From Plague to Pandemic Preparedness: mRNA–LNP Vaccines Against Bacterial Threats

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The increasing threat of emerging infectious diseases and antibiotic-resistant bacteria highlights the need for rapid, adaptable countermeasures beyond conventional vaccines and therapies. While mRNA-based vaccines have revolutionized the prevention of viral infections, their application against bacterial pathogens represents the next frontier in mRNA vaccinology. Our work outlines a technology-driven framework for combating bacterial infectious diseases using mRNA-LNP (mRNA-Lipid Nanoparticles) platforms. As a case study, we present a bivalent mRNA vaccine against *Yersinia pestis*, the causative agent of plague, a pathogen responsible for multiple pandemics and considered a potential biothreat. Our strategy, which integrates optimized antigen engineering with advanced delivery systems, elicits strong antigen-specific humoral and cellular immune responses and provides protection against lethal plague challenge in preclinical models. Importantly, the bivalent design addresses limitations related to antigenic composition and disease presentation, particularly in the context of pneumonic plague. These findings support mRNA vaccination as a promising approach against complex bacterial pathogens and position this technology as a rapid, scalable countermeasure for both natural outbreaks and engineered threats, with potential relevance to the growing challenge of antimicrobial resistance.