Upite and Jansone: *Intrinsic Activity*, 2017; **5**(Suppl.2):A2.44
doi:10.25006/IA.5.S2-A2.44
published online: 16 October 2017

INTRINSIC ACTIVITY

2nd International Conference in Pharmacology: From Cellular Processes to Drug Targets

Rīga, Latvia, 19–20 October 2017

MEETING ABSTRACT

A2.44

Are the peptide-based compounds the treatment candidates for Alzheimer's disease?

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Background: Alzheimer's disease (AD) is a neurodegenerative disease that affects more than 45 million people widespread [1]. Aggregation of intracerebrally generated amyloid β (Aβ) and tau proteins is the main neuropathological hallmark of AD [2]. The discovery of mutated Aβ to be protective in heterozygote family members in Italy and Island opens new roads for the treatment of amyloid protein depositions in the brain [3]. Recently, intensive research is focused on the role of short sequence peptides in dissolving Aβ aggregates in the central nervous system and providing their elimination from the brain through blood circulation.

Objectives: To advance our understanding about peptide-based Aβ aggregate inhibitors, based on natural Aβ sequence and containing modified amino acids.

Methods: A systematic search (1996–2017) of PubMed, Science Direct, EBSCO, Scopus, and Cochrane Library was performed by using key terms: AD, Aβ peptide, Aβ aggregation, and peptide-based AD inhibitors.

Results: The search yielded up to 658 records from 1996 to 2017. After screening of the titles and abstracts, 107 records met the criteria: AD, Aβ peptide, Aβ aggregation, peptide-based AD inhibitors, drug treatment and clinical trials. Widening of the knowledge of mechanism relying on the basis of Aβ fibril formation and protein misfolding has expanded the research interest of usefulness of peptide-based Aβ aggregate inhibitors in AD. In the last 25 years researchers' interest was directed on molecular structures of peptides suitable for potential treatment of AD, such as D-amino acid- and modified amino acid-containing peptides, retro-inverso peptide inhibitors, endogenous dipeptides, and peptides based on C-terminus, peptides derived from functional site sequence, cyclic peptides. Most of the synthesized peptides tested in AD studies have showed positive results in transgenic mouse models, however, have failed at different phases of clinical studies. The reasons identified were difficulties to cross the blood–brain barrier and low bioactivity. Peptide-based therapeutic agents might be one of the potential option for AD treatment that need to be further developed; however, there are still needs also for effective biomarkers to diagnose the disease at an early stage, thus gaining the most of the benefit of the used treatment before the neurodegenerative processes in the brain becomes irreversible.

Conclusions: The results of extensive research studies made in the last 25 years have shown the potential role of short peptide-based Aβ aggregate inhibitors in the treatment of AD.

Acknowledgements: Grant no. NFI/R/2014/023 of the EEA and the Norwegian Financial Mechanism project.

Keywords: Alzheimer's disease – amyloid aggregation – amyloid β peptide – drug treatment

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