

Adipose-secreted factors from peri-prostatic fat stimulate prostate cancer cell tumorigenicity

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Prostate cancer is a leading cause of death in Australian men. Epidemiological evidence shows that obesity is a significant risk factor for more aggressive prostate cancer and an independent predictor of disease recurrence and cancer-specific mortality. Despite this epidemiological association, the biological mechanisms linking adiposity to prostate cancer are not yet understood. The goal of this study was to investigate the effects of adipose-secreted factors produced by the peri-prostatic fat (PPAT) from men with prostate cancer, who were lean or obese. Adipose samples from PPAT and abdominal sub-cutaneous depot (AbAT) were obtained from 10 men undergoing radical prostatectomy surgery for localized prostate cancer. Adipose tissues were minced and incubated in serum-free media (CHO and glucose) for five hours. A prostate cancer cellularised co-culture assay model system was used to determine the effect of adipose secreted factors on the morphology and migration potential of prostate epithelial (BPH-1) cells. The data showed that both PPAT and AbAT significantly altered prostate epithelial cell morphology, which are hallmarks of cancer cell aggressiveness. PPAT conditioned media significantly increased the proliferation of prostate cancer (PC3 cells) compared to vehicle controls. PPAT from lean men was more potently tumorigenic than PPAT from obese men (n=5 respectively). Taken together, these data demonstrate a potent effect of human adipose tissues on prostate cancer cell tumorigenicity. Understanding how obesity or adipose tissue homeostasis increases prostate cancer aggressiveness is required to identify factors that promote prostate cancer progression, and how these could be applied to the clinical management of the disease.