Using Unique Ultrashort Inhibitor Peptide as BETA-Amyloid Modulator in C. elegans

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Alzheimer’s disease (AD) is a neurodegenerative disorder that causes progressively decreased memory functions. Nearly 44 million people have AD worldwide. Moreover, AD cannot be prevented, cured, or even slowed down. One of the main characteristics of AD is the aggregation of BETA-Amyloid (Abeta). This research proposes using novel ultrashort peptides, with inhibiting characteristics, to inhibit Abeta aggregation in C. elegans. Two C. elegans strains were used as in vivo model organisms. One is genetically engineered to expresses the full-length human Abeta (CL4176) and the other is the wild-type (N2). Three plates per strain were prepared with ultrashort peptides added on their food source (E. coli OP50), and the nematodes were left feeding. Both strains were subjected to 20 hours of temperature up-shift to induce Abeta aggregation in CL4176 strain. Abeta aggregation leads to paralysis, and the number of nematodes with paralysis were scored 20 hours after temperature up-shift, every 2 hours for a total of 10 hours. CL4176 strain with ultrashort peptides added to their food had fewer paralyzed nematodes compared to the CL4176 without ultrashort peptides (average paralysis inhibition 19% at 20mM, p-value <0.01) which suggests less Abeta aggregation. Moreover, ultrashort peptides showed no toxicity on the wild-type N2 strain. Thioflavin assays will be performed to observe the molecular mechanisms of the ultrashort peptides. These novel ultrashort peptides inhibitor proved to be efficient at inhibiting paralysis in an in vivo environment. This pre-clinical work suggests the potential use of these novel ultrashort peptides as a future therapeutic agent against AD.

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