CHARACTERIZATION OF LINE 61 OF MICE OVEREXPRESSING A-SYNUCLEIN (TNWT A-SYN): BEHAVIORAL AND HISTOLOGICAL CHANGES THROUGHOUT ADULTHOOD AND AGING

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Introduction: The accumulation of a-synuclein is a major feature in the pathology of Parkinson's disease. Transgenic mice over-expressing a-synuclein, driven by the Thy1-promoter, serve as an important model for research and development. Thus, a thorough understanding of the long-term effects of a-synuclein over-expression on both structure and function of the brain is essential for the planning of research projects and the interpretation of their outcomes.

Aims: Characterization of Line 61 with regard to age-related expression of murine and human isoforms of a-synuclein, and behavior of transgenic mice and wildtype littermates.

Methods: Quantitative histological analysis of a-synuclein levels and plaque load, and analysis of motor function.

Results: First behavioral tests show motoric deficits of a-synuclein transgenic animals, as observed in the Challenging BeamWalk and Beam Walk Test, starting at an age of 2 months. We present data on the age-dependent expression and distribution of endogenous (murine) and transgene (human) expression of a-synuclein isoforms throughout different regions of the mouse brain. In addition, we evaluate the formation of Lewy body-like inclusions throughout the brain.

Conclusions: We are able to show changes in the histological and behavioral profiles throughout the lifetime of mice. Most important is the correlation of the age-related morphological and functional changes. The results increase our understanding of the role of a-synuclein in normal function and disease and will provide us with a new Parkinson's disease animal model.