Research Theme: Infection and Immunity

Research Project Title: The lipidomics of *Enterococcus faecalis* infection

Principal Investigator/Supervisor: Assoc/Prof Kimberly Kline (SBS/SCELSE)

Co-supervisor/ Collaborator(s) (if any): Prof David Becker (LKC)

Project Description

a) Background:

Singapore has among the highest incidence of lower extremity amputations in the world and 85% of these amputations are preceded by diabetic foot ulcers. It is widely appreciated that diabetic ulcers are slow healing and difficult to resolve by standard antibiotic treatment. Enterococci are among the most frequently isolated bacteria from diabetic ulcers. Diabetic wound infections are often polymicrobial and biofilm-associated, and thus, inherently more tolerant to antimicrobials and more resistant to immune clearance. As such, *Enterococcus faecalis* wound infections are more difficult to treat and contribute to persistent and chronic infections. In addition, Enterococci are immunosuppressive and have niche-modulatory capacities that promote their virulence, as well as that of co-infecting organisms. Despite the prevalence of Enterococci in chronic diabetic wound infections, its strategies for surviving and persisting in the host during these infections are not well described. There is an urgent need to understand the host-pathogen interactions underlying Enterococcal wound infections because they will only become more prevalent as the global population ages, the incidence of correlated comorbidities continues to increase, and hospital stays become longer and more frequent.

b) Proposed work:

The specific goal of this project is to identify the mechanisms by which *Enterococcus faecalis* is able to survival and persistence within keratinocytes. Based on our preliminary data, we hypothesize that *E. faecalis* is internalized by both immune and epithelial cells, exports specific factors that promote its intracellular survival, and actively interferes with immune activation in the infected cells—all of which promotes wound infection in the mammalian host. This project will characterize the intracellular life cycle of *E. faecalis* in epithelial cells and identify the mechanism by which exported *E. faecalis* factors contribute to this process. The specific aims of this project are: 1) To define the intracellular life cycle of *E. faecalis* in keratinocytes, 2) To identify *E. faecalis* genes that contribute to intracellular survival.

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Please apply at the following:
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