Department of Molecular and Cellular Biology

Graduate Seminar MCB*7500

Friday, April 19th, 2024 @ 12:45 p.m.

presented by:

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"Mechanistic insights into fatty acid-mediated inhibition of Staphylococcus aureus signal transduction systems"

Staphylococcus aureus cell wall anchored (CWA) surface proteins are important virulence factors that enable host adhesion. CWA protein production involves an intricate network of signal transduction systems that respond to environmental cues. Recently, the Cox lab revealed that unsaturated fatty acids (uFAs) inhibit *S. aureus* adhesion to host molecules and reduce the abundance of fibronectin-binding proteins via inhibition of the SaeRS two-component system (TCS). However, it is unknown whether FA inhibition extends to other TCSs and transcriptional regulators. Additionally, the literature lacks a systematic study on the regulated production of CWA proteins. This project will examine whether FAs inhibit other TCSs and transcriptional regulators associated with the production of CWA proteins. Using a collection of single (TCS) knockout strains, I will quantify differential gene expression of key CWA protein genes to implicate their TCS regulators. To confirm these findings, I will use an enzyme-linked immunosorbent assay to detect surface protein abundance. Activation of SaeS, like other intramembrane sensing histidine kinases (IM-HKs), requires direct binding to cardiolipin. However, it is unknown how FAs interact and inhibit IM-HKs on a molecular level. By fusing the promoter of TCS-targeted genes to *lacZ*, I will quantify FA-mediated inhibition of signal cascades. Direct inhibition of the IM-HK will be investigated using its native promoter fused to a green fluorescent protein gene. A strain devoid of cardiolipin will be used as a negative control. Taken together, this project will disentangle FA-mediated inhibition of signal transduction systems that regulate virulence factor expression to protect against infection.