CHARACTERIZATION OF THE ROLE OF PROTOCADHERIN 11 X-LINKED IN ALZHEIMER’S DISEASE

Y. Levites¹, M. Carrasquillo², K. Jansen², C. Ceballos-Diaz¹, T. Golde¹
¹University of Florida, Gainesville, ²Mayo Clinic Jacksonville, Jacksonville, FL, USA

Introduction: Understanding the factors responsible for Alzheimer’s Disease (AD) is critical for the development of effective preventive and therapeutic strategies. In a recent genome-wide association study, an association of variants of the protocadherin 11 X-linked gene (PCDH11X) with late onset AD was described.

Aims: In this study we aim to further dissect the functional underpinnings of this association using somatic brain transgenesis technology we developed to knockdown and overexpress PCDH11X in murine brain.

Methods: Adeno-associated virus (AAV) was used to deliver anti-PCDH11X shRNAs to neonatal brains of transgenic AD mice and amyloid deposition was assessed using biochemical and immunohistochemical techniques.

Results: We were able to construct shRNA that efficiently knocked down PCDH11x levels in cell culture and our preliminary experiments in the CRND8 mouse model of AD suggest that knockdown of PCDH11X may prevent Aβ deposition - significant reductions in biochemical amyloid loads, and a decrease in apparent immunohistochemical amyloid loads in mice treated with PCDH11X shRNA were observed. Additionally we are analyzing whether an overexpression of full length or C-terminally truncated version of PCDH11X has an impact on amyloid levels and deposition in these mice.

Conclusions: Our results suggest a correlation between PCDH11X levels and amyloid pathology in CRND8 mice. Further studies on the role of overexpression of PCDH11X on APP-related pathology are of a great significance.