Natural and designed inhibitors of amyloid formation

https://www.neurodegenerationresearch.eu/survey/natural-and-designed-inhibitors-of-amyloid-formation/

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Natural and designed inhibitors of amyloid formation

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Research Abstract
We have pioneered experimental studies of the protein domain BRICHOS, initially driven by interest in the folding properties of the very aggregation-prone transmembrane region of prosurfactant protein C (proSP-C). These studies have recently generated several exciting findings; (i) BRICHOS prevents aggregation and fibril formation of the amyloid beta-peptide (Abeta) associated with Alzheimer´s disease (AD), (ii) mutations in proSP-C BRICHOS result in human amyloid disease, the first described amyloidosis secondary to chaperone malfunction, (iii) BRICHOS prevents Abeta aggregation and toxicity in fruit flies and hippocampal slices, and (iv) one BRICHOS structure is determined and a specific mechanism of action has been revealed. From this platform we now aim to (i) investigate if BRICHOS can reduce Abeta

aggregation and behavioral changes in AD mouse models, (ii) study structures and functions also of BRICHOS from Bri2 (associated with familial dementia), Bri3, and gastrokine 2 (associated with gastric cancer), (iii) use transgenic Drosophila flies to further study BRICHOS effects on Abeta aggregation and toxicity in vivo, (iv) search for compounds that potentiate the effect of endogenous BRICHOS. We also aim to study two other ways to prevent amyloid fibril formation, based on ligands designed to stabilize a non-aggregating conformation of Abeta and on structure-based inhibitors linked to a spider silk domain, another protein that we have analyzed in great detail.

Further information available at:

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