The ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter cloacae*) are believed to cause two-thirds of all hospital-acquired infections in the USA, and as many as 50% of all deaths resulting from bacterial infections. In addition, they have effectively "escaped" the ability to be treated by conventional therapeutics. As such, in the Shaw lab, we explore the pathogenic mechanisms of these bacteria (primarily focusing on MRSA) to understand how these dangerous organisms cause such widespread human morbidity and mortality. This is primarily driven through the study of regulation at all levels within the cell (transcriptional, translational and post-translational) using cutting edge genomic and proteomic techniques. In addition, we work with a wealth of medicinal chemists to rationally design and develop novel antibacterial agents targeting each of the ESKAPE pathogens. These efforts range from initial hit identification, to lead optimization and preclinical development.