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Vascularized Neuroimmune Organoids with Patient Brain Homogenates for Alzheimer's Research and Drug Discovery

Coumarin-amide analogs inhibit toxic alpha-synuclein and tau aggregation for Alzheimer's and Parkinson's therapies.

Researchers at Purdue University have developed a human pluripotent stem cell (hPSC)-based vascularized neuroimmune organoid model for Alzheimer's Disease (AD) modeling and drug discovery. AD is one of the most debilitating diseases in medicine, affecting more than 55 million people worldwide. Available treatments for AD are severely lacking, and current models mainly focus on inherited familial AD (fAD). However, models for studying fAD's counterpart, sporadic AD (sAD), are scarce, even though 95% of AD cases are without specific genetic mutations. It is therefore critical that appropriate models of sAD are developed.

This novel hPSC-based vascularized neuroimmune organoid model helps advance AD drug discovery, especially for sAD. The model incorporates multiple cell types affected in human AD brains, including neurons, microglia, astrocytes, and blood vessels. Moreover, the applicants have demonstrated for the first time that AD postmortem brain tissue-derived brain extracts containing amyloid beta (Aβ) and tau seeds can induce multiple AD pathologies within a relatively short time frame in the new organoid model. Thus, the new organoid model can be used for testing AD therapeutics, particularly antibody-based therapeutics, and studying AD disease mechanisms. As the widespread urgency for more translational human models to study AD progresses, this organoid model will serve as an invaluable tool for facilitating AD drug development.

Technology Validation:

Researchers demonstrated that brain homogenates from individuals with sAD can effectively induce multiple AD pathologies in organoids four weeks post-exposure, including amyloid beta (Aβ) plaques-like aggregates, tau tangles-like aggregates, neuroinflammation, elevated microglial synaptic

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pruning, synapse/neuronal loss, and impaired neural network. Furthermore, after treatment with Lecanemab, an FDA-approved drug targeting Aβ, AD brain extract exposed organoids showed a significant reduction of amyloid burden.

Advantages:

-Enables a more comprehensive understanding of cell-to-cell interactions and cell-type-associated pathological events in AD

-Can serve as an in vitro platform to advance AD drug development, particularly antibody-based therapeutics

-Effectively develops multiple AD pathologies within a short time frame

Applications:

-Pharmaceuticals

-Drug testing aimed at treating AD

-Disease mechanism studying

TRL: Pharmaceuticals

Intellectual Property:

Provisional-Patent, 2024-05-15, United States

Provisional-Patent, 2024-07-16, United States

PCT-Gov. Funding, 2025-05-15, WO

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