A molecular basis for enhanced cephalosporin resistance in vancomycin resistant Enterococci

Bacteria typically respond to changing environmental conditions by using a wide range of two-component systems (TCS) to initiate signal transduction pathways. *Enterococcus faecalis* and *Enterococcus faecium* are opportunistic pathogens on the WHO priority pathogen list that have used multiple TCSs to enable antibiotic resistance. Recently however, the role of the less abundant, eukaryotic-like serine threonine kinases (eSTKs) has been shown to play an important role in sensing external stimuli and generating an intracellular response. The *Enterococci* have a single eSTK called Irek, which has been previously implicated as important in the mediation of resistance to cephalosporins. We have previously shown a direct linkage between Irek and the two TCSs that control intrinsic cephalosporin and vancomycin resistance. In addition, genetic or chemical knock out of Irek function significantly reduces both vancomycin and cephalosporin resistance in Van_B phenotypic Enterococcal strains to below wild-type levels. This research describes experiments used to understand the relationship between TCS and Irek and therefore how enterococci initiate resistance to antibiotics. This understanding may provide a translational opportunity to develop an antibiotic adjuvant that will enable future antibiotic and chemotherapeutic strategies.