

アミロイド β を分解する JAL-TA9 (低分子酵素ペプチド) の発見

The discovery of JAL-TA9 which cleaves amyloid- β with proteolytic activity

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Amyloid- β ($A\beta$) 42, one of the causes of Alzheimer's disease (AD), is produced by the cleavage of amyloid precursor protein (APP) by β - or γ -secretases. Since $A\beta$ 42 oligomers exhibit strong neurotoxicity, $A\beta$ 42 is predicted to be a potentially efficient target for drug therapies. Recently, we screened peptides that activate MMP7 using our peptide library and found that the synthetic peptide JAL-TA9 (YKGSFRMI), which is derived from the BoxA region of Tob1 protein, showed proteolytic activity. It is generally accepted that an enzyme should be a large molecular protein consisting of more than thousands of amino acids. Thus, this is the first finding that a small synthetic peptide has protease activity, and we termed Catalytide as the general name of peptides with protease activity [1]. In this study, we demonstrate the cleavage activity of JAL-TA9 not only against the authentic soluble form of $A\beta$ 42 but also against the solid type of $A\beta$ 42 in the central region [2]. In addition, we demonstrated the cleavage activity using brain slices of AD patients. JAL-TA9 decreased the amount of accumulated $A\beta$ 42 in the brain of Alzheimer's patients. Taken together, JAL-TA9 is an attractive seed for the development of peptide drugs with a new strategy for Alzheimer's disease.

[1] Nakamura et al., Peptides, 116, 71 (2019)

[2] Nakamura et al., J. Royal, Sci., 1(2) 30–35 (2019)