

HUMAN AND MOUSE SEEDS DIFFERENTIALLY AFFECT A β AGGREGATION BY MODULATING THE INFLAMMATORY RESPONSE

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Abstract text: Alzheimer's Disease (AD) is a neurodegenerative proteinopathy in which A β can misfold and aggregate into seeds that structurally corrupt native proteins, mimicking a prion-like process. These amyloid aggregation and propagation processes are influenced by three factors: the origin of the A β seed, time of incubation and host. However, the mechanism underlying the differential effect of each factor is poorly known. Previous studies have shown that the A β source is relevant for the amyloid process, since its pathogenicity is different according to its origin. Furthermore, recent evidence suggests that microglia plays a key role in the amyloidogenic event, and can modulate the propagation and aggregation process. Here, we seek to perform a comparative study to determine whether A β seeds from humans vs a familial AD line (the 3xTg-AD model) are more efficient to generate amyloid aggregates, as well as the role of the microglia in the propagation process.

Methods: Amyloid seeds from AD patient (stage C for amyloid; from the Alzheimer's Disease Research Center at UCI) and 25 mo-3xTg-AD mice were injected into the hippocampus of 7-8-month-old 3xTg-AD mice. They were analyzed 10 months post-surgery for amyloid and microglia markers.

Results: Our findings demonstrated that amyloid seeds from the human patient seem to induce a more aggressive amyloid pathology compared to seeds from aged 3xTg-AD mice. Moreover, human and mice seeds differentially affect the presence of plaque-associated microglia in 3xTg-AD mice.

Conclusion: These results suggest that seeds from human patients seem to be more amyloidogenic than from aged 3xTg-AD mice, and also microglia cells may play a key role in this differential effect. Therefore, more profound understanding these factors will provide key insight on how amyloid pathology progresses in AD.

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