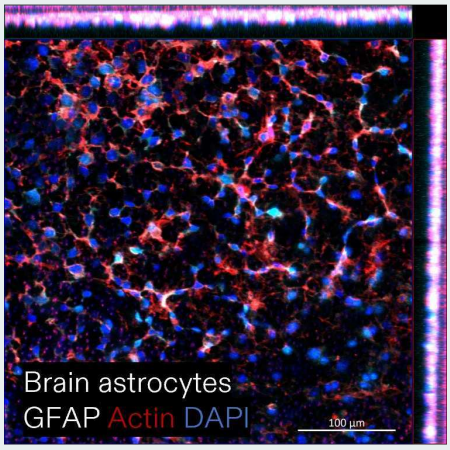
Summary

The blood-brain barrier is a highly regulated structural and functional interface between the vascular and the central nervous system. It plays a vital role in homeostasis but also decreases the effective molecular treatment of severe brain diseases.

We developed a high-throughput blood-brain barrier-on-chip composed of major cell types: astrocytes and endothelial cells. These are co-cultured on the opposing sides of semipermeable membrane and display *in vivo*-like permeability values.

We can achieve reversible barrier alteration to model strong neuro-inflammatory patterns. This enables in-depth studying of assisted and non-assisted transport from the vasculature to the brain for developing effective therapeutics.





Continuous model improvement

Contact us to be kept updated on our continuous improvement. The pharmacological validation of our mouse blood-brain barrier-on-chip model is ongoing. Also, the next-generation human-based model is currently being developed by our scientists.

Plate & service specifications

Providing	Plate-only & CRO testing service (plate + cell kit under development)
Plate formats	PLATE-96 (24 assays) flow or static culture PLATE-384 (96 assays) flow or static culture
Cells (CRO service)	Mouse primary astrocytes and mouse primary brain microvascular endothelial Cells (humanized model under validation)
Field of application	Research use only
Readouts (CRO service)	- Barrier leakage assessment - Compound permeability measurement - Immunofluorescence and histological characterization - Proteomics - Genomics

Document version 202208-1

Get in contact with us

Finnadvance provides AKITA® microfluidic plates and CRO services customized for your applications. Our experienced engineers and scientists are happy to work with you in order to understand your needs and support you meeting your objectives.

www.akita.bio

science@akita.bio

+358 40 653 7049

AKITA by Finnadvance

Human biology replicated reliably