Memory-Related Protein Synthesis in Alzheimers Disease Mouse Models

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USA

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Memory-Related Protein Synthesis in Alzheimers Disease Mouse Models

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Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is characterized by a severe loss of memories that causes great emotional suffering for patients and caregivers. There is currently no treatment for AD associated memory loss, because of insufficient understanding of the molecular mechanism that causes this memory loss. Memory loss is

present during early stages of AD. There is growing evidence that memory loss during the early stages of AD is caused by effects of soluble amyloid-beta (Abeta) oligomers on synapses. Since protein synthesis is essential for both memory storage and normal synapse physiology, altered protein synthesis provides a plausible molecular mechanism for mediating the effects of soluble Abeta oligomers on memories and synapses. This project will determine if soluble Abeta oligomers impair protein synthesis associated with memory storage. To achieve this, an AD mouse model based on the intracerebroventricular injection of Abeta oligomers will be used. Intracerebroventricular injection of Abeta oligomers acutely impairs the formation of a contextual fear memory. In addition, a transgenic AD mouse model will be studied. These AD mouse models will be combined with a unique transgenic mouse that was designed for the explicit purpose of measuring protein synthesis during memory storage. This transgenic mouse enables the isolation of translated mRNA from neurons in the hippocampus by expressing tagged ribosomes. By sequencing the mRNA associated with the tagged ribosomes, the synthesis rate of all neuronal proteins can be determined. By using this unbiased genome-wide approach, new unanticipated therapeutic targets can be discovered. Since the molecular pathway responsible for AD associated memory loss might also contribute to the progression of AD, these therapeutic targets might slow down or even prevent the progression of AD.

Further information available at:

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