



Chemical Biology Seminar

“Modulating the conformation and function of disease-relevant RNA with small molecules”

Abstract: Small molecules offer a unique opportunity to target structural and regulatory elements in therapeutically relevant RNAs, but understanding functional selectivity has been a recurrent challenge in small molecule:RNA recognition. In particular, RNAs tend to be more dynamic and offer less chemical functionality than proteins, and biologically active ligands must compete with the highly abundant and highly structured RNA of the ribosome. Indeed, the first small molecule drug targeting RNA other than the ribosome was just approved by the US FDA in August of 2020. Our recent survey of the literature revealed little more than one hundred reported chemical probes that target non-ribosomal RNA in biological systems.

As part of our efforts to improve small molecule targeting strategies and gain fundamental insights into small molecule:RNA recognition, we have analyzed patterns in both RNA-biased small molecule chemical space and RNA topological space privileged for differentiation. We have applied these principles to functionally modulate conformations of 3'-triple helix of the long noncoding RNA MALAT1 as well as an enterovirus (EV71) IRES structure, the latter in collaboration with the labs of Blanton Tolbert (Case Western Reserve University) and Gary Brewer and Mei-Ling Li (Rutgers Robert Wood Johnson Medical School). We have recently translated our success in developing an RNA-targeted antiviral for EV71 to targeting regulatory RNA in SARS-CoV-2.

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