Effect of CYP3A Inhibitor Bergamottin on Androgen Receptor Signaling in Prostate Cancer Cells

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BACKGROUND: The androgen receptor (AR) is the driving force of prostate cancer growth. The AR is a nuclear receptor which, upon activation, goes to the nucleus and promotes transcription of genes responsible for cancer growth. Previous studies have shown that inhibition of CYP3A5 blocks the activation process of the AR. Bergamottin, a compound found in grapefruit juice, is a known CYP3A4/5 inhibitor. Based on CYP3A5's ability to regulate AR activation, I tested the effects of bergamottin on AR activation to see if the compound can be utilized as a dietary supplement to block prostate cancer growth. METHODS: I used western blotting, and immunofluorescence to observe the effects of bergamottin on AR activation. Cell fractionation in combination with western blotting was used to determine cellular localization of AR. Cell growth measurement assay was used to monitor prostate cancer cell growth after treatment with bergamottin. RESULTS AND CONCLUSION: My experiment concluded that bergamottin successfully blocked AR activation and downstream signaling, and consequently slowed down prostate cancer cell growth. Even 2.4 uM of bergamottin reduced percentage growth of cells by 50%. Analysis of the western blot showed that bergamottin reduced total AR levels and nuclear AR even after R1881 induction. The implication of this experiment is the potential use of bergamottin as a food supplement alongside other prostate cancer treatments in order to aid in slowing down cancer growth.

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