TECHNOLOGY

Methylated Peptides Derived from Tau Protein and Their Antibodies for Diagnosis and Therapy of Alzheimer's Disease

OVERVIEW

Alzheimer's disease (AD) is a neurologically degenerative disease that is defined in part by the accumulation of aberrant tau proteins (neurofibrillary tangles) within the brain. The mechanisms which drive tau aggregation is not fully understood and existing treatments do little to delay the inevitable decline of Alzheimer's patients. UMB researchers, however, have discovered new insights into the structural isolates of tau proteins which have revealed a previously unrecognized tau modification, lysine methylation that is distinct in AD brains compared to that of normal brain tissues. Utilizing these unique markers, specific methylation site signatures have been isolated in AD brains that can be used to create synthetic methylated peptide antigens for production of antibodies capable of detecting tau methylation in biological samples. Brain tissue sections from late-stage AD patients confirm high incidence of localization of anti-methyl lysine antibodies with that of neurofibrillary tangles. This approach provides a unique possibility for the development of an early diagnostic screen to detect AD during a time when treatment is likely to be most effective. Potential also exist for drug-antibody conjugate therapies for targeted treatments for all stages of disease progression in Alzheimer patients.

APPLICATIONS

Alzheimer's disease is the sixth-leading cause of death and affects 5.4 million Americans. With no cure, prevention method, or effective medication to slow disease progression, it is estimated for 2012 alone, that the cost for direct care of Alzheimer's patients will be an approximate $200 billion. While the death rates have declined for most major disease such as heart disease (-13 percent), breast cancer (-3 percent), prostate cancer (-8 percent), stroke (-20 percent), and HIV/AIDS (-29), Alzheimer's has risen 66% within the same period. Five FDA-approved Alzheimer's drugs (Aricept, Razadyne, Namenda, Exelon, Cognex) currently exist, but the average effectiveness is 6-12 months for only half of the individuals that are treated. A large interest exists for the development of newer drugs with several in late-stage development (bapineuzumab-Pfizer and J&J; solanezumab-Eli Lilly). However, setbacks such as Genentech's AN-1792, a vaccine for clearance of amyloid plaques, with no effect on dementia, suggest ineffectiveness for this approach. Current drugs help to mask the symptoms of Alzheimer's, but does little to treat the underlying disease itself. This invention has the potential to be first of its kind to not only screen but target therapeutic drugs to the disease site.

ADVANTAGES

-Compositions include antigenic tau peptides that are capable of inducing immune responses to target abnormally methylated tau proteins for clearance, effectively targeting and treating the disease. -Utilizes unique epitopes specific to pathological tau to provide increased accuracy and sensitivity compared to current methods of use in distinguishing tau isoforms and diagnosing Alzheimer. -Method can be used to diagnose pre mortem states, allowing for early treatment to intervene with disease progression. -Allows for ongoing monitoring of patients to examine effectiveness of drug treatments over time. -Methylated peptides can be used as antigens to identify compounds for use in treatment of Alzheimer.

STAGE OF DEVELOPMENT

This invention provides immunogens, immunogenic compositions, and/or pharmaceutical compositions including peptides for the diagnosis or treatment of neurological disorders such as AD. Methyl lysine content in intact tissue, were prepared from post mortem late-stage AD cases and subjected to double-label confocal fluorescence microscopy using anti-tau and anti-methyl lysine antibodies. Anti-methyl lysine immunoreactivity colocalized with 78 +/- 13% of neurofibrillary tangles in these specimens.

R&D REQUIRED

Additional in vitro and in vivo experiments are required for validation.

LICENSING POTENTIAL

UM seeks to develop and commercialize by an exclusive or non-exclusive license agreement and/or sponsored research with a company active in the area.

CONTACT INFO

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PATENT STATUS

-Issued, US, No. 9,738,709

LICENSE STATUS

Available for non-exclusive license

CATEGORIES

- Diagnostics
- Therapeutics

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EXTERNAL RESOURCES

- Dual modification of Alzheimer's disease PHF-tau protein by lysine methylation and ubiquitylation...
- Alzheimer disease-specific conformation of hyperphosphorylated paired helical filament-Tau is polyubiquitinated through...

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