EXOGENOUS TGF-βI UPREGULATES VEGF TRANSCRIPTION UNDER NORMOXIC CONDITIONS IN DU145 PROSTATE CANCER CELLS

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Abstract: Prostate cancer is the most common malignancy in American males, and the second leading cause of cancer deaths. Transformed cells break free of cell cycle regulation and proliferate uncontrollably. The resulting cellular mass continues to grow until the microenvironment of the cells at the tumors interior becomes hypoxic. These conditions promote the stabilization of the transcription factor HIF-1α and subsequent transcription of VEGF, a known pro-angiogenic factor that recruits and reorganizes adjacent blood vessel endothelium into new blood vessels. TGF-βI has been linked to tumor neovascularization and enhanced metastasis in prostate cancer cells. However, in normal prostate cells, and some cancers, TGF-βI functions as a tumor suppressor. The mechanisms regulating these divergent influences on normal and cancerous prostate cells are not well understood. In advanced prostate cancer, increased expression of TGF-βI is associated with poor prognosis. This may mean that TGF-βI contributes to enhanced metastasis in prostate cancer by promoting angiogenesis. We have previously shown that TGF-βI significantly down-regulates VEGF protein expression in HPV7 prostate epithelial cells under normoxic conditions. We hypothesize that TGF-βI plays a potential role in the enhanced metastasis of prostate cancer by advancing neovascularization. In this investigation, we treated DU145 prostate cancer cells with 1ng/ml of recombinant human TGF-βI under normoxic and hypoxic conditions for three and six hours respectively. We observed that TGF-βI up regulated VEGF transcription in DU145 cells under normoxic conditions. Furthermore, we saw that the addition of TGF-βI did not appear to significantly upregulate VEGF transcription in DU145 prostate cancer cells exposed to hypoxia. Taken together, these results suggest that TGF-βI effects on VEGF transcription in DU145 prostate cancer cells under normoxic and hypoxic conditions are governed by a shared pathway. Further studies are underway to elucidate the mechanism involved in this VEGF response to TGF-βI under normoxic conditions in DU145 prostate cancer cells.