METHOD FOR IMPROVING TRANSCYTOSIS PROPERTIES OF A HUMAN BLOOD-BRAIN BARRIER MODEL

View U.S. Patent Application Publication No. US-2025-0092369 in PDF format.

WARF: P230318US02

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The Invention

UW-Madison researchers have developed a blood-brain barrier (BBB) model with in vivo-like BBB transcytosis properties using a new method that improves the fidelity of highly selective, cross-barrier transport. The BBB is composed of specialized vascular endothelial cells that maintain brain homeostasis and regulate the passage of blood solutes into the central nervous system (CNS) by restricting both transcellular and paracellular transport. In vitro human pluripotent stem cell (hPSC)-derived BBB models have proven useful for the study of barrier regulation, molecular transport, and brain drug delivery. Such models offer improved recapitulation of human development and disease as compared to animal models, and offer greater accessibility as compared to primary human tissues. However, the brain microvascular endothelial cells (BMECs) that form the BBB in vivo exhibit reduced expression of vesicular transcytosis proteins relative to non-BBB endothelial cells, and this is not reflected in existing BBB models. As a result, existing BBB models do not accurately model trans-BBB transport of substances that utilize the caveolae-mediated transport pathway. The researchers addressed these limitations using a small molecule and overexpression (lentiviral or doxycycline-induced) of certain receptors. This combination reduces the expression of certain transport proteins while maintaining high expression of certain BBB-enriched proteins, resulting in the desired characteristics. These models could be used to test the ability of therapeutic agents to cross the BBB.

Additional Information

For More Information About the Inventors

- Sean Palecek
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Tech Fields

- Pluripotent Stem Cells : Differentiation
- Research Tools : Biomanufacturing

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