Targeting Estrogen- and Hedgehog-Signaling Pathways in Prostate Cancer

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ABSTRACT

Botanical compounds, implicated as cancer protective either by traditional medicine or in modern cancer research are shown to inhibit prostate tumorigenesis both *in vivo* and *in vitro*. Using a transgenic mouse as an animal model to study the development and treatment of prostate cancer, we were investigating a selection of botanical compounds, specifically apigenin, baicalein, curcumin, EGCG, genistein, quercetin, and resveratrol and the importance of Estrogen Receptors (ERs) in Prostate Cancer. All compounds combinations were able to inhibit or delay prostate cancer incidence when fed to TRAMP (TRansgenic Adenocarcinoma of the Mouse Prostate) mice. The protective effects were only present in mice WT for ER α and β indicating a need for both receptors for these compounds to act on the prostate cancer incidence. All seven compounds were also able to delay prostate cancer cell growth of both human (LNCaP, PC3, PC3M) and mouse (TRAMP-C2) prostate cancer cell lines. The compounds inhibited the hedgehog signaling pathway as indicated by decreasing Gli1 levels. Additionally, we observed a protective effect in TRAMP mice KO for ERα, which had a significantly decreased incidence of aggressive (poorly differentiated) carcinoma, whereas ERβKO mice displayed double the PDC incidence.

My research sheds light on an additional mechanism by which phytoestrogens are potentially protecting against cancer. My work suggests a new treatment target for addressing both slow and fast growing prostate cancers. Based on data presented here, we propose that a combination of ERα antagonists, ERβ agonists and selected botanicals should present a comprehensive prostate cancer remedy.