



**Chemistry Department
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Research Group of Karen Buchmueller

The Buchmueller lab focuses on AT hook containing proteins, including the High Mobility Group A (HMGA) family of proteins. AT hook motifs are named because these regions of protein bind A/T rich DNA sequences. As a result of their binding to DNA, AT hook containing proteins regulate a wide variety of genomic functions. Of particular interest are the HMGA proteins, which are primarily expressed during development; however, high levels of HMGA1 proteins have been detected in many adult human malignant tumors, such as pancreatic and breast carcinomas. Increased levels of HMGA1 proteins are indicators of poor prognosis for cancer patients and correspond to metastasized cancer.

To develop effective inhibitors of HMGA1, it is necessary to characterize the affinity and thermodynamic contributions of the competition between small molecules and AT hook peptides for binding DNA. We have utilized isothermal titration microcalorimetry (ITC), filter binding and fluorescence experiments to robustly quantify the interplay between small molecules, AT hook and DNA.

In another group of projects, we are investigating the dynamic nature of AT hook variants and their roles DNA binding. AT hooks lack well-defined three dimensional structures and understanding the changes in dynamics as a function of DNA binding will shed light on their role in specific DNA binding proteins.