BERBERINE SUPPRESSES ANDROGEN RECEPTOR SIGNALING IN PROSTATE CANCER CELLS.

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Abstract

The androgen signaling axis, activated by binding of androgens to the androgen receptor (AR), plays a critical role in all stages of prostate cancer. Androgen deprivation therapy (ADT) is a major component of the treatment regimen for advanced prostate cancer. However, after a moderate and short-term response, the disease eventually progresses to castration-resistant prostate cancer (CRPC), which is incurable. Recent evidence suggests that continued AR activation is essential for the progression to CRPC. Therefore, novel agents targeting AR directly are in critical need in the fight against prostate cancer. Berberine is a phytochemical isolated from plants of the genera Berberis and Coptis. It has been shown previously to inhibit the growth of prostate cancer cells. In this study, we examined the effect of berberine on androgen signaling in prostate cancer cells. Treatment with berberine decreased the transcriptional activity of AR and reduced the expression of AR-regulated genes. The suppression of AR activity by berberine is achieved by inhibition of AR nuclear translocation and induction of AR degradation. A proteasome inhibitor, but not a pan-caspase inhibitor, reversed AR degradation by berberine, suggesting that berberine-induced AR degradation is mediated by a proteasome pathway. This report is the first to show berberine suppresses the AR signaling pathway and provides strong support for berberine as a preventive and therapeutic agent for prostate cancer.