

## **Epigenetic Modifications Involving RECK to Inhibit Prostate Cancer Metastasis**

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Prostate cancer is the second leading cause of death in the United States males with estimated 174,650 cases to be diagnosed and 31,620 deaths alone in 2019. Treatments of prostate cancer such as radiation therapy and chemotherapy are often physically, mentally, and financially taxing on the patient. Emerging research has shown that the imbalance of matrix metalloproteinases (MMPs) is responsible for the uncontrolled growth of prostate cancer. During prostate cancer growth, the reversion-inducing cysteine-rich protein with kazal motifs (RECK) gene is under expressed through epigenetic modifications which allows the unrestricted expression of MMPs. RECK is critical to preventing cancer growth as it is a tumor suppressor and inhibits metastasis and angiogenesis. Green Tea polyphenols (GTP) has recently gained attention for its anticancer properties. GTP and its major constituent, EGCG can reverse epigenetic changes. Thus, we hypothesize that GTP can reduce prostate cancer growth through the reactivation of RECK. Initial experiments demonstrate that human prostate cells viz. RWPE, C42B, and RC77T expressed high levels of RECK whereas it was under-expressed in LNCaP, 22Rv1, DU145, PC-3, PC-3M, and DuPro cells. We selected DuPro and LNCaP cancer cells for further analysis and were treated with 3-Deazaneplanocin A (DZNep), Trichostatin A (TSA), a combination of DZNep, TSA, GTP and EGCG. A 72-h treatment time of GTP and EGCG showed a significant decrease in the growth of DuPro cells as compared to the control. GTP and EGCG had a similar effect on cell growth as TSA, a histone deacetylase inhibitor and DZNep, an EZH2 inhibitor. The effects of GTP and EGCG on RECK in DuPro and LNCaP cells were also tested at 24 and 48 h intervals. Although DuPro cells does not exhibit much change after 24 h, both cell lines demonstrated an increase in RECK expression after 48 h. Our studies display an increase in RECK expression and a decrease in cell growth after treatment with GTP and EGCG. In conclusion, GTP and EGCG led to reversal of the expression of RECK, and this effect was superior to DZNep and TSA having significant effect on its reactivation. Further mechanistic studies with green tea are warranted.