Potentiation of the Growth Inhibitory Effects of Vitamin D in Prostate Cancer By Genistein

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Calcitriol, the hormonally active form of vitamin D, inhibits the growth and progression of several cancers. Inflammation has been postulated to play a role in the carcinogenic process of many cancers, including prostate cancer (PCa). Our recent research indicates that calcitriol exhibits anti-inflammatory actions that may contribute to its anti-cancer effects in PCa. Calcitriol inhibits the synthesis and actions of pro-inflammatory prostaglandins (PG) by three mechanisms: (i) inhibition of the expression of cyclooxygenase-2 (COX-2), the enzyme that synthesizes PGs, (ii) induction of the expression of 15-prostaglandin dehydrogenase (15-PGDH), the enzyme that inactivates PGs and (iii) decreasing the expression of EP and FP PG receptors, the mediators of PG actions. Our research also shows that genistein, an active component in soy is a potent inhibitor of vitamin D-24-hydroxylase, the enzyme that initiates the catabolism of calcitriol, thereby increasing its biologically activity.

In addition, genistein also exerts independent regulatory effects on the PG pathway in PCa cells. Like calcitriol, genistein inhibits COX-2 expression in PCa cells leading to decreased synthesis of PGE_2. Genistein also decreases EP and FP PG receptor expression thereby reducing the biological effects of PGE_2. The combination of calcitriol and genistein acts in a cooperative way to inhibit the PG pathway as well as retard PCa cell growth. Both calcitriol and genistein are relatively safe with little toxicity associated with their intake. We therefore postulate that the combination of calcitriol and genistein is an attractive therapeutic option for the treatment and/or prevention of PCa.