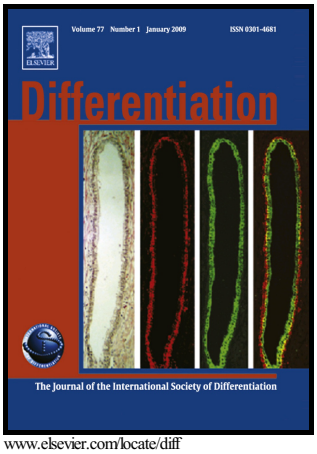

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The role of E2F1-topoIIβ signaling in regulation of cell cycle exit and neuronal differentiation of human SH-SY5Y cells

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Abstract

This study aims to test the role of E2F1-topo Ⅱβ signaling in neuronal differentiation of SH-SY5Y cells. With retinoic acid (RA) induction, a high percentage of cells were found to be arrested at the G_0/G_1 phase, with decreased levels of cyclinD1, CDK4, phosphorylation status of pRb and E2F1, in addition to an elevated level of p27. The cells were shown to differentiate into neuronal phenotypes characterized by highly expressed neuronal markers, MAP2 and enriched topo Ⅱβ, and remarkable neurite outgrowth. Exogenously forced E2F1 expression with a specific E2F1 plasmid led to suppression of topo Ⅱβ expression and disruption of the neuronal differentiation of SH-SY5Y cells. On further examination using the ChIP assay, we found that E2F1 bound directly to the promoter region of topo Ⅱβ, and its binding ability was inversely correlated with topo Ⅱβ expression in response to RA induction. Thus, our findings suggest that E2F1-topo Ⅱβ signaling may play a role in regulation of cell cycle exit and neuronal differentiation.

Abbreviations

topo Ⅱβ, topoisomerase Ⅱβ; E2F-1, Adenovirus E2 promoter-binding factor-1; RA, All-trans retinoic acid; CDKs, cyclin-dependent kinases; ChIP, chromatin immunoprecipitation;

Key words

Topo Ⅱβ; E2F-1; Neuronal differentiation; RA; Cell cycle