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Re-sensitizing drug-resistant bacteria to antibiotics by designing Antisense Therapeutics COLLEEN COURTNEY, ANUSHREE CHATTERJEE, University of Colorado Boulder — "Super-bugs" or "multi-drug resistant organisms" are a serious international health problem, with devastating consequences to patient health care. The Center for Disease Control has identified antibiotic resistance as one of the world's most pressing public health problems as a significant fraction of bacterial infections contracted are drug resistant. Typically, antibiotic resistance is encoded by "resistance-genes" which express proteins that carryout the resistance causing functions inside the bacterium. We present a RNA based therapeutic strategy for designing antimicrobials capable of re-sensitizing resistant bacteria to antibiotics by targeting labile regions of messenger RNAs encoding for resistance-causing proteins. We perform in silico RNA secondary structure modeling to identify labile target regions in an mRNA of interest. A synthetic biology approach is then used to administer antisense nucleic acids to our model system of ampicillin resistant *Escherichia coli*. Our results show a prolonged lag phase and decrease in viability of drug-resistant E. coli treated with antisense molecules. The antisense strategy can be applied to alter expression of other genes in antibiotic resistance pathways or other pathways of interest.

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