PrimeSurface™ Plate 96V application
Blood-brain barrier (BBB)

【Data Provided】
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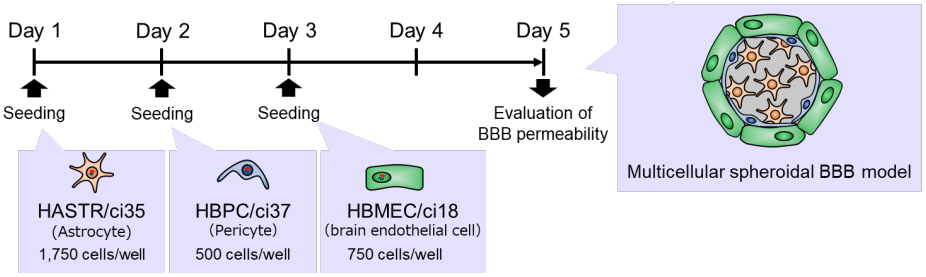
Background

The human brain is an important organ composed of numerous neurons and is protected by the blood-brain barrier (BBB), which restricts the movement of substances from the blood to the brain and prevents the entry of toxic substances. However, it also limits the delivery of drugs into the brain, posing a significant obstacle in the development of therapeutics for central nervous system disorders. There is a need to develop a functional *in vitro* BBB models model to evaluate BBB permeability for delivery mechanism for therapeutics to the brain.
Here, we introduce a new human BBB model developed by Professor Furihata's group at Tokyo University of Pharmacy and Life Sciences. This multicellular spheroidal BBB model, which is formed by using PrimeSurface™ Plate 96V, has been used to evaluate BBB permeability study and is expected to be useful in understanding the molecular mechanisms of BBB physiology and pathophysiology.

BBB model formation

The cells to form BBB spheroid were seeded on PrimeSurface™ Plate 96V as follows:



Multicellular spheroidal BBB model (self-assemble astrocytes and brain pericytes as a spheroid core covered with brain endothelial cells as an outer layer) is formed using PrimeSurface™.

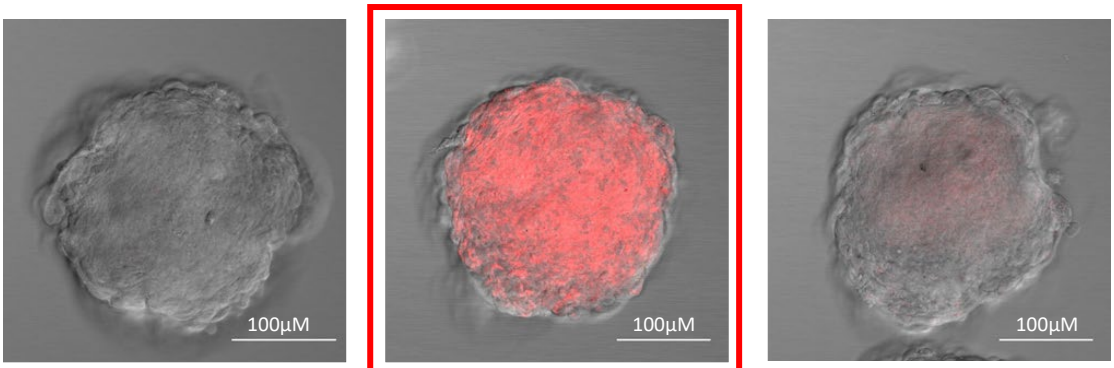
Please refer to the paper for more details:
Generation of a Human Conditionally Immortalized Cell-based Multicellular Spheroidal Blood-Brain Barrier Model for Permeability Evaluation of Macromolecules. Isogai R, Morio H, Okamoto A, Kitamura K, Furihata T. Bio Protoc. 2022;12:e4465.

Evaluation of BBB permeability

Receptor-mediated transcytosis is a known transport pathway that involves the transport of macromolecules such as transferrin and insulin (peptide hormones and proteins) across the BBB using intracellular vesicles. In this BBB model, a novel peptide (labeled with Cy5), which is expected to be used as a brain drug delivery system, was tested for permeability in the brain.

[Methods]
1.Collect spheroids on Day 5 and wash them with HBSS (+). Add the peptide to the medium to achieve a final concentration of 1 μM.
2.Treat the spheroids at 37°C for 40 minutes and wash them with PBS (+).
3.Fix the spheroids with 4% PFA and mount them on glass slides for observation using confocal microscopy.

[Results]
Red fluorescence from Cy5 was observed inside the spheroid, confirming that the novel peptide has BBB permeability.



Brightfield image of the spheroid | Peptides with BBB permeability | Peptides without BBB permeability

PrimeSurface™ can be used to form multicellular spheroids with a structure close to BBB *in vivo*.

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