Molecular basis of the anti-cancer effects of genistein isoflavone in LNCaP prostate cancer cells


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Abstract
Background: Prostate cancer is the most common form of non-skin cancer within the United States and the second leading cause of cancer deaths. Survival rates for the advanced disease remain relatively low, and conventional treatments may be accompanied by significant side effects. As a result, current research is aimed at alternative or adjuvant treatments that will target components of the signal transduction, cell-cycle and apoptosis pathways, to induce cell death with little or no toxic side effects to the patient. In this study, we investigated the effect of genistein isoflavone, a soy derivative, on expression levels of genes involved in these pathways. The mechanism of genistein-induced cell death was also investigated. The chemosensitivity of the LNCaP prostate cancer cells to genistein was investigated using ATP and MTS assays, and a caspase binding assay was used to determine apoptosis induction. Several molecular targets were determined using cDNA microarray and RT-PCR analysis.
**Results:** The overall data revealed that genistein induces cell death in a time- and dose-dependent manner, and regulates expression levels of several genes involved in carcinogenesis and immunity. Several cell-cycle genes were down-regulated, including the mitotic kinesins, cyclins and cyclin-dependent kinases. Various members of the Bcl-2 family of apoptotic proteins were also affected. The DefB1 and the HLA membrane receptor genes involved in immunogenicity were also up-regulated.

**Conclusion:** The results indicate that genistein inhibits growth of the hormone-dependent prostate cancer cells, LNCaP, via apoptosis induction through regulation of some of the genes involved in carcinogenesis of many tumors, and immunogenicity. This study augments the potential phytotherapeutic and immunotherapeutic significance of genistein isoflavone.

**Key words:** Genistein isoflavone, prostate cancer, expression of genes, phytotherapeutic adjuvant, immunotherapy and chemotherapy