COMBATTING FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

Advanced Phage-based Strategies For Biodefense Against Burkholderia Pseudomallei

Apichai Tuanyok University of Florida **Pacharapong Khrongsee** University of Florida **Herbert Schweizer** Northern Arizona University **Nawarat Somprasong** Northern Arizona University

The global rise in antibiotic resistance has significantly escalated the threat posed by Burkholderia pseudomallei, a Tier-1 select biowarfare agent responsible for melioidosis. Addressing this, our research explores innovative bacteriophage-based solutions tailored for biodefense. This abstract encapsulates pivotal findings from three comprehensive studies that underscore the potential of phages to revolutionize diagnostics and therapeutics in combating biothreats. Our initial study breaks new ground by overcoming the bacterial O-antigen specificity barrier, a critical challenge in phage application. Screening 145 phage isolates, we identified candidates with the capacity to infect diverse B. pseudomallei strains, enhancing their utility across various environmental and clinical scenarios. Subsequent genetic analysis revealed nine integration hotspots within the B. pseudomallei pangenome, linked primarily to tRNA genes, which are crucial for phages' adaptability and horizontal gene transfer. This genetic plasticity is pivotal for developing phage therapies with enhanced host range and resilience. The final phase of our research involved engineering phages with modified repressor and integrase genes, significantly amplifying their lytic capabilities. These engineered phages present a formidable tool against antibiotic-resistant pathogens, offering a sophisticated alternative to conventional treatments. Collectively, our studies not only advance the understanding of phage biology but also highlight their transformative potential in biodefense, providing a viable strategy against biological threats like melioidosis, particularly in regions most impacted by this disease.

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