Targeting Signaling Molecules of P. aeruginosa by Using Mucin as an Anti-Quorum Sensing Drug: A Novel Design To Evaluate Efficacy in the Context of Multidrug Resistance

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Pseudomonas aeruginosa is a gram-negative opportunistic pathogen involved in several human diseases such as cystic fibrosis. This bacterium is highly resistant to antibiotic treatments due to its biofilm and pyocyanin production abilities which are regulated by quorum sensing (QS), the process of cell-to-cell communication between bacteria. Bacteria bind to signaling molecules released by their local population to gather information about cellular density, and once a certain threshold has been reached, bacteria turn into their virulent state. The objective of this study is to curb virulent properties of pathogenic bacteria by suppressing QS to eliminate drug resistance. QS signaling molecules, HHQ in P. aeruginosa, were specifically targeted to downregulate QS. A gene responsible for the synthesis of HHQ was knocked out and measured amounts of external HHQ molecules and mucin as an anti-QS drug were then added to cultures. Mucin was shown to downregulate QS by targeting HHQ signaling molecules. An in-depth statistical method for evaluating the impact of anti-QS drugs on bacterial virulence by adjusting for bacterial growth, temperature, and linear and quadric trends of time within treatment was developed. By controlling for these covariates, the accuracy of the results improved, allowing for more reliable evaluations. In this study, we demonstrated that targeting signaling molecules of highly specific pathways curbs virulence of pathogenic bacteria. This research opens the door for the development of anti-QS drugs in the clinical setting.

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