Department of Molecular and Cellular Biology Graduate Seminar MCB*6500

Friday, May. 25, 2018 in SSC 1511 @ 12 noon

presented by:

Faris Halawa

(Advisor: A. Clarke)

"Development of a novel assay for the putative ligation reaction carried out by lytic transglycosylases"

Bacteria rely on a muropeptide network known as peptidoglycan (PG) that envelops the bacterial cell wall for structural stability. Glycan strands of PG consist of repeating disaccharide units formed by the β 1-4 glycosidic linkage of N-acetylglucoasmine and N-acetlymuramic acid. A class of enzymes employed by bacteria known as the lytic transglycosylases(LTs) are autolysins that cleave the glycosidic linkage in PG for a variety of cellular processes such as cell division, cell growth, and flagella insertion. LTs are known to give disease-causing bacteria virulence as well as antibiotic resistance. Thus there is great interest in studying LTs to potentially target them with antibiotics. The cleavage of PG by LTs results in 1,6 anhydrosugar products via an intramolecular cyclization. This mode of cleavage is in contrast to lysozymes, eukaryotic immunity enzymes, that cleaves the same bond via hydrolysis irreversibly. Theoretically, the energy reserve in the PG glyosidic bond is conserved during LT activity due to the role of LTs in housekeeping and cell division. Thus, the unique mode of action of LTs may serve a constructive purpose. The present study hypothesizes that LTs catalyze the formation of the novel 1,6 anhydrosugar products and subsequently re-ligate them back to PG when needed. The study will isolate these 1,6 anhydrosugars from the LT digestion of a chemoenzymatically synthesized polymer of the PG precursor, Lipid II. A novel liquid chromatography- mass spectroscopy assay will be developed to determine the kinetics of this putative ligation reaction.