

## 7<sup>th</sup> International Conference on AD/PD (2005) – Sorrento, Italy

### **Behavioral deficits and increased mGluR5 immunoreactivity in CNS of transgenic mice overexpressing alpha-synuclein**

D.L. Price<sup>1,3</sup>, E. Rockenstein<sup>1,2</sup>, N.A.B. MacLean<sup>1,3</sup>, M.H. Ellisman<sup>1,3</sup> E. Masliah<sup>1,2</sup>  
*Depts. of Neuroscience<sup>1</sup> and Pathology<sup>2</sup>, and National Center for Microscopy and Imaging Research<sup>3</sup>, University of California, San Diego, La Jolla, CA USA*

Glutamatergic system components are well positioned within the CNS to play important roles in the pathogenesis of neurodegenerative disorders and have received interest as a therapeutic target for Parkinsonian motor dysfunction via restoration of dopamine-glutamatergic homeostasis. Transgenic mice overexpressing wild-type human alpha-synuclein ( $\alpha$ -syn) exhibit  $\alpha$ -syn immunopositive inclusions and neurites in multiple regions of the brain including the hippocampus, cerebellum and cortex. Drawing on the methods of multi-scale imaging, behavioral pharmacology and bioinformatics, we are using a multi-disciplinary approach to characterize a transgenic mouse overexpressing human alpha-synuclein. We conducted large scale mapping studies of mGluR5 immunoreactivity in regions of the brain previously shown to contain  $\alpha$ -syn immunopositive inclusions. Overall increased mGluR5 immunoreactivity was observed in many brain regions of  $\alpha$ -syn transgenic mice associated with motor and cognitive functions. In addition, focal regions of mGluR5 immunoreactivity are laminar in distribution and correspond to  $\alpha$ -syn immunolabeling patterns in hippocampal and cortical regions. Transgenic animals also exhibit cognitive and motor deficits as measured in water maze and pole test paradigms. The current studies indicate that this mouse model is an appropriate choice for evaluation of mGluR5 antagonist treatment on pathological and behavioral indices. Furthermore, these data will be used to explore the role of mGluR5 receptors in the CNS regions vulnerable to formation of protein aggregations in this and other transgenic mouse models of Parkinson's syndromes. Our findings highlight the advantages of using a multi-disciplinary approach to evaluating mouse models of human neurodegenerative diseases.

*Supported by The Branfman Family and MJ Fox Foundations, NCRN RR04050, NIDCD DC03192 (CCDB), RR043050 (Mouse BIRN), and NIH LM 07292.*