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Bcl-Xl Enhances Resistence to Parkisonian Toxin Mpp+ in Nurr1-Induced Dopamine Neurons

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In-vitro expanded CNS precursors provide a potentially unlimited source of dopamine (DA) neurons for the experimental treatment in Parkinson's disease. An efficient dopaminergic differentiation from CNS precursors in vitro is limited to mesencephalic precursors isolated from early embryonic ages (embryonic day 11.5 (E11.5)-E12.5). The nuclear orphan receptor Nurr1 is essential for the development of midbrain DA neurons in vivo. We have previously demonstrated that Nurr1 induce naive CNS precursors to differentiate into DA neurons regardless of gestational ages and brain region from which CNS precursors were isolated. The Nurr1-induced DA neurons, however, were less mature and showed lower survival than those derived from mesencephalic precursors. In this study, we demonstrate that the precursor cells transfected with a Bcl-2 family anti-apoptotic protein Bcl-XL along with Nurr1 (NB cells) differentiate into DA neurons with more extensive neurite outgrowths and less susceptible to Parkinsonian toxin 1-methyl-4-phenylpyridium (MPP+), compared to cells transfected with Nurr1 alone (N cells). These data suggest a role for Bcl-XL during in vitro DA neuron differentiation and provide an improved system for cell transplantation in a preclinical animal model of Parkinson's disease.

Keyword : CNS precursors, dopamine neurons, Nurr1, Bcl-XL, MPP+