A-SYNUCLEIN CONFERS RESISTANCE TO STAUROSPORINE-INDUCED APOPTOSIS NOT ONLY IN NEURONAL SH-SY5Y CELLS, BUT ALSO IN MELANOMA SK-MEL28 CELLS

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The Synuclein family members, α-, β-, and γ-Synuclein, are a family of neuronal proteins with elusive functions. Initially termed as Breast Cancer-specific Gene 1, γ-Synuclein is involved in carcinogenesis. On the other hand, α-Synuclein is a central player in the pathophysiology of Parkinson's disease (PD). Its wild-type form can inhibit apoptosis in response to various pro-apoptotic stimuli, making it another attractive candidate in carcinogenesis besides γ-Synuclein. Recently, Matsuo & Kamitani (2010), PLoS ONE, 5, e10481 showed that α-Synuclein is highly expressed in the human melanoma cell line, SK-MEL28, but is undetectable in non-melanocytic cutaneous carcinoma and normal skin. Therefore, the objective of this study was to re-investigate the anti-apoptotic property of α-Synuclein in neuronal SH-SY5Y and melanoma SK-MEL28 cells, by overexpression and knockdown, respectively. SH-SY5Y and SK-MEL28 cells were stably transfected with pcDNA3.1-human α-Synuclein and three pLKO.1 short hairpin RNAs (shRNAs) targeting human α-Synuclein, respectively, and were subjected to staurosporine treatment. MTT cell viability assay showed that SH-SY5Y cells overexpressing wild type α-Synuclein were significantly less vulnerable to staurosporine cytotoxicity compared to mock or untransfected controls and those expressing familial PD α-Synuclein mutants - A30P, E46K, A53T. In SK-MEL28 cells, depletion of endogenous α-Synuclein significantly enhanced staurosporine cytotoxicity, consistent with reduced Bcl-2 and Bcl-XL, and increased Bax and cleaved caspase 9 expression levels. Flow cytometric analysis with Propidium Iodide staining also revealed that the proliferative index was significantly reduced in α-Synuclein knockdown SK-MEL28 cells. These results suggest that the fundamental property of wild type α-Synuclein may be anti-apoptotic.