Dietary protein restriction inhibits tumor growth in human xenograft models.


Abstract

Purpose: Data from epidemiological and experimental studies suggest that dietary protein intake may play a role in inhibiting prostate and breast cancer by modulating the IGF/AKT/mTOR pathway. In this study we investigated the effects of diets with different protein content or quality on prostate and breast cancer. Experimental Design: To test our hypothesis we assessed the inhibitory effect of protein diet restriction on prostate and breast cancer growth, serum PSA and IGF-1 concentrations, mTOR activity and epigenetic markers, by using human xenograft cancer models. Results: Our results showed a 70% inhibition of tumor growth in the castrate-resistant LuCaP23.1 prostate cancer model and a 56% inhibition in the WHIM16 breast cancer model fed with a 7% protein diet when compared to an isocaloric 21% protein diet. Inhibition of tumor growth correlated, in the LuCaP23.1 model, with decreased serum PSA and IGF-1 levels, down-regulation of mTORC1 activity, decreased cell proliferation as indicated by Ki67 staining, and reduction in epigenetic markers of prostate cancer progression, including the histone methyltransferase EZH2 and the associated histone mark H3K27me3. In addition, we observed that modifications of dietary protein quality, independently of protein quantity, decreased tumor growth. A diet containing 20% plant protein inhibited tumor weight by 37% as compared to a 20% animal dairy protein diet. Conclusions: Our findings suggest that a reduction in dietary protein intake is highly effective in inhibiting tumor growth in human xenograft prostate and breast cancer models, possibly through the inhibition of the IGF/AKT/mTOR pathway and epigenetic modifications.