AMYLOID-β SEEDING AND PROPAGATION PROCESSES IN A hAβ-KI MODEL OF ALZHEIMER'S DISEASE

Laura Trujillo-Estrada[1], Kelly Do Huynh[2], Marie Minh Thu Nguyen[2], Alwin Cheung[2], Janine Pham Tran[2], Cristina Nunez-Diaz[1], Stefania Forner[2], Alessandra C Martinie[2], Celia da Cunha[2], Mohammad Shahnawaz[3], Claudio Soto[3], Ines Moreno-Gonzalez[1], Antonia Gutierrez[1], Frank M LaFerla[2], David Baglietto-Vargas[1]

[1]University of Malaga/CIBERNED/IBIMA, Cell Biology, Malaga, Spain, [2]University of California Irvine, Institute for Memory Impairments and Neurological disorders, Irvine, CA, [3]University of Texas Health Science Center at Houston, The Mitchell Center for Alzheimer's Disease and Related Brain Disorders, Department of Neurology, Houston, TX

Recent evidence indicates that Aβ can misfold and aggregate into seeds that structurally corrupt native proteins, mimicking a prion-like process. Several studies using FAD animal models have demonstrated that intracerebral infusion of brain extracts from APP-transgenic mice or AD patients induce Aβ deposition and cerebral amyloid angiopathy. To carry out most of these Aβ-seeding studies, APP-transgenic animal have been used. Nevertheless, it remains to be elucidated whether Aβ deposition can be induced by Aβ-seeds in a sporadic AD model that does not overexpress APP and produces wild type human Aβ.
We used an innovative model to better understand the amyloidogenic events that occur in sporadic AD. This hAβ-KI model, expresses wild-type human Aβ under the control of the endogenous mouse APP gene. Aβ-seeds from AD patients (stage C) from the AD Research Center (UCI) were administered into 7-8-month-old hAβ-KI and as positive controls 3xTg-AD mice were employed.
We demonstrated that amyloid seeds can stimulate Aβ aggregations in 3xTg-AD and hAβ-KI models. We found that Aβ aggregates occur earlier in the 3xTg-AD vs hAβ-KI and that a longer term of treatment is necessary to accelerate diffusible Aβ pathology in the hAβ-KI mice. Thereferoe, this hAβ-KI model represents an important step towards the development of next-generation animal models that will provide better predictive outcomes for human patients.