Amyloid propagation in a sporadic model of Alzheimer disease

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Background: Most age-associated neurodegenerative disorders involve the aggregation of specific proteins within the nervous system, as occurs in Alzheimer's disease (AD). Recent evidence indicates that Aβ can misfold and aggregate into seeds that structurally corrupt native proteins, mimicking a prion-like process of template protein corruption or seeding. In fact, studies in FAD-based animal models show that Aβ deposition and cerebral amyloid angiopathy may be induced by intracerebral infusion of brain extracts from AD patients or from aged APP-transgenic mice. These studies have shown that the characteristic of both the seeding agent and the host influence the pathologic signature of the Aβ seeds. In this regard, the majority of the Aβ-seeding studies have been done in APP-transgenic animal models that overproduce APP and/or Aβ. However, it remains to be elucidated whether Aβ deposition can be induced by Aβ seeds in an animal model that does not overexpress APP and produces wild type human Aβ and if these aggregates are similar to the human condition.

Method: Here, we used an innovative animal model to better understand the amyloidogenic events that occur in the sporadic form of the disease. Our model, termed hAβ-KI, expresses wild-type human Aβ under the control of the endogenous mouse APP gene. Thus, amyloid seeds from AD patients (stage C for amyloid) from the Alzheimer's Disease Research Center (ADRC) at UCI were administered into 7-8-month-old hAβ-KI and as positive controls 3xTg-AD mice were employed.

Result: Our findings demonstrated that amyloid seeds differentially occur in 3xTg-AD and hAb-KI mice and these aggregates are developed earlier in the familial model, 3xTg-AD mice.

Conclusion: These results suggest that multiple factors such as the seed, recipient model and time are critical factors that can modulate the amyloid pathology onset and progression. Thus, more profound understanding these factors will provide key insight on how amyloid pathology progress in AD.