CHRISTINE A. RODEN
Postdoctoral Fellow, Biology
University of North Carolina at Chapel Hill

"Control of viral RNA via SARS-CoV-2 nucleocapsid protein condensation"

Biomolecular condensation partitions cellular contents to maintain homeostasis. Many nuclear and cytoplasmic condensates are rich in RNA and RNA-binding proteins (RBPs). Hidden within RNA primary sequence is the code which specifies protein-binding, condensation, and sorting of RNAs to their destined condensates for function. Deciphering this code is challenging in cells because of the complex composition and redundancy of many different RNAs and RBPs in promoting a given condensate. Viral condensates offer a distinct advantage for study over endogenous cellular condensates because a limited set of viral proteins must engage with specific viral nucleic acid. Condensation of viral proteins and nucleic acids is an emerging mode of regulation for viruses conferring modular biochemical complexity to minimal viral genomes and proteomes. An example is the SARS-CoV-2 nucleocapsid protein (N-protein) which is required for multiple steps in viral replication. N-protein condenses with viral RNA sequences at specific human body temperatures making it a powerful model for deciphering the role of RNA sequence and structure specificity in condensates. I discovered that two separate and distinct double-stranded, RNA motifs promote N-protein condensation via its two structured RNA-binding regions and these interactions impart specific droplet physical properties that could support varied viral functions including translation repression, sub-genomic RNA generation, and viral RNA packaging. Thus, SARS-CoV-2 can achieve biochemical complexity, performing multiple functions in the same cytoplasm, with minimal protein components by utilizing distinctly patterned RNA motifs that control N-protein interactions with RNA and condensation. I am now leveraging the RNA code for condensation to condensates in live cells, during the viral replication cycle, and to engineer synthetic condensates for novel functions.