Influence of alpha-synuclein overexpression on DNA damage in neuronal cell lines

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Parkinson's disease (PD) is a neurodegenerative disease characterized by the loss of dopaminergic neurons and the presence of intracellular aggregates enriched in alpha-synuclein (alpha-syn). Its underlying cause is still unknown. Recent findings of somatic mutations in human brains might provide evidences associating environmental genotoxicity with the etiology of some neurodegenerative diseases. On the other hand, misfolded alpha-syn has been hypothesized to cause DNA damage in some neuronal cells and to increase the sensitivity of cells to oxidative stress.

Mycotoxins are naturally occurring food contaminants produced as secondary metabolites by filamentous fungi. Among them, ochratoxin A (OTA) is one of the most relevant ones due to its genotoxic and carcinogenic potential as well as to its ability to induce oxidative stress. Recently, our group has demonstrated *in vitro* and *in vivo* that OTA replicates several PD features.

In order to study whether the over-expression of alpha-syn affects the response of cells to DNA damage and oxidative stress, SH-SY5Y neuronal cells and a clone of the same cell line over-expressing full-length human alpha-syn were exposed to the oxidant agent potassium bromate ($KBrO_3$) and OTA. Both cell types were exposed to $KBrO_3$ (0.15 - 2.5 mM) for 3 h or to OTA (0.2 - 25 µM) for 1, 3 and 6 h. The standard and the Fpg-modified comet assays were used to detect DNA strand breaks and oxidized bases, respectively. The proliferation assay was carried out at the same time to study cell viability. $KBrO_3$ showed a dose-dependent increase of oxidized bases, whereas OTA did not produce significant levels of DNA strand breaks or oxidative damage at any concentration or time tested. In general, the response in both cell types was similar. In conclusion, results suggest that over-expression of alpha-synuclein does not change the response to oxidative stress of the cell line and that OTA does not induce DNA damage (i.e, DNA strand breaks, alkali labile sites or oxidized bases) in SH-SY5Y cells.

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