Antioxioxidant and antiapoptotic effects of Thymosin β4 in Aβ-induced SH-SY5Y cells via the 5-HTR1A/ERK axis

ABSTRACT

Alzheimer's disease (AD) is a common amnestic cognitive impairment characterised by β-amyloid (Aβ) plaques deposit in the brain of the elderly. AD is a yet incurable disease due to its unknown exact pathogenesis and unavailability of effective remedies in clinical application. Thymosin β4 (Tβ4) is a housekeeping protein that plays important role in cell proliferation, migration and differentiation. It has the ability to protect and repair neurons however it is still unclear involvement in AD. Therefore, the aim of this study is to elucidate the role and mechanism of Tβ4 in mediating the improvement of AD. AD-like cell model was constructed in neuroblastoma cell line SH-SY5Y treated with Aβ. Overexpression of Tβ4 were done using lentivirus infection and downregulation through siRNA transfection. We performed western blot and flow cytometry to study the apoptosis and standard kits to measure the oxidative stress-associated biomarkers. There is significant increased in viability and decreased apoptosis in Tβ4 overexpression group compared to control. Furthermore, overexpression of Tβ4 suppressed the expression of pro-apoptotic markers such as Caspase-3, Caspase-8, and Bax meanwhile upregulated the expression of anti-apoptotic gene Bcl-2. Tβ4 alleviated oxidative damage by reducing MDA, LDH and ROS and increasing SOD and GSH-PX in Aβ-treated SH-SY5Y cells. We found that Tβ4 inhibit ERK/p38 MAPK pathway and intensify the expression of 5-HTR1A. Additionally, we showed that upregulation of 5-HTR1A dampened the Tβ4 to activate ERK signalling. In conclusion, our study revealed the neuroprotective role of Tβ4 in AD which may open up new therapeutic applications in AD treatment.