RNA-Metabolite Relationships and Their Implications for the Emergence and Development of Metabolism.
M. A. Ditzler and D. H. Burke, Molecular Microbiology and Immunology, University of Missouri School of Medicine, USA

The characteristics of RNA in modern biology support a central role for RNA in the early development of life. The existence of ribozymes coupled with the capacity of RNA to serve as the genome of several RNA viruses, lends tremendous support to the RNA world hypothesis by establishing RNA's ability to both store genetic information and catalyze chemical reactions in nature. More recently, the discovery of naturally occurring metabolite-binding RNAs (riboswitches), and cofactor-RNA conjugates provides support for a central role for RNA in the emergence of complex metabolisms.

Our work is focused on understanding the relationship between RNA and metabolites in modern biology and its implications for the emergence and development of metabolism. Metabolite-binding RNA motifs have been identified in both natural and artificially selected RNAs. In nature these motifs occur within the context of riboswitches. Riboswitches are gene regulation elements that couple metabolite binding to structural changes within a messenger-RNA. Riboswitches exhibit broad phylogenic distribution among bacteria, and in at least one instance (a TPP responsive riboswitch) appear in all three domains of life. At least 14 small molecules have been demonstrated to bind to 17 distinct classes of riboswitches and thereby regulate gene expression. These include amino acids (glycine, lysine), nucleobases (adenine and guanine), coenzymes (S-adenosylmethionine, S-adenosylhomocysteine, flavin mononucleotide, adenosylcobalamine, thiamin pyrophosphate), ions (Mg^{2+}) and the secondary messenger cyclic-di-GMP. For most of the small molecules, only one RNA aptamer motif has been identified; however, there are at least four different structural motifs that bind S-adenosylmethionine (SAM). Here, we test the binding specificity of multiple riboswitches. We also discuss the potential of motifs present in riboswitch to serve as substrate binding domains in metabolic ribozymes.