Conjugative Transfer of Cytotoxic Genes for Targeted Cell Elimination

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With the increasing problem of antibiotic resistance in bacteria, a different approach is needed to combat bacterial infections without continual overuse of antibiotics. This experiment demonstrates the viability of an alternative strategy: using horizontal gene transfer of cytotoxic genes within a bacterial population for rapid and sustainable toxin delivery. Conjugation is a defense mechanism commonly employed by bacteria to rapidly transmit advantageous antibiotic resistance genes within populations; this experiment takes advantage of this efficient transfer process to deliver a custom cytotoxic ccdB gyrase inhibitor-encoding plasmid, activated by the sugar L-arabinose. To emulate conjugation dynamics of a one-way plasmid transfer system, a MatLab-based predictive simulator using conditional probabilities ran 80 iterations of 5 minute conjugation intervals and yielded that 35 iterations allowed for transfer of the toxin-encoding plasmid into all potential recipient cells; simulation results were lab tested using custom plasmid constructs of the arabinose-induced ccdB toxin system facilitated by the araBAD promoter. Cytotoxic ccdB experimental and YFP control plasmids verified in vitro viability for elimination of antibiotic resistant bacterial populations. The plasmid transfer-mediated toxin system successfully targeted and inhibited bacterial growth, and conjugation of the genetic ccdB cytotoxin shows potential as an efficient gene delivery method for sustainable and highly effective toxins for inducible cell death for gram negative bacteria. Future research could expand upon this genetic system to combat antibiotic resistant bacterial infections, as well as induce genetic cell death in other pathogens and illnesses using other specific promoters and toxin genes.

Awards Won:
Fourth Award of $500