TREATMENT WITH MONOCLONAL ANTIBODIES REDUCES INTRACELLULAR DIMERIZATION/OLIGOMERIZATION OF ALPHA-SYNUCLEIN IN A CELL CULTURE MODEL


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Introduction: Lewy bodies are present in the cytoplasm of certain neurons in brains with Parkinson's disease and dementia with Lewy bodies. These intracellular aggregates mainly consist of fibrillary forms of the presynaptic protein alpha-synuclein. Natively, alpha-synuclein is unfolded but a range of intermediate species are formed during the aggregation process. Such oligomeric forms have particular neurotoxic properties and could therefore be attractive targets for immunotherapy or other treatment strategies.

Aims: To study the effect of passive immunotherapy on a cell model for alpha-synuclein dimerization/oligomerization.

Methods: Bimolecular fluorescence complementation (BiFC) was used to measure the extent of intracellular alpha-synuclein dimerization/oligomerization. Constructs of full-length alpha-synuclein fused with either halves of the green fluorescent protein (GFP) were transiently co-expressed in H4 neuroglioma cells. Next, the cells were incubated in conditioned media with different monoclonal alpha-synuclein antibodies. Finally, cells were analyzed by fluorescence microscopy.

Results: After 48 hrs, cells transfected with the two alpha-synuclein-GFP constructs displayed robust GFP signals, indicating alpha-synuclein dimerization/oligomerization. Transfected cells treated with alpha-synuclein monoclonal antibodies displayed significantly reduced intracellular GFP signals compared to cells treated with irrelevant antibodies. Antibodies against C-terminal epitopes proved to be more efficient in preventing alpha-synuclein dimerization/oligomerization.

Discussion: Here, we show that alpha-synuclein dimerization/oligomerization can be significantly reduced in a cell culture model by extracellular treatment with monoclonal alpha-synuclein antibodies. Our data thus suggest that passive immunotherapy could be a useful strategy against alpha-synuclein pathology in spite of its intracellular nature.