NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

SBS-IAS Seminar:

Strategies to Slow the Development of Daptomycin Resistance in Enterococcus faecalis

24 Nov 2020 (Tue), 11am (GMT+8) **Zoom**

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Abstract

Most cationic antimicrobial peptides (CAMPs) possess a well-characterized ability to preferentially interact with anionic membrane lipids leading to bacterial membrane poration and cell death. Emerging research suggests that anionic lipids cluster in membrane microdomains in many bacteria, suggesting that CAPs may preferentially interact with the bacterial membrane within anionic domains. We investigated the interaction between human beta defensins with the human pathogen Enterococcus faecalis. At sublethal concentrations, these CAMPs preferentially target and disrupt virulence-associated functions that occur in these microdomains. Modification of anionic lipids by multiple peptide resistance factor (MprF), a protein that confers CAP resistance by electrostatic repulsion, renders E. faecalis more resistant to killing by defensins and less susceptible to focal targeting by the cationic antimicrobial peptides. MprF is also involved in daptomycin resistance, a cationic antibiotic of last resort for E. faecalis and other Gram positive pathogens. Interestingly, MprF mutants are both more sensitive to killing by daptomycin and evolve daptomycin resistance more slowly. Understanding the mechanism by which MprF mutants slow antimicrobial resistance acquisition has enabled the proposal of new combinatorial strategies to prolong the efficacy of this last line antibiotic.



Speaker:
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Speaker's Biography

Kimberly Kline is an Associate Dean for Faculty Affairs in the College of Science and Associate Professor of Microbiology at Nanyang Technological University in Singapore; and a Principal Investigator at the Singapore Centre for Environmental Life Sciences Engineering. Prior to coming to Singapore, Kimberly received an MPH in Biostatistics and Epidemiology and PhD in Microbiology and Immunology from Northwestern University. Kimberly completed postdoctoral training at Washington University in St. Louis and at the Karolinska Institute in Stockholm Sweden.

Kimberly has received multiple awards for her contributions to the field of microbiology, including a NIH K99 Career Development Award in 2011, the Singapore National Research Foundation Fellowship in 2011, the ICAAC Young Investigator Award from the American Society of Microbiology in 2014, and the Nanyang Education Award in 2017.

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