MASTER'S THESIS

Expression of brain-derived neurotrophic factor in reactive astrocytes provides neuroprotection to SH-SY5Y cells against six-hydroxydopamine toxicity invitro

Tsang, Yuen Ting

Date of Award:
2012

Expression of Brain-derived Neurotrophic Factor in Reactive Astrocytes Provides Neuroprotection to SH-SY5Y Cells Against Six-hydroxydopamine Toxicity *in vitro*

TSANG Yuen Ting

A thesis submitted in partial fulfillment of the requirements

for the degree of

Master of Philosophy

Principal Supervisor: Prof K.K.L.Yung

Hong Kong Baptist University

August 2012

ABSTRACT

Brain-derived neurotrophic factor (BDNF) has been shown to enhance the survival of dopaminergic neurons and to protect them against the neurotoxic effects of 6-hydroxydopamine (6-OHDA), a specific neurotoxin to dopaminergic neurons (Spina et al., 1992). Nestin is an embryonic protein and is a marker for neural stem cells (Lendahl et al., 1990). Nestin is not found in mature normal astrocytes. In our previous studies using rodent models of Parkinson's disease (Chen et al., 2004), a few nestin-immunoreactive reactive astrocytes were found to appear and express BDNF after the onset of Parkinson's disease. In order to investigate the neuroprotective roles of BDNF in reactive astrocytes, primary cell cultures of rat astrocytes were employed in the present study. By immunocytochemistry and Western blot analysis, a vast proportion of astrocytes in culture were found to be nestin-immunoreactive. In addition, most of these reactive astrocytes were found to express BDNF immunoreactivity. Reactive astrocytes were treated with BDNF (5, 50, 100, 200 ηg/ml). The levels of BDNF expression were found to be further enhanced in some culture, upregulation of p-MEK and p-Erk1/2 in astrocytes were illustrated via Western blot analysis. Moreover, BDNF endanced reactive astrocytes were co-cultured with neuroblastoma SH-SY5Y cells, activation of Akt and MAPK pathway were illustrated via Western blot analysis. The cells co-cultures were treated with 6-OHDA (40mM), significant reductions of cell death of SH-SY5Y cells were found. The present results as a whole indicate that astrocytes in vitro display characterizations of reactive astrocytes and express high levels of BDNF. Besides, administration of BDNF could stimulate further expression of BDNF in reactive astrocytes through the MAPK pathway. These reactive astrocytes provide neuroprotective

to neuron-like cells in vitro via activation of Akt and MAPK signaling pathway in SH-SY5Y cells. The neuroprotective effects are likely to be related with the expression of BDNF in the reactive astrocytes.

Table of Contents