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Abstract

The Development of an Early Diagnostic Method for Alzheimer's Disease †

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Alzheimer's disease (AD) is the most common form of dementia, characterized by neuronal degeneration and death. The appearance of aggregated forms of the Aβ42 peptide is a key biochemical marker indicating the possible initiation of the pathological cascade in Alzheimer's disease [1].

The goal of this study is to develop an approach for the early diagnosis of AD by detecting Aβ42 multimers in the blood and lymph.

We adapted the Protein Misfolding Cyclic Amplification (PMCA) method [2] for the detection of Aβ42 aggregates in blood samples. One of the main challenges in using the PMCA method for detecting Aβ42 aggregates is that the synthesized or recombinant Aβ42 peptide spontaneously aggregates with high yield. Therefore, it is difficult to distinguish spontaneous aggregation from aggregation induced by externally added aggregated Aβ42, e.g., from the patient's samples.

Previously, using a yeast model [3], we identified mutations in human Aβ42 that reduce its aggregation propensity. In this study, we isolated and purified the wild-type Aβ42 and five recombinant Aβ42 variants with mutations that decrease Aβ42 aggregation via metal-affinity chromatography. We investigated the aggregation kinetics of these Aβ42 variants in the presence of thioflavin T using fluorometry. Currently, we are studying the aggregation kinetics of different Aβ42 variants in the presence of aggregated wild-type Aβ42.

We believe that our findings will help develop an effective system for detecting multimeric forms of the Aβ peptide in the blood at extremely low levels to be used as a biomarker for diagnosing AD before the onset of any clinical symptoms.

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