ENGINEERING BETTER QUORUM QUENCHING ENZYMES

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Many clinically relevant bacterial pathogens (*e.g. Pseudomonas aeruginosa)* use chemical signals to communicate with one another as a precursor to initiating infection and/or biofilm formation (a process called quorum sensing). This process enables bacteria to replicate without displaying virulent behaviour until a population capable of overwhelming the host defences is reached. Once they have reached a critical mass, they activate their arsenal of virulence genes, establish infection, and/or begin forming biofilms. Due to the important role of quorum sensing in bacterial pathogenesis, the disruption of this system (quorum quenching) is a promising new antimicrobial strategy. Our goal is to engineer highly active and specific 'quorum quenching' enzymes that irreversibly degrade the signalling molecules used in quorum sensing. Our main focus is degrading *N*-acyl-L-homoserine lactones (AHLs), as they are the most common type of quorum sensing molecules used by Gram-negative pathogens. Iterative rounds of site-saturation mutagenesis have been used to identify amino acid substitutions that confer improved activity and/or specificity. Variants have been tested against *P. aeruginosa* biofilms, using a variety of techniques including crystal violet assays, scanning electron microscopy, and confocal microscopy. The results of these studies will be presented.