Development of a Method to Treat Alzheimer's Disease by Protection of Synapses

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BACKGROUND

NMDA receptors (NMDARs) are principal regulators of synaptic signaling in the brain. Modulation of NMDARs' function and trafficking is important for the regulation of synaptic transmission and several forms of synaptic plasticity. Postsynaptic density protein 95 (PSD-95) acts as a scaffolding protein and stabilizes the surface and synaptic expression of NMDARs. NMDA receptors (NMDARs) are ionotropic glutamate receptors that are expressed throughout the nervous system and play crucial roles in neuronal development, synaptic plasticity, learning and memory.

PSD-95 (Post Synaptic Density protein) or SAP90, a membrane-associated guanylate kinase (MAGUK), is the major scaffolding protein in the excitatory postsynaptic density (PSD) and a potent regulator of synaptic strength. It is almost exclusively located in the post synaptic density of neurons and is involved in anchoring synaptic proteins. Its direct and indirect binding partners include neuroligin, NMDA receptors, AMPA receptors, and potassium channels. Postsynaptic loss does not precede obvious Aβ (beta-amyloid or amyloid beta) and Tau deposition, but instead appears to occur as Aβ and Tau pathologies advance. This indicates that PSD-95 is an excellent intrinsic biomarker for post synaptic mechanisms and its expression is reduced in brain tissue from patients with Alzheimer's Disease (AD) as well as in mouse models of AD.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have shown that increased PSD-95, a major synaptic scaffolding molecule, blocks the effects of Aβ on synapses. These results indicate that increased PSD-95 protects synapses from Aβ toxicity by interfering with ion-flux independent NMDAR CTD signaling. Using a chemical inhibitor to block its depalmitoylation increases PSD- 95 at synapses and rescues deficits caused by Aβ; possibly opening a new therapeutic avenue against AD.

APPLICATIONS

The inventors have developed a method for treating a neurodegenerative disease by administering a therapeutically effective amount of a polypeptide or an effective amount of an inhibitor of a palmitoylation pathway to increase the amount of PSD-95 in the synapse.

STATE OF DEVELOPMENT

The state of the development is in the experimental stage.

INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Post Synaptic Density protein, PSD-95, neurodegenerative diseases, NMDA receptors, inhibitors of palmitoylation, Alzheimer's disease

CATEGORIZED AS

- **Medical**
  - Other
  - Therapeutics

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