Blocking fatty acid uptake reduces prostate cancer progression

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Alterations in metabolism are a hallmark of cancer pathogenesis. Rapidly dividing cancers have an exponential increase in energy requirements, and hence the Warburg effect has been postulated. However, prostate cancer is slowly proliferating and clinical observations indicate that classic Warburg reprogramming is not important in driving progression of this cancer. Here, we used a series of radiometric techniques to show that fatty acid uptake is increased in human prostate cancer tissue and that these fatty acids are preferentially directed towards biomass production rather than energy provision. Global transcriptomic analysis revealed marked regulation of genes encoding lipid metabolism in prostate cancer and alterations of the fatty acid transporter CD36 correlated with poor survival in prostate cancer patients. CD36 silencing in prostate cancer cells reduced fatty acid uptake and cancer proliferation and aggressiveness as determined by migration studies using wound healing and transwell assays. *In vivo* xenograft experiments using CD36 silenced PC3 prostate cancer cells demonstrated a slower rate of tumour growth compared to parental PC3 cells. Genetic deletion of Cd36 in the prostatic epithelium of cancer susceptible Pten-null mice reduced fatty acid uptake and storage, and slowed the progression of prostate cancer, as demonstrated by a reduction in the incidence of invasive carcinoma *in situ*. In summary, our results identify a critical role for fatty acid uptake in prostate cancer progression, which is in contrast to other rapidly proliferating cancers such as melanoma. Our data suggest that blocking fatty acid uptake may offer a novel therapeutic pathway for the treatment of this prostate cancer.