AN ANTIBODY SHOWING HIGH REACTIVITY FOR OLIGOMERIC ALPHA-SYNUCLEIN REVEALS EXTENSIVE PATHOLOGY

G.G. Kovacs¹, U. Wagner², M. Pikkarainen³, B. Dumont⁴,⁵, A.A. Osman², A. Perret-Liaudet⁴, H. Budka¹, I. Alafuzoff³,⁶, I. Lachmann²

¹Institute of Neurology, Medical University of Vienna, Vienna, Austria, ²AJ Roboscence GmbH, Leipzig, Germany, ³Institute of Clinical Medicine - Neurology, University of Eastern Finland, Kuopio, Finland, ⁴Neurobiology Dept., GHE, Hospices Civils de Lyon, ⁵Neuropharmacology Lab., ISPZ-University of Pharmacy, Lyon, France, ⁶Department of Genetics and Pathology, Uppsala University, Uppsala, Sweden

Introduction: Alpha-synuclein is the major protein associated with Lewy body dementia, Parkinson’s disease and multiple system atrophy. Since it is present in the brain in physiological conditions as a presynaptic protein, it is crucial to characterize disease-associated modifications to develop an in vivo biomarker. Indeed, recent studies emphasize that the oligomer form of alpha-synuclein may be a candidate to distinguish diseased from non-diseased conditions.

Aims: To develop and validate antibodies showing high specificity and sensitivity for disease-associated alpha-synuclein.

Methods: Recombinant human alpha-synuclein or synthetic peptides containing different amino acid sequences were used for immunization of mice. After generation of alpha-synuclein oligomers, ELISA and Western blotting was used to test the specificity of antibodies. Using tissue microarray sections originated from different human alpha-synucleinopathies we compared the novel antibodies with commercially available antibodies.

Results: We generated three anti-alpha-synuclein antibodies. Antibody 5G4 was able to trap oligomeric alpha-synuclein preparation in sandwich ELISA or coated on magnetic beads, whereas no signal was found for monomeric alpha-synuclein. 5G4 proved to be superior to other antibodies in comparative immunohistochemical studies and showed more prominent pathological deposits even in tissue that was in fixative for a long time (up to 14 years).

Conclusions: On one hand antibody 5G4 may be suitable for re-evaluation of archival material and may reveal more widespread alpha-synuclein pathology than a panel of commercially available antibodies and on the other hand it may be a reliable tool for the development of in vivo diagnostic assays for detecting alpha-synuclein oligomers in body fluids.