

The Arms Race Between Bacteriophages and Antibiotics

Antimicrobial resistance is one of the greatest threats to public health. *Staphylococcus aureus* and particularly methicillin resistant *S. aureus* (MRSA) is the leading cause of community acquired and health care associated infections. The recommended treatment for MRSA complicated bacteremia is vancomycin. Due to treatment failure and/or the development of vancomycin non-susceptible strains during therapy, daptomycin is considered as a well-tolerated alternative to vancomycin for complicated bloodstream infections. However, daptomycin resistance has been increasingly reported, especially as post-vancomycin failure. Due to these circumstances, the exploration of adjuvant antibacterial options has become a necessity in current practice. With the scarcity of effective treatment options, bacteriophages (“phages”) represent a very promising alternative approach against infections due to multi-drug resistant pathogens. Here, daptomycin non-susceptible isolates with various mutation profiles are targeted to achieve the three fundamental components of synergy including eradication of bacterial infection, prevention of resistance development and re-sensitization of already resistant isolates. For this purpose, a cohort of isogenic isolate pairs are exposed to phage-daptomycin combinations to verify the utility of adjunctive phage-daptomycin combinations. Phages exert an immense selective pressure on bacteria which leads to broad arsenal of defense mechanisms including fitness loss against other environmental pressures such as antibiotics. Elevated sensitivity to phage was observed in daptomycin non-susceptible isolates in comparison to their susceptible parents. The mechanism of this phenomenon is probably compounded over modification of phage receptors located on the surface of the cell membrane. Understanding the factors that affect antibiotic-phage synergy can accelerate transition of phage to the hospital system for better management of complicated infections.