

Amyloid-binding Peptoids with Broad-spectrum Antiviral, Antibacterial, and Antifungal Activity

Background

Amyloid β ($A\beta$) is a key protein involved in the pathogenesis of Alzheimer's Disease (AD). A key property of $A\beta$ that is now believed to be at the core of its toxicity in AD is its ability to form soluble, toxic oligomers. Targeting such oligomers remains a promising avenue for AD therapeutic development. It has been found that 1:1 equimolar LL-37/ $A\beta$ 40 mixtures are totally prevented from forming $A\beta$ fibrils, while lower relative molar amounts of LL-37 slow the kinetics of fibril formation; and in this patent, a synthetic peptoid mimic of LL-37 is also shown to bind $A\beta$.

It has also become clear that sporadic AD (not resulting from a unique familial predisposition to disease) is either caused by or accompanied by the occurrence of polymicrobial brain infections and dysfunction of the blood-brain barrier (BBB). Certain oral pathogens that are associated with dementia—including *Porphyromonas gingivalis* (PG), Herpes Simplex Virus-1 (HSV-1) and *Candida albicans*—can be killed or inactivated by the LL-37 peptide, which is produced by the human innate immune system, as well as by peptoid mimics of LL-37 described in this patent.

Although $A\beta$:LL-37 interactions offer an interesting starting point in the development of new therapeutic approaches that block $A\beta$ aggregation and toxicity, the relatively complex, poorly understood, pleiotropic immunomodulatory effects of LL-37, as well as its relatively high molecular weight (~4500 g/mol, 37 amino acids) and extreme vulnerability to cleavage by proteases, are substantially disadvantageous features from the standpoint of using the peptide as an exogenous AD therapeutic. Thus, a biostable peptoid mimic of LL-37 is more promising.

Technology

It was recently discovered that certain peptoid mimics of LL-37 share the same anti-amyloid activity of the peptide, while also exhibiting potent antimicrobial and antiviral activity against both *P. gingivalis*, HSV-1, and *C. albicans*. Thus, these peptoids have the potential to be developed as antimicrobial treatments that may also serve as anti-amyloid treatments.

Figure:

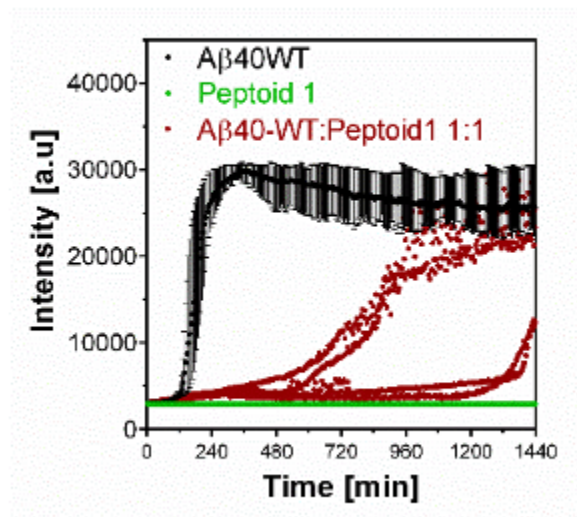


Figure Description: *Thioflavin T (ThT) fluorescence measurements of the process of A β amyloid formation and A β :peptoid formation following A β 40 fibril formation.*

(image credit: the inventors)

Applications

- Therapeutic or prophylactic treatments for Alzheimer's Disease

Advantages

- Leverages recently discovered aspects of A β amyloid formation, A β :LL-37 interactions and A β :peptoid interactions
- Simultaneously reduces A β amyloid loads and addresses the polymicrobial brain infections that frequently accompany AD

Patents

- Published Application: [WO2022165539](#)
- Published Application: [20230390222](#)

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