Novel Treatment For Alzheimer’s Disease and Dementia

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BACKGROUND

Pathological accumulation of phosphorylated Tau (pTau) and accumulation of amyloid-beta (Ab) fragments are the two major biochemical hallmarks of Alzheimer’s disease (AD). Effective strategies to remove Ab in AD-patient brains have been developed, but have not yet shown efficacy to slow cognitive decline in clinical trials. This finding has led to the idea that targeting Tau or combinatorial strategies that target both Tau and Ab are required to treat AD.

Genetic, epidemiologic, and biochemical evidence suggests that predisposition to AD may arise from altered cholesterol metabolism, although the molecular pathways that may link cholesterol to AD phenotypes are only partially understood. Stimulation of a brain specific cytochrome that converts cholesterol to 24-hydroxycholesterol, which in turn reduces cholesteryl ester. Reduction of cholesteryl ester has been demonstrated to reduce pathological Tau phosphorylation in human neurons made from induced pluripotent stem cells. Also, low dose Efavirenz/Sustiva reduces neurofibrillary tangles in a mouse model. The pathway may run from cholesteryl ester to Tau via the proteasome.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have shown that very low doses of Efavirenz reduced neurofibrillary tangles in AD and in fronto-temporal dementia. Low dose studies using *in vivo* mouse models and in iPSC, demonstrated that the pathway and targets are independent of amyloid.

The invention provides a method of reducing cholesteryl ester in a patient by administering an effective amount of efavirenz or a derivative thereof. The cholesteryl ester is associated with tauopathy that causes neurofibriliary tangles, while in other cases the tauopathy is AD and/ or frontotemporal dementia.

ADVANTAGES

This discovery offers a novel treatment for Alzheimer’s Disease and Dementia.

STATE OF DEVELOPMENT

The state of development is based on experimental data from human neurons made from iPSC and *in vivo* mouse brain studies. Clinical testing of human Alzheimer’s disease is currently in the planning stages.

INTELLECTUAL PROPERTY INFO

The invention is patent-pending and is available for licensing and collaborations

RELATED MATERIALS

- van der Kant R, Langness VF, Herrera CM, Williams DA, Fong LK, Leestemaker Y, Steenvoorden E, Rynearson KD, Brouwers JF, Helms JB, Ovaa H, Giera M, Wagner SL, Bang AG, Goldstein LSB. Cholesterol Metabolism Is a Druggable Axis that Independently Regulates Tau and Amyloid-ß in iPSC-Derived Alzheimer’s Disease Neurons Cell Stem Cell. 2019 Mar 7;24(3):363-375.e9. 10.1016/j.stem.2018.12.013. Epub 2019 Jan 24 - 01/24/2019

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Alzheimer’s disease, Tau; amyloid beta; cholesterol metabolism; cholesteryl esters; disease modeling; drug screening; induced pluripotent stem cells; lipids; proteostasis

CATEGORIZED AS

- **Medical**
  - Disease: Central Nervous System
  - Therapeutics

RELATED CASES

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