Novel peptide can selectively detect and neutralize an early molecular trigger of Alzheimer's disease

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A study published today (December 5) in the *Proceedings of the National Academy of Sciences* (*PNAS*) demonstrates a customized, synthetic peptide's ability to selectively detect Alzheimer's disease.

The novel approach detailed in "SOBA: Development and testing of a soluble oligomer binding assay for detection of amyloidogenic toxic oligomers" allows detection of Alzheimer's disease at all stages, including presymptomatic cases, as well as differentiation from different amyloid-related neurodegenerative diseases.

The technology was developed in the Daggett lab at the University of Washington, and AltPep is a spinout company developing a revolutionary platform based on this technology focusing on early detection and treatments, with the aim to change the course of amyloid diseases.

"Early diagnosis and treatment for Alzheimer's disease and other amyloid diseases have been elusive," said Valerie Daggett, Ph.D., Founder and CEO of AltPep. "We are targeting an early molecular trigger of amyloid diseases, a goal once thought to be unattainable. Our novel peptide platform is designed to selectively bind toxic oligomers, which is like finding a needle in a haystack.

"AltPep's technology is different from other approaches because it rationally targets a specific nonstandard protein structure discovered in the Daggett lab, called alpha-sheet. These toxic oligomers form both early and throughout the disease process."

Amyloid diseases are associated with protein misfolding and aggregation of different toxic soluble oligomer proteins. For Alzheimer's disease, the formation of toxic amyloid beta-peptide (Aβ) oligomers is an early molecular trigger before other downstream events, such as plaque deposition and abnormal tau phosphorylation, take place. The aim is to intervene early in the disease pathway, before irreparable damage occurs, estimated to begin 10 to 20 years before clinically evident disease.

Current treatment options are deployed too late, after a patient has signs and symptoms of the disease. This study demonstrates the ability of custom-designed, alpha-sheet peptides to both neutralize and detect these toxic oligomers in cerebrospinal fluid (CSF) and blood.

"This peer-reviewed publication highlights the unique and broad

potential of AltPep's platform to target multiple amyloid diseases," said Chad Robins, Board Member of AltPep and Co-founder and CEO of Adaptive Biotechnologies. "This is a pivotal time for the company, with groundbreaking science and a fantastic team to execute on its important mission."

Study results

In the study, Alzheimer's disease detection was achieved by testing 379 human plasma samples from 310 patients. The SOBA assay detected Aβ toxic oligomers in patients on the Alzheimer's disease continuum and discriminated from other forms of dementia with 99% sensitivity and specificity. In addition, the assay identified 13 samples from cognitively normal controls with high toxic oligomer levels.

In subsequent years, 12 of the 13 were confirmed to progress to mild cognitive impairment (follow-up was not available for one individual). These results suggest that the SOBA assay can detect early Alzheimer's disease molecular pathology prior to clinical symptoms.

To demonstrate the broader application of the technology, CSF samples from patients with Parkinson's disease and Lewy body dementia were evaluated using the SOBA assay adapted for detection of Parkinson's disease-associated toxic oligomers. Strong signals and good discrimination between Parkinson's and Alzheimer's disease patients were seen, confirming proof of concept of the platform's modular and broad approach.

About SOBA diagnostics and SOBIN therapeutics

SOBA diagnostics are highly sensitive, simple blood tests in development to aid in the diagnosis of amyloid diseases. SOBIN

therapeutics are in development for use in concert with early detection to target and neutralize the toxic soluble oligomers associated with amyloid diseases.

AltPep has received Breakthrough Designation from the FDA for its SOBA-AD diagnostic for Alzheimer's disease. The inclusion in the FDA Breakthrough Devices Program means that AltPep can expect prioritized review of the submission of the diagnostic test.

More information: Shea, Dylan et al, SOBA: Development and testing of a soluble oligomer binding assay for detection of amyloidogenic toxic oligomers, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2213157119. doi.org/10.1073/pnas.2213157119

Provided by AltPep Corporation