Soy isoflavones augment the effect of TRAIL-mediated apoptotic death in prostate cancer cells.

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Source

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Abstract

Prostate cancer represents an ideal disease for chemopreventive intervention. Genistein, daidzein and equol, the predominant soy isoflavones, have been reported to lower the risk of prostate cancer. Isoflavones exert their chemopreventive properties by affecting apoptosis signalling pathways in cancer cells. Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) is an endogenous anticancer agent that induces apoptosis selectively in tumour cells. Soluble or expressed in immune cells, TRAIL molecules play an important role in immune surveillance and defense mechanisms against tumour cells. However, various types of cancer cells are resistant to TRAIL-mediated apoptosis. We examined the cytotoxic and apoptotic effects of genistein, daidzein and equol in combination with TRAIL in LNCaP cells. Cytotoxicity was measured by MTT and LDH assays. Apoptosis was analyzed by flow cytometry and fluorescence microscopy using Annexin V-FITC. Mitochondrial membrane potential (ΔΨm) was evaluated by fluorescence microscopy using DePsipher staining. Flow cytometry detected the expression of death receptor TRAIL-R1 (DR4) and TRAIL-R2 (DR5) on cell surfaces. The soy isoflavones sensitized TRAIL-resistant prostate cancer cells to apoptotic death. The isoflavones did not alter death receptor expression, but significantly augmented TRAIL-induced disruption of ΔΨm in the LNCaP cells. We showed for the first time that the chemopreventive effects of soy foods on prostate cancer are associated with isoflavone-induced support of TRAIL-mediated apoptotic death.

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