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Can diet influence cancer cell growth? Effects of phytoestrogens on the hedgehog-signaling pathway in prostate cancer.

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Prostate cancer continues to be one of the most common cancers affecting American men. By better understanding the mechanisms involved in prostate cancer cell proliferation, better treatments can be developed and more cases can be prevented. One mechanism that has been linked to prostate cancer is the Sonic hedgehog-signaling (Shh) pathway. Normally, the hedgehog pathway is active only during embryonic development. Several types of tumors, including those of the prostate, demonstrate inappropriate activation of the hedgehog pathway in the adult. Cyclopamine, a steroidal alkaloid isolated from , is able to inhibit the pathway and has been shown to inhibit prostate cancer cell growth both and using xenograft models, . Despite the promising initial results of cyclopamine treatment, the compound is a very potent teratogen, and its cost makes it an unrealistic answer as a widespread cancer cure. Botanical compounds may provide a cost effective and abundant alternative. We hypothesize that various botanicals including genistein, EGCG, curcumin, and quercetin will disrupt the Shh pathway and inhibit cell growth. TRAMP-C2 and PC3 prostate cancer cell lines were used as models for hedgehog pathway response to phytoestrogens. Protein assays measuring cell growth following treatment with each botanical were performed. Real-Time RT-PCR experiments to measure mRNA concentrations of hedgehog target genes were also performed. Initial results indicate that phytoestrogens are decreasing prostate cancer cell growth up to 70 percent with genistein being the strongest inhibitor. An approximate IC50 value of 30μM was found for genistein. The Shh pathway also responds to the presence of phytoestrogens with decreased hedgehog target mRNA concentration following phytoestrogen treatment.