Involvement of both extracellular signal-regulated kinase and c-Jun N-terminal kinase pathways in the TPA-induced upregulation of p21 in colon cancer cells

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摘要

Abstract

Protein kinase C (PKC), a family of serine-threonine kinases, has been implicated in the regulation of colon tumorigenesis. However, the specific isoform of PKC involved in this process is not clear. In the present study, we found that treatment of the cultured human colon cancer cell line COLO-205 with a PKC agonist, 12-O-tetradecanoylphorbol-13-acetate (TPA), resulted in cell-cycle arrest at the G(0)/G(1) phase, decrease in cell number, PKCgamma isoform translocation, and upregulation of p21(Cip1) protein. Pretreatment of the cells with a PKC inhibitor, staurosporine, prevented the TPA-induced upregulation of p21(Cip1) protein. Based on the findings of the present study including that (a) both extracellular signal-regulated kinase (ERK) and c-jun N-terminal kinase (JNK) were activated in the TPA-treated COLO-205 cells, (b) pretreatment with the mitogen-activated protein kinase kinase inhibitor PD98059 but not with the p38 mitogen-activated protein kinase inhibitor SB203580 blocked the TPA-induced p21(Cip1) in COLO-205 cells, and (c) transient transfection of the COLO-205 cells with dominant negative ERK or JNK plasmid significantly suppressed the TPA-induced p21(Cip1) protein induction, we conclude that both the ERK and JNK pathways are involved in the TPA-induced upregulation of p21(Cip1) protein in the COLO-205 cells..

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