PHYSIOLOGY AND BIOCHEMISTRY

Cell proliferation and Cathepsin L expression are inversely correlated during bladder cancer progression. DAN STELZER\*, MICHELLE ROBILLARD, MARIAH DOOLEY, JAMES DEDDENS, LARRY DOUGLASS, and JULIA CARTER, Wood Hudson Cancer Research Laboratory, Newport, KY 41071.

Bladder cancer will account for 80,000 new cases and 17,000 deaths during 2017. To better understand factors controlling progression of bladder cancer, we studied archived specimens from 142 patients of formalin fixed paraffin embedded surgical specimens of bladder cancer donated to Wood Hudson Cancer Research Lab. Patient survival in this cohort was significantly related to stage and grade of disease (p < 0.0001). The increase in pathologic staging of bladder cancer involves invasiveness into deeper layers of tissue such as subepithelial connective tissue, muscularis propia, perivesical fat tissue, and finally metastasis as the cancer progresses. Grading of these tumors is determined by the amount of cells that deviate in structure and function from normal urothelial cells. The lysosomal protein Cathepsin L is a cysteine protease that is capable of degrading extracellular matrix. We hypothesized tumors that expressed Cathepsin L in greater amounts would correlate with higher stage and grade in these tumors. Histologic sections (5μm thick) of formalin fixed paraffin embedded surgical specimens of bladder cancer were stained immunohistochemically using a rabbit monoclonal antibody to Cathepsin L (DAKO). Cell proliferation was determined by a mouse monoclonal antibody to KI-67. Area of tissue expressing Cathepsin L was determined by image cytometry. The number of nuclei expressing KI-67 was counted in the same tumor areas. We found that the number of nuclei was highly correlated with pathologic stage, grade, malignancy, and survival for patients. Conversely, in contrast to our hypothesis, Cathepsin L was inversely correlated with progression in bladder cancer tumors.