

Chemical Biology Seminar

Breaking Down Bacterial Cell Walls to Understand Inflammation



ABSTRACT: We are interested in understanding how the bacterial cell wall is processed both by bacteria and the human host. Both commensal and pathogenic bacteria are believed to produce peptidoglycan fragments and misrecognition can lead to the development of inflammatory bowel disease (IBD), such as Crohn's disease (CD), asthma and gastrointestinal (GI) cancers. Importantly, a long-standing debate around the biological relevance of the immunoactive synthetic fragment muramyl dipeptide (MDP) remains unclear due to a lack of NAM-based probes. We hypothesize that there are unidentified enzymatic targets and bacterial cell wall fragments that will be useful in the design of novel antibiotics and anti-inflammatory therapies.

We have taken a two-pronged approach towards testing this hypothesis. From the small molecule side, we have established an in vitro assay, which allows us to assess the affinity of Nod2, an innate immune receptor that binds to bacterial cell wall fragments. This assay has allowed us to tease apart binding from activation and we have begun to derive rules for molecular recognition by intracellular innate immune receptors. In addition, we have developed a robust synthetic method to readily access a library of bacterial cell wall derivatives. These derivatives will be used as affinity reagents to capture both human and bacterial enzymes that are responsible for bacterial cell wall processing. From the larger polymer side, we have embedded carbohydrates with small modifiable tags into the bacterial cell wall. We developed a method to label the NAM glycan backbone of *E. coli*, *P. putida*, and *B. subtilis* in whole cells. The results reveal fundamental architectural details of the glycan chains of the peptidoglycan, and further enable us to track the engulfment and breakdown of bacteria by macrophages, ultimately revealing a peptidoglycan digestion mechanism for invasive bacteria.

Prof. Catherine Leimkuhler Grimes

University of Delaware

Thursday April 19th, 2018

11:00 am in Room 1315 Chemistry

Refreshments will be available at 10:40 am in the Shain Tower atrium.

For more information, please call Kristi Heming in the Chem Biol path office (262-6815).