

P041 Exploring new roles for Cathepsin K in prostate cancer
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Prostate cancer has a propensity to metastasize to the bone and locally disrupt normal bone remodeling. **Cathepsin K is an osteolytic enzyme implicated in bone resorption and a target of the pharmaceutical industry for treatment of osteoporosis.** We have previously demonstrated an involvement of cathepsin K in prostate cancer-mediated osteolysis of the bone, possibly through cleavage of extracellular matrix proteins (e.g. SPARC). The present studies were designed to further examine the role of the bone microenvironment in regulation of cathepsin K and the subsequent effect on prostate cancer growth. We used primary human bone marrow cells grown in 3D collagen I gels with prostate carcinoma cells. We demonstrated increased expression and activity of cathepsin K upon interaction of tumor cells with bone marrow cells. In addition, we observed a significant upregulation of SPARC and VEGF, two proteins that we have shown to be cleaved, and possibly regulated by cathepsin K. Interestingly cathepsin K as well as SPARC and VEGF have been recently linked to obesity. Their upregulation in obese subjects correlates with decreased levels of adiponectin, an adipocyte (fat cell) hormone with anti-inflammatory, anti-angiogenic and anti-tumorigenic properties. Levels of adiponectin also are significantly reduced in prostate cancer. Our recent data demonstrates that cathepsin K cleaves adiponectin and thereby potentially modulates its activity. Studies to determine whether adipocyte cathepsin K correlates with aggressive prostate cancer are in progress.