Peptide Nucleic Acids as Potential Designer Antimicrobials

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The overuse of antimicrobials in many aspects of daily life has ushered in a wave of antimicrobial resistance to antibiotics that have been effective for decades. Resistance to antibiotics is spread between bacteria through mechanisms of gene transfer and mutations. Peptide nucleic acids (PNAs) are 8 to 10 nucleotide synthetic sequences that are complementary to start sites, due to their peptide backbone instead of sugar backbone bind stronger and less prone to mutations. They can be used to inhibit synthesis of specific proteins by binding to the target gene as well as mRNA and thereby prevent transcription and translation. PNAs can be designed for specific essential genes to inhibit bacterial growth or for drug resistance genes to make them susceptible to the antibiotic. In this experiment, PNAs were designed for the essential gene tsf and the gene TetA associated tetracycline resistance in Salmonella typhimurium (S. typhimurium). These PNA molecules with attached cell-penetrating peptides (CPPs) were incubated with S. typhimurium with reducing concentrations of tetracycline to determine the minimal inhibitory concentration and minimal bactericidal concentration. S. typhimurium was also incubated with a scrambled control PNA sequence that was not specific to any gene in the S. typhimurium genome and CPPs only to determine their effects if any. Results showed that essential gene (tsf) PNAs did inhibit growth for 18 hours at a concentration of 8 ug/mL tetracycline, while the use of PNAs to inhibit the associated resistance gene TetA significantly inhibited growth after 4 hours with 8 ug/mL of tetracycline. PNA treatment groups also significant displayed growth inhibition and bactericidal activity at a lower tetracycline concentration.

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