A Novel Strategy for Definitive Antibiotic Therapy via Initiation of Targeted Programmed Cell Death

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The overuse of broad-spectrum antibiotics and lack of new drug development has resulted in widespread emergence of antibiotic resistant bacterial infections, posing a substantial threat to public health and economic security. Previously, Curcumin-encapsulated lipid nanocarriers were shown to successfully induce programmed cell death (PCD) in a cyanobacterial colony via inhibition of the Thioredoxin system, the major antioxidant pathway in bacterial cytosol. Subsequently, initiation of targeted PCD utilizing nanoparticles coated with bacterial membrane vesicles (BMVs) was postulated to act as a biomimetic mechanism for definitive antibiotic therapy, isolating PCD to target cells from which the vesicles are derived. In the present study, blank and Curcumin-encapsulated poly(lactic-co-glycolic acid) (PLGA) nanoparticles were prepared using single emulsion-solvent evaporation and biofunctionalized with BMVs isolated from Staphylococcus epidermidis via ultrasonication. Effective extraction of protein-rich vesicles was achieved using a combination of differential centrifugation, microfiltration, and washing. Successful fusion to the nanoparticle surface was confirmed with dynamic light scattering. The treatments were then applied to cultures of S. epidermidis and Escherichia coli to compare efficacy. Following incubation, spectrophotometric analysis yielded inconclusive results. However, TrxR inhibition in the free Curcumin groups indicates an alternative role for PCD as a mechanism for altruistic suicide. Future studies will involve utilizing higher concentrations of the treatments and fluorescent microscopy to observe intermittent stages of cell death. Overall, this research marks an important step in the development of a novel strategy for definitive antibiotic therapy.

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