

Macrocyclic Anti-Amyloid Peptides

Aberrant amyloid self-assembly and cytotoxicity of A β and α -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.

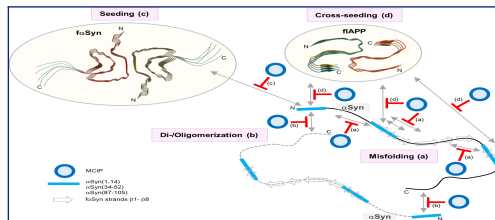


Nanomolar inhibitors with drug-like properties

Macrocyclic peptides designed to mimic IAPP self-/cross-interaction sites and previously found to inhibit amyloidogenesis of IAPP and/or amyloid- β peptide A β 40(42) of Alzheimer's Disease, are nanomolar inhibitors of both self- and IAPP-cross-seeded amyloid self-assembly of α Syn.



Hornung et al., 2025



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

IP RIGHTS

PCT phase initiated

2025

CHALLENGE

AD- and PD-related neurodegeneration in the brain are linked to the self-assembly of A β and α -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 2b and 2e is mediated via interactions with α Syn via three α Syn segments identified as key sites of both α Syn self- and its cross-interactions with IAPP. MCIP 2b and 2e are also able to block A β 42-mediated cross-seeding of α Syn. 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 α Syn 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

TRL 08

TRL 07

TRL 06

TRL 05

TRL 04

TRL 03

TRL 02

TRL 01

Technology Readiness Level (TRL)



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