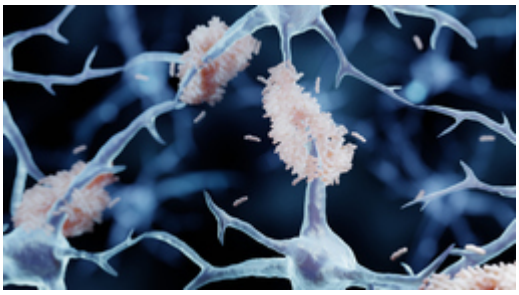
INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Amyloid-Specific Antibodies and uses Thereof

TECHNOLOGY NUMBER: 2020-510



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Medical Devices
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OVERVIEW

A novel class of affinity-matured conformation antibodies against Alzheimer's alpha-beta fibrils

- Superior affinity and lower levels of non-specific interactions compared to existing antibodies
- An new affinity maturation process which could develop diverse amyloidogenic disorders

BACKGROUND

Neurodegenerative disorders such as Alzheimer's and Parkinson's diseases are expected to become more prevalent as life expectancy increases due to significant advances in treating other human disorders such as cancer and heart disease. These neurodegenerative diseases are linked to the formation of toxic prefibrillar oligomers and amyloid fibrils in the brain. Natural antibodies specific to amyloid-forming proteins may detect, disrupt, and reverse toxic protein aggregation in these illnesses. While there is interest in generating exogenous antibodies to treat Alzheimer's and Parkinson's diseases, the production of antibodies to these antigens is difficult because amyloid is relatively insoluble, heterogenous in size and conformation, hydrophobic, and multivalent. Also, the use of immunization to generate such antibodies is limited due to variable presentation of antigens to the immune system. So, a need exists for higher quality antibodies directed at the protein aggregates associated with both Alzheimer's and Parkinson's disease.

INNOVATION

Researchers at the University of Michigan have discovered a novel class of affinity-matured conformation antibodies against Alzheimer's alpha-beta fibrils. The investigators designed antibody libraries based on a lead conformational antibody by sampling combinations of amino

acids in the antigen binding site predicted to lead to high antibody specificity. These antibodies were found to display superior affinity properties against alpha-beta fibrils and lower levels of non-specific interactions compared to existing antibodies, providing the potential to improve the diagnosis and prognosis of this category of illnesses. This affinity maturation process could furthermore be applied to the development of antibodies with even more specificity to alpha-beta fibrils, or alternatively it could be used to evolve the conformational specificity of existing antibodies against diverse types of amyloidogenic aggregates. So, both the newly discovered antibodies and the nascent means by which they were discovered provide potential routes for exploring and addressing neurodegenerative disorders.

References

1. Desai A, et al. , Rational affinity maturation of anti-amyloid antibodies with high conformational and sequence specificity. J Biol Chem. 2021 Jan-Jun:296:100508. doi: 10.1016/j.jbc.2021.100508.