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Research report

# Bacterial enzymes effectively digest Alzheimer's β-amyloid peptide

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ABSTRACT

Aggregated β-amyloid peptides play key roles in the development of Alzheimer's disease, and rec evidence suggests that microbial particles, among others, can facilitate their polymerization. Bacte enzymes, however, have been proved to be beneficial in degrading pathological fibrillar structures clinical settings, such as strepto-kinases in resolving blood-clots. The purpose of this study was to inv tigate the ability of bacterial substances to effectively hydrolyze β-amyloid peptides. Degrading produ of several proteinases from *Bacillus pumilus* were evaluated using MALDI-TOF mass-spectrometry, a their toxicity was assessed *in vitro* using cell-culture assays and morphological studies. These enzyn have proved to be non-toxic and were demonstrated to cleave through the functional domains of amyloid peptide. By yielding inactive fragments, proteinases of *Bacillus pumilus* may be used as candid anti-amyloid agents.



## 1. Introduction

Alzheimer's disease (AD) is a slowly progressive primary neuro-degenerative disorder. Its histo-pathological hallmark features, the senile plaques, are extra-cellular deposits of β-amyloid-peptide (βAP) and impaired cellular brain structures associated with inflammatory elements such as microglia. Although a number of hypotheses exist around the patho-mechanism of AD, there is perhaps no single causative agent. It is also dubious if plaques are responsible for and actively involved in the degenerative process, or just innocent by-products formed during the course of the disease that is triggered by yet unknown other factors. According to the amyloid-theory, soluble monomeric βAP is a physiological peptide with several vital functions in the brain (Wu et al., 1995; Schulz, 1996; Huber et al., 1997; Kamenetz et al., 2000), and aggregation is key to its neuro-toxicity (Pike et al., 1993; Dumery et al., 2001), however it is not clearly established what causes polymerization.

Converging lines of evidence suggest that bacterial and viral p ticles might play a role in cerebral amyloidosis seen in AD, a bacterial endotoxins, among others, have been demonstrated promote βAP fibrillo-genesis (Reis et al., 2010; Asti and Giog 2014). Neuro-infections may also lead to global cerebral infla mation similar to that is seen in AD brains. In order to facilit trans-migration of mono-nuclear leukocytes from the periphe into the central nervous system (CNS), inflammatory mediat such as cytokines enhance the permeability of blood-brain b rier (BBB) (de Vries et al., 1996). Similarly, *Helicobacter pyl* also releases products that could induce break-down of the B (Kountouras et al., 2014). Other micro-organisms such as *Herp simplex* virus type 1 (HSV1) and *Chlamydia pneumoniae* are post lated to be risk factors for AD (Itzhaki et al., 2004).

In addition to their role in infection, bacteria are also kno for their therapeutic effects. Microbial proteinases are widely us as medicinal agents, such as the thrombo-lytic drugs staphy and strepto-kinase. Bacterial proteases have several advantag over similar products of animal origin: they are secreted into t medium and can easily undergo purification, they have high s bility with low patho-genicity and toxicity, and cultivation of t micro-organisms is also more cost effective. Their role in β metabolism, however, is not yet characterized.

βAP is continuously produced in low concentrations, and rapidly turned over in the normal brain: reduced catabolism m

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