

P040 Regulation of ADAMTS expression in prostate cancer and stromal cells by androgen and TNF.

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Prostate cancer is the most common cancer and second leading cause of cancer mortality in men. A group of ADAMTS enzymes (A Disintegrin And Metalloproteinase with Thrombospondin motifs) are proteases that cleave structural proteoglycans in the extracellular matrix (ECM) such as versican and aggrecan. ECM breakdown and remodelling is essential for cancer progression. Dihydrotestosterone (DHT) is a growth factor for prostate cancer cells, and serum TNF levels are elevated in men with advanced prostate cancer. Work by our group has shown the expression profile of ADAMTS enzymes in prostate cancer and stromal cell lines. We proceeded to analyse the effect of DHT and TNF on the expression of these enzymes, and investigate the role of ADAMTS-1 in prostate cancer progression.

Expression levels of ADAMTS-1, -15 and -20 mRNA in prostate cancer and stromal cells were determined using real-time PCR. The effect of treatment with DHT and TNF on mRNA expression was analysed. Using shRNA, expression of ADAMTS-1 was inhibited. The effect of enzyme inhibition on cell migration was assessed.

ADAMTS-1 and -15 mRNA expression was modulated by DHT and TNF. ADAMTS-1 inhibition slowed down initiation of migratory activity in tumour spheroids.