

B8 Role of polyamines in prostatic cancer

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The importance of polyamines in prostatic growth and differentiation has prompted studies to evaluate the clinical relevance of the ornithine decarboxylase/polyamine system in prostatic cancer. These studies show that differences in biological behaviour of prostatic (cancer) cells are accompanied with changes in polyamine levels and/or the activity of their metabolic enzymes. A faulty antizyme regulation of polyamine homeostasis may play an important role in the growth and progression of prostatic carcinoma. Treatment of human prostate carcinoma cells with inhibitors of polyamine metabolic enzymes or polyamine analogues induces cell growth arrest or (apoptotic) cell death. Our recent *in vitro* studies using conformationally restricted polyamine analogues show that these compounds inhibit cell growth, probably by inducing antizyme-mediated degradation of ornithine decarboxylase. Sensitivity of human prostate cancer cells for these compounds was increased in the absence of androgens. These results suggest that these analogues might have chemotherapeutic potential in case prostatic cancer has become androgen-independent. Pilot data in an *in vivo* xenograft model show that these analogues have effects on tumour growth, vascularity, blood perfusion and tissue hypoxia. Overall, these studies show that polyamines may serve as important biomarkers of prostatic malignancy and provide a promising target for chemotherapy of prostatic cancer.