FORMATION OF A-SYNUCLEIN AGGREGATES IN A CELL CULTURE MODEL

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Introduction: Aggregation of the cytosolic protein α-synuclein plays a central role in neurodegenerative disorders such as Parkinson’s disease (PD) and dementia with Lewy bodies (DLB). The Lewy bodies, a characteristic feature of these diseases, are predominantly composed of fibrillar α-synuclein. However, recently it has been shown that small presynaptic α-synuclein aggregates, not Lewy bodies, cause neurodegeneration in DLB.

Aims: Based on the hypothesis that small α-synuclein aggregates play an important role for the pathogenesis of PD/DLB our aim was to establish a cellular model for the reproducible production of small α-synuclein aggregates in order to investigate the possible pathological function of these molecules in more detail.

Methods: Human α-synuclein overexpressing SH-SY5Y cells were treated with retinoic acid/FeCl2 and analyzed by immunofluorescence. To further study the formation of aggregates we used the previously established protein aggregate filtration (PAF) assay and characterized the molecules after proteinase K digestion and separation in a density gradient, in order to compare them with aggregates isolated from human brain samples.

Results: We detected partially proteinase K-resistant and thioflavin S-positive α-synuclein aggregates in our cell culture system after treatment with retinoic acid and FeCl2. The aggregates were comparable with small aggregates from human brain.

Conclusions: Here we present a cellular model for the effective and reproducible production of α-synuclein aggregates showing characteristics like small aggregates from DLB patients. This model can be used to investigate the process of α-synuclein aggregation in more detail, as well as the molecular mechanisms of neurodegeneration in PD/DLB.