

Inhibition of prostate cancer cell colony formation by the flavonoid quercetin correlates with modulation of specific regulatory genes.

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The natural product quercetin is a flavonoid found in many fruits and vegetables. Previous research has shown that quercetin has antitumor, anti-inflammatory, antiallergic, and antiviral activities. In the present investigation we studied the effect of quercetin on the ability of prostate cancer cell lines with various degrees of aggressive potential to form colonies in vitro. Specifically, we examined the molecular mechanisms underlying this effect, including the expression of cell cycle and tumor suppressor genes as well as oncogenes. We observed that quercetin at concentrations of 25 and 50 micro M significantly inhibited the growth of the highly aggressive PC-3 prostate cancer cell line and the moderately aggressive DU-145 prostate cancer cell line, whereas it did not affect colony formation by the poorly aggressive LNCaP prostate cancer cell line or the normal fibroblast cell line BG-9. Using the gene array methodology, we found that quercetin significantly inhibited the expression of specific oncogenes and genes controlling G(1), S, G(2), and M phases of the cell cycle. Moreover, quercetin reciprocally up-regulated the expression of several tumor suppressor genes. In conclusion, our results demonstrate that the antitumor effects of quercetin directly correlate with the aggressive potential of prostate cancer cells and that the mechanism(s) of quercetin-mediated antitumor effects may involve up-regulation of tumor suppressor genes and reciprocal down-regulation of oncogenes and cell cycle genes. The results of these studies provide a scientific basis for the potential use of flavonoids as nutraceuticals in the chemoprevention of cancer.

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