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Genistein의 암세포 성장 억제 기전
(Genistein Induces G2/M Arrest of the Cell Cycle in Human Cancer Cells)

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Genistein, a natural isoflavonoid phytoestrogen, is a strong inhibitor of protein tyrosine kinase and DNA topoisomerase II activities. Genistein has been shown to have anticancer proliferation, differentiation and chemopreventive effects. In the present study, we have addressed the mechanism of action by which genistein suppressed the proliferation of p53-null human prostate carcinoma cells. Genistein significantly inhibited the cell growth, which effect was reversible, and induced dendrite-like structure. The inhibitory effects of genistein on cell growth proliferation were associated with a G2/M arrest in cell cycle progression concomitant with a marked inhibition of cyclin B1 and an induction of Cdk inhibitor p21 (WAF1/CIP1) by p53-independent manner. Following genistein treatment of cells, an increased binding of p21 with Cdk2 and Cdc2 paralleled a significant decrease in Cdc2 and Cdk2 kinase activity with no change in Cdk2 and Cdc2 expression. Genistein also induced the activation of a p21 promoter reporter construct, utilizing a sequence distinct from the p53-binding site. Analysis of deletion constructs of p21 promoter indicated that the response to genistein localized to the 300 base pairs proximal to the transcription start site. These data suggest that genistein may exert a strong anticarcinogenic effect, and that this effect possibly involves an induction of p21, which inhibits the threshold kinase activities of Cdks and associated cyclins, leading to a G2/M arrest in the cell cycle progression.