Use of Neurotrophic Factor-alpha1/Carboxypeptidase E (CPE) to Treat Alzheimer Disease

Summary
The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) seeks research licensees and/or co-development partners under a Cooperative Research and Development Agreement (CRADA) to advance preclinical and clinical development of methods to treat Alzheimer Disease using Carboxypeptidase E (CPE).

NIH Reference Number
E-200-2021

Product Type
- Therapeutics

Keywords
- Brain, “Cognitive impairment”, Memory, Mild Cognitive Impairment, MCI, AD, Alzheimer’s Disease, Hippocampus, Neurodegeneration, Neurotrophic, Carboxypeptidase E, CPE, Brain-Derived Neurotrophic Factor, BNDF, Loh

Collaboration Opportunity
This invention is available for licensing.

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Description of Technology
There is no known cure for Alzheimer’s disease, a brain disorder that severely affects memory, thinking, learning, and organizing skills. It eventually decreases a person’s ability to carry out simple, daily activities. It is predicted that over 14 million Americans will develop Alzheimer’s without effective treatment options. Mild cognitive impairment (MCI) is a stage prior to Alzheimer’s when memory problems become noticeable. A patient’s ability to function and live independently remain intact as the brain compensates for disease-related changes. Disease symptoms worsen over a period that may progress over 10 years. In some people, MCI can hold steady at this stage. However, people with MCI are at high risk for progressing to dementia. Alzheimer’s disease is the
most common form of dementia.

MCI is associated with neurological cell death in the hippocampus. The technology from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), describes that direct administration of an adenovirus carrying the Carboxypeptidase E (CPE) gene to the hippocampus results in overexpression of the CPE protein in an experimental mouse model of AD. CPE protein overexpression averts neurological cell death in the hippocampus. Treated mice do not develop memory impairment. This technology was effective in mice with normal expression of brain-derived neurotrophic factor (BNDF). It may be applicable to a wider range of patients, including those with BNDF deficiency and no deficiency of BNDF expression. Further, this technology may provide for a combination therapy with CPE and BNDF to treat AD.

This technology protects neurons prior to the appearance of cell damage due to accumulation of intracellular tau-containing neurofibrillary tangles and extracellular β-amyloid (Aβ) deposits in the brain.

The use of CPE as an early intervention in the initial diagnosis of MCI may stabilize the neurological condition of patients and avoid progression of AD in a large population of aging patients.

The NICHD technology is available for commercial licensing to develop as a therapy for MCI or AD. There is also opportunity for preclinical co-development of the technology with the NICHD laboratory of Dr. Peng Loh.

Potential Commercial Applications

- Treatment of patients
  - Diagnosed with mild cognitive impairment (MCI)
  - Diagnosed with neurologic damage to the hippocampus
  - With early signs of Alzheimer’s Disease (AD)
- Combination therapy with Brain-Derived Neurotrophic Factor (BDNF)

Competitive Advantages

- Halt the progression from MCI to AD
- Combination therapy with CPE and BNDF
- Neuroprotective prior to the appearance of cell damage

Inventor(s)

Peng Loh PhD (NICHD)

Development Stage

- Pre-clinical (in vivo)

Publications

Xiao L, et.al. Neurotrophic factor-α1, a novel tropin is critical for the prevention of stress-induced hippocampal CA3 cell death and cognitive dysfunction in mice: comparison to
BDNF. [PMID 33414376]

**Patent Status**
- **U.S. Provisional:** U.S. Provisional Patent Application Number 63/273,312, Filed 29 Oct 2021

**Therapeutic Area**
- Central Nervous System

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