

Research Theme: Infection and Immunity
Research Project Title: Mechanisms of <i>E. faecalis</i> Subversion of Neutrophil-mediated killing
Principal Investigator/Supervisor: Assoc/Prof Kimberly Kline (SBS/SCELSE)
Co-supervisor/ Collaborator(s) (if any): Assist/Prof Christine Wong (LKC)
Project Description
<p>a) Background:</p> <p>Inflammation is a critical component of nearly every human disease. It is also a vital part of the protective response to most pathogens, and it is therefore highly advantageous to bacterial pathogens to have evolved mechanisms to suppress inflammation. So it is not surprising that diverse bacteria have evolved sophisticated mechanisms to interfere with the signaling pathways involved in inflammation to escape or hijack immune system. Understanding the mechanisms by which pathogens suppress inflammation will inform not only our treatment of those particular pathogens/diseases by identifying potential immunotherapeutic targets, but may also enable the development of novel approaches to the suppression of the inflammatory components of many other diseases.</p>
<p>b) Proposed work:</p> <p>We have defined experimental systems in which <i>Enterococcus faecalis</i> antagonizes various antimicrobial pathways typically used by neutrophils. Our goal is to identify the molecular mechanisms, on the host and bacterial side, involved in these neutrophil subversion phenotypes. A Transposon library will be screened for mutations that affect the ability of <i>E. faecalis</i> to evade neutrophil-mediated killing. The identified genes will be further studied via reverse genetics and recombinantly expression to study their cellular and biochemical activities. At the same time, we will determine the host pathways that are affected by interaction with <i>E. faecalis</i>, leading to their inability to clear <i>E. faecalis</i> infection. Mechanistic discoveries made <i>in vitro</i> will be validated in a variety of <i>in vivo</i> mouse infection models, including urinary tract infection, wound infection, and gastrointestinal infection. Methodologies that may be employed in these studies include bacterial and mammalian genetic screens (transposon and CRISPR), tissue culture, animal infection, RNA-sequencing, metabolomics, fluorescent and super-resolution microscopy, flow cytometry, high content screening, and more.</p>
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Please apply at the following:
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