Redox sensitive RNA Aptamers to Flavin Adenine Dinucleotide. R. R. Poudyal[1], M. Roychordhury-Saha[2], I. Emahi[3], D. A. Baum[3], D. H. Burke[4]. [1]Department of Biochemistry (rrpfz5@mail.missouri.edu), University of Missouri, [2]Sequenom Laboratories, San Diego, California, [3]Saint Louis Univeristy-Department of Chemistry, [4]Life Sciences Center, University of Missouri (burkedh@missouri.edu)

Nucleotide cofactors used by modern biochemistry are sometimes considered to be remnants of catalytic elements from an RNA world. While it is well established that RNA can bind redox-active cofactors, there has been little direct attention paid to differential binding of oxidized and reduced forms of those cofactors. It is not yet clear whether RNA aptamers can differentiate between redox states of these cofactors. Differential binding to specific redox states of cofactors can be used as a means by RNA enzymes to enhance redox potential of bound cofactors.

Our lab has used directed evolution to identify aptamers that differentially bind to FAD and its reduced form $FADH_2$. Several of the selected aptamers bind to a column immobilized with FAD is considerably greater than the fraction of aptamers that bind to $FADH_2$. For four promising candidates, we used in-line probing to identify nucleotides that are either sensitized or protected from in-line attack by the 2'OH upon ligand binding. Aptamer 12.29 showed maximum modulation of in-line cleavage in the presence of FAD at several sites, indicating that structural changes due to the binding of FAD modulate in-line attack of the 2'OH. Based on the predicted secondary structure of aptamer 12.29, we truncated the original 91-nt aptamer to a much smaller 51-nt version which still retained FAD binding function. Preliminary data based on in-line probing suggests this truncated aptamer binds to FAD but not $FADH_2$. Studying how RNA molecules can distinguish between redox states of cofactors will enable us to understand how prebiotic RNA enzymes may have used these cofactors for electron transport reactions.