Transcription Nuclear Factor of Activated T-Cells (NFAT) Involved in Parkinson's Disease (PD)

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INTRODUCTION: Studies suggesting that the mechanism which leads to neuronal loss in PD consists by an abnormal accumulation of a protein α-synuclein and subsequent formation of intracellular protein aggregates called Lewy bodies. Studies have shown that α-synuclein aggregates alter membrane fluidity and increase calcium (Ca+2) influx, rise levels of intracellular Ca+2 lead to the activation of calcineurin phosphatase. Although, the main calcineurin target are (NFAT), its contribution to the PD is very poorly understood. NFAT proteins directly regulate the expression of genes involved in control of cell death by apoptosis, as well as gene involved in inflammation.

OBJECTIVES: to evaluate the involvement of NFAT in the neurodegenerative process induced by aggregates of α-synuclein

MATERIAL AND METHODS: Purification of α-syn protein, A30P mutant was performed as previously established protocol (CONWAY 1998).

DISCUSSION AND RESULTS: Only oligomers are capable of triggerin cell death in primary cultures of dopaminergic neurons and this effect is partially reversed by the inhibition of enzyme CnA. The same was observed in N2A neuroblastoma cell where the specific inhibitor of NFAT, the VIVIT peptide, was able to block programed cell death induced oligomers. Alpha synuclein oligomers and fibers were able to reduce the number of presynaptic events, as seen by the expression of synapsin protein I. This effect was also reversed when the cells were pre treated with an inhibitor of CnA. Alpha synuclein oligomers modulate the expression of genes involved in progammed cell death such as Bcl2A1A, Bcl-2L11 and TNFRSF21 as well as genes involved in formation and maintenance of synaptic events as SYN1, Tubb4 and Kalrn. Inhibition of NFAT was able to normalize the expression of this genes being possibly involved in their regulation of transcription.

CONCLUSION: NFAT ability to regulate genes involved in the regulation of apoptosis and dynamic formation of functional synapses in neurons and possibly in PD neurodegeneration process.

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