Abeta-Targeted Fluorinated Liposomes for 19F MRI Detection of Abeta Pathologies in APP/PSEN1 Mice

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Abeta-Targeted Fluorinated Liposomes for 19F MRI Detection of Abeta Pathologies in APP/PSEN1 Mice

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Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is the leading cause of dementia in individuals over the age of 65 and the prevalence in the United States this year is estimated at 5.2 million. 83,494 Americans died from the disease in 2010 and an estimated

70,000 more will die from AD this year, and it remains without a cure. Empirical data strongly suggest that amyloid-? (A?) deposition and blood-brain barrier (BBB) compromise may precede clinical manifestation of the disease by over 20 years. Methods to quantify A? in vivo are therefore actively investigated by the medical research community as a means of early detection. Our long term goal is to develop a magnetic resonance imaging (MRI) contrast agent for visualization of A? plaques in vivo. We recently showed that fluorescent A?-targeted liposomes cross the BBB and avidly label A? pathologies in the brains of APP/PSEN1 mice. In a second generation formulation, we loaded similar particles with a gadolinium contrast agent and obtained MRI data which confirm that they cross the BBB of Tg2576 mice. However, the contrast-to-noise ratio of this agent does not allow unequivocal interpretation of images due to the background signal that exists in proton-based MRI. 19F MRI presents an alternative to address this problem because there is no endogenous 19F MRI detectable signal in soft tissue. Current 1H MRI hardware can be used for 19F MRI with little modification and 19F is a stable atom with 100% natural abundance, easily available, non-radioactive, and inexpensive. Unfortunately, almost all 19F-based agents currently under use for biomedical applications utilize perfluorocarbons (PFCs) which have low aqueous solubility and not amenable to aqueous core liposome formulations protocols. We have designed and synthesized two new hydrophilic fluorinated molecules with this capacity. In this application, we propose to prepare a A?-targeted liposome formulation bearing one of the molecules as a 19F contrast payload and explore its potential as a tool to define and quantify noninvasively, the longitudinal accumulation of amyloid plaques (using 5, 7, 9 and 12-month old APP/PSEN1 mice) by 19F MRI. Completion of this work will result in a potential novel MRI platform for noninvasive detection and quantification of amyloid plaque burden in vivo and a potential contrast agent to other molecular imaging applications.

Further information available at:

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