

[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 Chung¹, Jung-Hwan Kim¹, Joo-Seob Keum², Seung Sei Lee²
and Young-Joon Surh¹

¹College of Pharmacy, Seoul National University

²School 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 PGE₂ 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- κ B. TPA stimulated both NF- κ B DNA-protein binding and COX-2 promoter activity. However, genistein did not inhibited TPA- or TNF- α -induced NF- κ B DNA-protein binding, but suppressed the transcriptional activity of NF- κ B induced by TPA. Immunofluorescence staining also demonstrated that increased nuclear translocation of the active NF- κ B 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 PGE₂ 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