Anti-myeloid peptides to combat Alzheimer's

Alzheimer's disease (AD) is a yet incurable neurodegenerative disease that slowly and progressively worsens. The most common early symptom is difficulty in remembering recent events and as the disease advances, symptoms include problems with language, disorientation, mood swings, loss of motivation, self-neglect and behavioral changes. Ultimately, bodily functions are lost leading to death.

Nanomolar inhibitors with drug-like properties

IP RIGHTS
US granted, EP pending
2021

Our lead synthetic macrocyclic peptide, termed MCIP 2E, belongs to a new class of highly potent inhibitors of Aß-amyloid self-assembly and related cytotoxic effects.

REFERENCES:

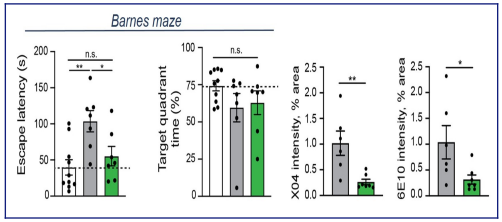
- Published patent application
- Spanopoulou et al., 2018

01 Effective production by routine solid phase peptide synthesis

02 Good proteolytic stability in human plasma (in vitro)

03 Effective crossing of human blood brain barrier (in a cell model)

04 Promising data from behavioral tests with no observed in vivo toxicity in mouse model



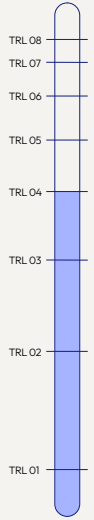
Treatment of 5XFAD mice with the macrocyclic peptide 2E reduces amyloid pathology and improves their learning and memory; data from 5-month-old mice (Ji, Dalla Volta, Bernhagen, Kapurniotu, Gökce et al., manuscript in preparation, LMU and TUM).

CHALLENGE

AD is characterized by extracellular deposition of amyloid-ß (Aß). Despite the established link to amyloid plaques of ß-amyloid peptide (Aß) in the brain, all anti-Aß therapeutic strategies have so far failed e.g. antibody-based approaches aimed at blocking amyloid self-assembly. However, the development of anti-amyloid compounds is an important target of AD-related research. For this reason, there is an urgent need to develop novel classes of amyloid inhibitors.

INNOVATION

MCIP 2E was confirmed as a potent inhibitor of amyloidogenesis in several in vitro assays and a mouse model of Alzheimer's disease (unpublished data). Its drug-like properties include small size (<20 amino acids), high solubility, potent amyloid inhibitor function (nanomolar IC50) and Aß-40(42) binding affinity, target selectivity and blood brain barrier (BBB) permeability (determined using in vitro models). In light of the extremely low BBB as one of the weak points of antibody-based approaches, the above listed properties make MCIPs suitable drug candidates.



01 Basic principles observed · **02** Technology concept formulated · **03** Experimental proof of concept · **04** Technology validated in lab · **05** Technology validated in relevant environment · **06** Technology demonstrated in relevant environment · **07** System prototype demonstrated in operational environment · **08** System complete and qualified

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