[P-2]

INHIBITORY EFFECTS OF THE SOY ISOFLAVONE GENISTEIN ON INDUCTION OF COX-2 AND ACTIVATION OF ERK1/2 IN CULTURED MCF10A CELLS

Myung-Hoon Chung[1], Jung-Hwan Kim[1], Joo-Seob Keum[2], Seung Sei Lee[2] and Young-Joon Surh[1]

[1] College of Pharmacy, Seoul National University
[2] School of Medicine, Sung-Kyun-Kwan university

We have investigated the effects of genistein on induction of cyclooxygenase-2 (COX-2) that plays an important role in the pathophysiology of carcinogenesis as well as in cellular response to inflammatory stimuli. Treatment of MCF10A cells with 12-O-Tetradecanoylphorbol-13-acetate (TPA) or TNF-α resulted in increased COX-2 expression and PGE_2 production, which was inhibited by genistein. There are multiple lines of evidence supporting that the induction of COX-2 is regulated by the eukaryotic transcription factor NF-κB. TPA stimulated both NF-κB DNA-protein binding and COX-2 promoter activity. However, genistein did not inhibited TPA- or TNF-α-induced NF-κB DNA-protein binding, but suppressed the transcriptional activity of NF-κB induced by TPA. Immunofluorescence staining also demonstrated that increased nuclear translocation of the active NF-κB p65 subunit was not abolished by genistein. Genistein treatment attenuated TPA- or TNF-α-induced activation of ERK1/2. Above findings, taken together, suggest that genistein inhibits COX-2 expression and PGE_2 production in MCF10A cells by acting at the transcription initiation complex via a tyrosine kinase- or ERK-dependent pathway.

keyword : Genistein, Cyclooxygenase-2, MCF10A cells