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The involvement of caspase family in Parkinson's disease: A study of neurotoxicity in human dopaminergic neuron differentiated from stem cells

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Parkinson's (PD) disease is characterized by the death of dopamine-containing neurons (DCN), which clinically translates into impaired motor functions and neuropsychiatric problems. Since the majority of studies have been using animal models of PD or post-mortem samples from PD patients, the progression of the disease in human cells still remains to be fully characterized. Therefore, there is an imperative need to go back to basics and understand the mechanism of the events happening prior to the dopaminergic cell death. To this aim, a human dopaminergic cell model was developed from a human neural progenitor ReNcells, and to which a neurotoxin 6OHDA was applied to mimic the different stages of PD. The objective of this study was to investigate the progression of the disease particularly in relation to the involvement of the caspase, a family of cysteine proteases which acts as pro-apoptotic proteins that promote cell death via activation of the caspase cascade. Our results showed that 6OHDA-induced toxicity triggered caspases-2 and -8 activation, which in turn activated caspase-3 leading to death of DCN. Additionally, activation of caspases-2, -3, and -8 was reduced by z-VAD-FMK in 6OHD-treated cells. Our results suggest that caspase-2 cause's cell death might be via an indirect NF kappaB route. This study has established a PD model which can provide better insight to PD pathogenesis on a biochemical and molecular level, leading to a better understanding of PD and potential for new treatments.

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