Multifunctional Anti-Amyloid Peptides

Aberrant amyloid self-assembly and cytotoxicity of Aß and a-Synuclein are linked to the pathogenesis of more than 50 cell-and neurodegenerative diseases including Alzheimer's (AD), Parkinson's disease (PD) and type 2 diabetes (T2D), the latter being epidemiologically linked to both AD and PD. For this reason, there is an urgent need to develop molecules that suppress both amyloid self-assembly and cross-seeding interactions of above peptides can be promising leads for therapeutics in AD, PD and T2D.

Nanomolar inhibitors with drug-like properties

IP RIGHTS
PCT phase initiated
2025

Macrocyclic peptides designed to mimic IAPP self-/cross-interaction sites and previously found to inhibit amyloidogenesis of IAPP and/or amyloid-β peptide Aβ40(42) of Alzheimer's Disease, are nanomolar inhibitors of both self- and IAPP-cross-seeded amyloid self-assembly of αSyn.

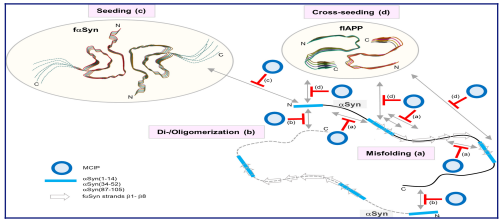
Hornung et al., 2025

01 MCIPs 2b and 2e as candidates for treatment of AD, T2D, PD incl. related synucleinopathies

02 High stability toward proteolytic degradation in human plasma and by brain proteases (in vitro)

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

04 Promising molecules for potential biomarkers - detection/quantification of (pre)amyloidal aggregates



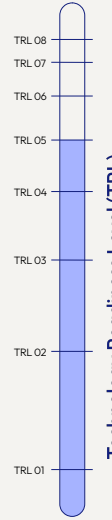
Multi-Targeting Macrocyclic Peptides as Nanomolar Inhibitors of Self- and Cross-Seeded Amyloid Self-Assembly of α-Synuclein.

CHALLENGE

AD-and PD-related neurodegeneration in the brain are linked to the self-assembly of Aß and a-Synuclein while T2D-related pancreatic beta-cell degeneration is linked with amyloid self-assembly of IAPP. Cross-seeding interactions between different amyloid polypeptides/proteins have emerged as possible molecular links between various different cell-/neurodegenerative diseases. Molecules that suppress both amyloid self-assembly and cross-seeding are urgently needed, however.

INNOVATION

The results suggest that the anti-amyloid function of MCIP 2 b and 2 e is mediated via interactions with αSyn via three αSyn segments identified as key sites of both αSyn self- and its cross-interactions with IAPP. MCIP 2b and 2 e are also able to block Aβ42-mediated cross-seeding of αSyn. Based on their broad spectrum amyloid inhibitor activity and additional drug-like properties, MCIPs are promising leads for multifunctional anti-amyloid drugs in PD, T2D, AD, and their comorbidities. The identified key αSyn segments shall serve as valuable targets for the design of novel, multi-site targeting molecules as effective anti-amyloids in PD and related synucleinopathies.



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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