Identifying novel anti-amyloid targets in psychogeriatric disorders

https://neurodegenerationresearch.eu/survey/identifying-novel-anti-amyloid-targets-in-psychogeriatric-disorders/

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Sweden

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4

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Research Abstract
During the past decade important roles for proteoglycans (PG) in psychiatric diseases have been discovered. We have been focusing on the importance of glypican-1 (an amyloid associated heparan sulfate (HS) PG abundant in the adult human brain) in psycogeriatric disorders including prion, Niemann-Pick and Alzheimer´s disease (AD) and found evidence for its anti-amyloid properties. Our studies on in vitro and in vivo models (transgenic AD mice) as well as human brain tissues from AD patients show accumulation of HS released from glypican-1 in amyloid plaques. Further, treatment with reducing agents like vitamin C induces release of HS from glypican-1 that forms conjugates with aggregation prone proteins, modulates their oligomerization, suppresses their toxicity and targets them to proteasomes for degradation.

Here, we aim to elucidate the role of glypican-1 as a regulatory factor for amyloid beta trafficking, oligomerization, degradation and toxicity using in vitro and in vivo AD models. The anti-amyloid properties will be investigated in primary cortical neurons (in vitro) and hippocampal slices (ex vivo) from wild type and AD mice. Attempts will be made to purge amyloid beta burden in transgenic AD mice (in vivo). We will also investigate the role of exosomes as vehicles for transfer of toxic amyloids and elucidate the role of PG as receptors for exosomal amyloid uptake. Involvement of PG in spread of amyloid beta will also be investigated in vivo using transgenic AD mice.

Further information available at:

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