Drug Discovery & Development

Enhanced Blood-Brain Barrier Model Outperforms All Others

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WARF: P130017US02

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing an improved *in vitro* model of the blood-brain barrier that is derived from human pluripotent stem cells and enhanced with retinoic acid.

Overview

The blood-brain barrier (BBB) is made up of brain microvascular endothelial cells (BMECs), which line brain capillaries and control trafficking between the bloodstream and neural tissue. Although essential to healthy brain function, the BBB interferes with drug delivery, preventing most pharmaceuticals and therapeutics from entering the brain from the bloodstream. This hinders the treatment of brain disorders such as stroke and Alzheimer's disease.

Accurately reproducing the BBB in an *in vitro* setting would help identify compounds capable of entering the brain. A robust human model especially is needed for accurate screening and study. Current methods for creating an *in vitro* human BBB model require the independent isolation of multiple cell types, and the quality of these preparations varies.

UW–Madison researchers previously created a simpler, more reproducible BBB model using primary BMECs and neural progenitor cells. However, primary BMECs are difficult to isolate and grow reproducibly.

The Invention

UW–Madison researchers have developed a more realistic, reproducible *in vitro* model of the BBB. The model uses either human embryonic or induced pluripotent stem cells as a source of BMECs.

These cells are treated with retinoic acid to produce further BBB maturation and improve barrier properties. They are purified and co-cultured with other types of neurovascular cells, including pericytes, astrocytes and differentiated neural progenitor cells (NPCs).

Applications

- Screening for compounds capable of crossing the BBB for treatment of brain disorders
- Identifying compounds for treatment of other diseases that have the potential to cross the BBB and cause brain toxicity
- Researching brain function

Key Benefits

- More accurately predicts *in vivo* behavior than other models
- Treatment with retinoic acid leads to dramatic improvement in tightness.
- Much higher transendothelial electrical resistance (TEER) measurements than other models
- Less labor intensive
- Reproducible and reliable

- Expresses important BBB markers
- Good permeability properties

Stage of Development

The TEER measurements of this model have exceeded 5,000 Ωcm^2, which is higher than any known model.

Additional Information

For More Information About the Inventors

- Eric Shusta
- Sean Palecek

Related Technologies

- WARF reference number P100219US02 describes an efficient protocol for producing highly pure populations of BMECs.

Publications

- Lippmann E.S., Al-Ahmad A., Palecek S.P. and Shusta E.V. 2013. Modeling the Blood-Brain Barrier using Stem Cell Sources. Fluid Barriers CNS. 10, 2. DOI: 10.1186/2045-8118-10-2

Tech Fields

- Drug Discovery & Development : Disease models
- Drug Discovery & Development : Preclinical testing

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854