Novel Application of a Quorum-Sensing Based Genetic Circuit within an Antimicrobial Bioengineered Probiotic

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There is a growing concern worldwide that extensive use of antibiotics is resulting in the development of antibiotic resistance among pathogenic bacteria. Pseudomonas aeruginosa is a multidrug-resistant human pathogen, of which some strains have even developed resistance to carbapenems, an extremely effective class of antibiotics. I predicted that the creation of an bioengineered probiotic that incorporates a genetic circuit will be more effective at sensing and eliminating P. aeruginosa than conventional antibiotics. I proposed the use of a genetic circuit with the integration of XOR Boolean logic that is able to sense for pathogens through quorum sensing, an organic chemical signaling cascade used by P. aeruginosa to elicit activation of a gene once a threshold concentration of chemical signals is attained. Once the presence of pathogens is detected, then the probiotic will begin to produce antimicrobial peptides in order to eliminate the pathogens, and will signal the immune system of the host organism through the production of chemoattractive autoinducers. In order to design the bioengineered probiotic, I employed the use of synthetic biology softwares such as CellDesigner, TinkerCell, and CelloCAD to computationally design the genetic logic circuit. Similar software was used to simulate the circuit, which allowed for the analysis of the results of the engineered probiotic. Simulations displayed that the bioengineered probiotic was able to inhibit P. aeruginosa by 99% after 15 hours. Simulations clearly depicted the improvement in the response to P. aeruginosa infections between commonly used antibiotics to the bioengineered probiotic developed in my project. The next steps would be to obtain the appropriate DNA plasmids and implement the genetic circuit.