

QCB Evenings

Wednesday, February 28 • 5:30pm • Chemistry C033

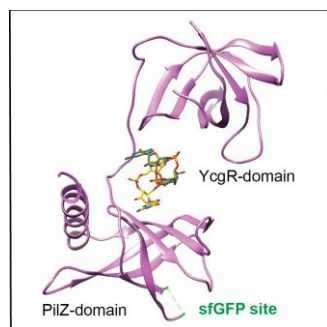
Identification of compounds that inhibit Chikungunya virus infection

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Chikungunya virus, an arbovirus, is transmitted to humans via infected mosquitos. Previously, Chikungunya infections were limited to Asia, Africa, and Europe; but recently, outbreaks have occurred in the Americas and the Caribbean. Most infected individuals experience some symptoms which can range from short term fatigue and fever to debilitating arthritic disease that can last for months or years. No current vaccine is available and treatment options are limited. The capsid protein of Chikungunya virus forms a protective shell around the viral RNA genome during virus transmission. With the correct environmental trigger, this proteinaceous shell dissociates, releasing the viral genome and initiating infection. Capsid also interacts with the E2 protein, one of the viral spike proteins, and these interactions are important for virion formation and egress from the cell. We hypothesize that compounds that interfere with capsid: viral nucleic acid interactions inhibit the release of viral genomes as well as virus assembly and egress. We suspect that viruses treated with anti-viral compounds that target structural proteins, such as capsid, are less likely to develop resistant mutants than viruses treated with drugs that target viral enzymes. We designed a high-throughput, *in vitro* FRET-based assay to monitor core-like particle assembly. We screened 10,000 compounds and found 106 that altered core-like particles. A subset was selected to study their effects in virus-infected vertebrate cells. Our results show that 3 and 4 compounds inhibit infectious, but not total, virus production by at least 90 and 50%, respectively. Further, we tested if these compounds were capable of inhibiting other viruses and if they were effective in invertebrate mosquito cells. Future studies will clarify the mechanisms by which these compounds inhibit Chikungunya virus production.

MotI (DgrA) acts as a clutch on the flagellar stator protein MotA in *Bacillus subtilis*

Sundharraman Subramanian, Dann LAB



Bacterial flagella are nanomachines rotated by powerful motors, which drive motility that is often associated with virulence. The bacterial flagellum is structurally complex and requires tens of thousands of subunits from over 30 different proteins. Further, flagella are integrated in the cell envelope and are seldom degraded perhaps because flagellar synthesis is costly in the consumption of metabolic building blocks and in the multigenerational time they take to assemble. Regulators that inhibit flagellar rotation are potentially reversible, preserving the energy investment on the machine and arrest flagellar rotation either as a brake, increasing resistance, or as a clutch, cutting power to the machine. In this seminar, data will be presented that describe the behavior of YcgR-homolog MotI (formerly DgrA) of *B. subtilis* as a clutch. I will present the three-dimensional structure of MotI bound to c-di-GMP, followed by fluorescent localization studies with MotI-fluorescent protein fusions and their dependence on MotA. Finally, I will present data showing that the MotI-inhibited flagella rotate freely by Brownian motion. We propose a model in which flagellar stators are disengaged and sequestered from the flagellar rotor when bound by MotI indicating its behavior as a clutch.

All QCB Trainer Lab Personnel are invited to attend.
Refreshments will be provided.