Molecular Dynamics Studies of RNA Recognition

Lauren A. Michael, Billy R. Miller III, Nina E. McCrate, Bryan Sitzmann, Emily E. Hopson and Elizabeth E. Koballa and Maria C. Nagan*

Truman State University, Department of Chemistry, Kirksville, MO 63501

Subtle changes in the chemical structure of RNA can dramatically affect its structure and stability. RNA structural properties are correlated to biochemical activity to draw conclusions about how specific functional groups affect biological function. Employing molecular dynamics simulation techniques, our research primarily examines two types of RNA recognition, messenger RNA - transfer RNA (mRNA-tRNA) recognition, a key step in the translation of proteins, and protein-RNA interactions in human immunodeficiency virus (HIV). In the first area, the role of naturally occurring, posttranscriptionally modified bases in affecting tRNA-mRNA recognition is examined. In human $tRNA^{Lys,3}$, we find that the threonyl-*N6*-modification of 2-methylthio-6-threonylcarbamoyl-adenosine at position 37 (ms^2t^6A37) is required to maintain a canonical stair-stepped conformation in the anticodon bases (34-36). *Ab initio* studies examining the underlying stabilizing forces in retaining a stair-stepped conformation are underway. Interestingly in *E. coli* $tRNA^{Phe}$, we find that presence of a modified base at position 37 is not sufficient to retain a stair-stepped conformation and that modifications probably act in concert with Mg^{2+} to stabilize the tRNA structure. In the second area of research, we are examining the role of water and electrostatics in RNA-peptide recognition. In late phase Rev-RRE recognition mediates nucleocytoplasmic export of partially and unspliced HIV mRNA. From *in vitro* selection studies performed by Frankel and coworkers, a synthetic peptide known as RSG-1.2 has been found to bind RRE with greater affinity and specificity than the native Rev peptide. MD simulations of the RSG-1.2-RRE complex have been performed and compared to an analogous Rev-RRE system.