## CHEMISTRY & BIOCHEMISTRY SEMINAR SERIES:

Ringing the alarm: cyclic nucleotides mediate bacterial immunity against phages

## **Abstract:**

Bacteria have evolved a variety of strategies to combat viral infections and many of these are surprisingly conserved in eukaryotic innate immune systems. Bacteriophages have, in turn, evolved their own counter-defenses which can inhibit bacterial immunity and safeguard viral replication. Several ant-phage defenses depend on generation and sensing of cyclic nucleotide second messengers and recent research has revealed that phages can counteract these pathways through directly sequestering or 'sponging' the nucleotide signal. We have discovered that remarkably, bacteria can encode a form of 'back-up' defense which only comes into play when these nucleotides are depleted. Through a combination of biochemical, structural, and comparative genomics approaches, we explore the nucleotide specificity for this system and establish that other anti-sponge defense mechanisms may be more widespread in prokaryotes than previously appreciated.

## **About the Speaker:**

Dr. Morehouse is currently as Assistant Professor at the University of California Irvine in the Department of Molecular Biology and Biochemistry. He grew up in Connecticut and then came to Worcester, MA for his undergraduate degree at WPI (Worcester Polytechnic Institute) in Biochemistry (class of 2012) with a minor in Chemistry. He was recruited as a graduate student at Brandeis University where he did his Ph.D. in Daniel Oprian's lab and studied plant terpene biosynthesis and cyclic GMP signaling in fungi. He defended his Ph.D. in 2017 and started a postdoc position at Harvard Medical School in the lab of Philip Kranzusch (pronounced cran-chess). He transferred out of the field of terpene research to the areas of human and bacterial antiviral immunity in the Departments of Microbiology (HMS) and Cancer Immunology & Virology at Dana-Farber Cancer Institute. He began his independent faculty career at UC Irvine in 2022. His research is on the evolution of immune signaling with a particular emphasis on non-canonical cyclic nucleotide signaling during viral infection. He has published many papers on the subject of the immune defenses employed by bacteria to prevent viral replication and how those defenses have conserved attributes across living systems- even humans. His research team employs biochemical and structural biology approaches to understand mechanisms of cyclic nucleotide producing enzymes and the receptors that recognize and respond to those signals. He has been supported by a T32 during his PhD, again during his postdoc, and then secured an F32 to study human cyclic nucleotide signaling. Recently, he received his first major NIH grant, the MIRA (R35), for work like what he is going to share with us today. Dr. Morehouse has also been the recipient of several awards and honors including winning a SPROUT award for research on Taxol biosynthesis as a graduate student, an Outstanding Postdoctoral award for Harvard Medical School, and a Young Investigator Award for cyclic nucleotide signaling research. Most recently he was awarded the Chancellor's Award for Distinguished Fostering of Undergraduate Research at UC Irvine.



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