UC RIVERSIDE

BCH 252 Seminar Series

Matthew Guevara, Biochemistry & Molecular Biology Graduate Student, UC Riverside

Seminar Title: "Dynamic Molecular Reprogramming of Human and Viral Protein Synthesis by SARS-CoV-2 Nucleocapsid Protein"

Abstract: Viruses need to hijack their host cell's machinery, including its ribosomes, to replicate and cause infection. Coronaviruses like SARS-CoV-2 hijack ribosomes with their viral RNA genome by mimicking host messenger RNAs (mRNA). They also suppress host mRNA translation by sophisticated mechanisms involving their non-structural proteins. However, non-structural proteins are not available when the viral genome enters the cell. They are synthesized at a later point, raising the question of how the virus initially hijacks host protein synthesis. We have found that the nucleocapsid (N) protein, which enters host cells with the viral genome, selectively promotes translation driven by viral RNA, even in the absence of other viral factors. Viral RNA structural features allow N protein to bind the RNA very tightly to exert this effect. Mechanistically, N protein enhances the activity of human translation initiation factor 4F (eIF4F), which recognizes mRNAs to begin translation. With real-time single-molecule fluorescence experiments, we found that N protein stabilizes the "closed loop" mRNP complex, that includes eIF4F and enhances ribosome recruitment and mRNA stability *via* mRNA 5'-3' circularization. Thus, N protein reprograms eukaryotic translation to privilege viral protein synthesis at the outset of infection. Our findings provide insight into potential new antiviral therapeutic strategies.

Tuesday, February 18th, 2025 12:00 p.m. - 12:50 p.m. PST

In-Person: Genomics Auditorium 1102A

Host: Dr. Sean O'Leary