Library Synthesis of antimicrobial peptide targeting *Staphylococcus aureus*

Due to the overprescribing of antibiotics bacteria have adapted and developed mechanisms to combat the antimicrobial agents. One example is *Staphylococcus aureus,* which causes common skin infections, and can be easily treated. But amidst the abuse of antibiotics, *S. aureus* has become resistant to most known antibiotics; resistant strains are termed Methicillin-resistant *Staphylococcus aureus* (MRSA). This is a major concern in hospitals where the bacteria evolve under constant pressure developing multi-drug resistance. Thus significant efforts have been made to develop either stronger antibiotics or investigating alternate pathways to target the resistant strains. The mevalonate pathway appears to be critical for the survival of many bacteria including *S. aureus*. Recently, Matsumoto *et. al.* concluded that the mevalonate pathway is essential for cell wall synthesis. Gram-positive bacteria have a thick cell wall layer and interrupting assembly of this layer generates antimicrobial activity. The same group identified Farnesyl diphosphate as an important intermediate in cell wall synthesis and depletion of this molecule compromises the cell wall layer making the bacteria susceptible to osmotic fluctuations. In another study, Qingrong Huang and co-workers, isolated a dipeptide pyrophosphate from a common beverage -kefir. This peptide inhibited fungi and several Gram-positive bacteria and showed a synergistic effect with Erythromycin in Gram-negative bacteria. We hypothesize that this dipeptide competes with the Farnesyl diphosphate in the synthesis of the cell wall. To test our hypothesis, we are synthesizing various analogs of the dipeptide pyrophosphate. These molecules will help us deduce the structural elements required for activity. We will then test our hypothesis by probing the mechanism of action. This poster highlights our synthetic efforts at building the compound library.

Keywords: Antibiotic resistance, MRSA, antimicrobial peptides, mevalonate pathway, library synthesis