alpha-synuclein

BACKGROUND

A positive association between PD and melanoma has been well established, but biologic explanation for this association is still lacking. The findings that α-synuclein is pathogenically related to PD and the fact that α-synuclein is robustly expressed in melanoma cell lines and in primary/metastatic melanoma tissues suggest that α-synuclein could play a role in the link between PD and melanoma. We, therefore, explored the role of α-synuclein in ultraviolet B (UVB) light-induced injury in neuronal PC12 cells and in human melanoma cells.

METHODS

Stable inducible PC12 cells expressing α-synuclein were maintained at Dulbecco’s modified Eagle’s medium (DMEM) containing 10% horse serum, 5% fetal bovine serum (FBS), 75 μg/ml hygromycin B, and 100 μg/ml G418. The α-synuclein transgene was induced by doxycycline. SK-MEL-28 melanoma cells with high α-synuclein expression were maintained in DMEM containing 10% FBS. All cells were cultured at 37°C, 10% CO2. For UVB light irradiation, cells culture medium was replaced by PBS. After UVB exposure, the cultures were brought back to standard cell culture conditions and cultivated for specific time periods followed by MTT and immunoblotting assay to determine the viability and apoptosis of cells.

RESULTS

Alpha-synuclein was highly expressed in SK-MEL-28 melanoma cells as compared to that in PC12 neuronal cells and A375 melanoma cells (Fig. 1A). The transgene expression of α-synuclein in stable inducible PC12 cells could be induced when cells were treated with doxycycline for 48 h (Fig. 1A). The protein level of α-synuclein in SK-MEL-28 melanoma cells was decreased when cells were transfected with SNCA siRNA (Fig. 1B).

UVB light exposure caused loss of cell viability by 37% in A375 melanoma cells and by 19% in SK-MEL-28 melanoma cells. The cell viability was decreased by 30% in PC12 cells after UVB light exposure, which was further reduced by 46% in α-synuclein transgene overexpressed PC12 cells (PC12/Dox) (Fig. 2).

Additionally, UVB light exposure caused apoptosis in A375, SK-MEL-28 melanoma cells and in PC12 neuronal cells by showing increased protein levels of cleaved PARP (Fig. 3A). The increase of cleaved PARP protein level was lower in SK-MEL-28 cells as compared to than in A375 cells (Fig. 3A). The apoptosis was enhanced when α-synuclein gene was suppressed in SK-MEL-28 melanoma cells (Fig. 3B). Additionally, increased transgene expression of α-synuclein enhanced susceptibility of PC12 cells to UVB light-induced apoptosis (Fig. 3B).

REFERENCES


ACKNOWLEDGEMENT

The authors acknowledge the joint participation by Diana Heis Henry Medical Research Foundation through its direct engagement in the continuous active conduct of medical research in conjunction with Baylor College of Medicine and this program and the support from the Michael J. Fox Foundation for Parkinson’s Research, Rapid Response Innovation Awards.