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

Vaccine Efficacy Against Antigenically Novel Anthrax Causing Pathogens

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Background information: Anthrax is primarily a zoonotic disease caused by bacteria in the Bacillus cereus complex, including Bacillus anthracis, toxigenic B. cereus, and toxigenic encapsulated Bacillus cereus biovar anthracis. The spore-forming organism evolves slowly due to extended quiescenct periods. Though slowly accumulating, mutation and gene transfer result in changes to Bacillus physiology and virulence.
Purpose: Ensure gapless coverage in warfighter protection by assessing current vaccination strategies against emerging anthrax pathogens.
Objective: Characterize physiologic and pathogenic differences of emerging anthrax bacteria in vitro and in vivo. Quantify protection afforded by current veterinary vaccine standards and a deprecated human vaccine against emerging anthrax threats.
Rationale of the research: By understanding how emerging pathogens cause anthrax we can design effective preventative measures and maintain efficacy of current defense strategies to decrease risk of warfighter exposure to anthrax.
Relationship to other areas of study: Threat protection against anthrax using next-generation vaccine platforms, such as OMV and glycoconjugate vaccine technologies, can benefit from challenge panels composed of emerging anthrax causing pathogens. Microphysiological systems or organoids treated with emerging anthrax pathogens can correlate in vitro and in vivo data.
Methods: Genome sequencing and phylogenetics confirmed nucleic acid signatures of emerging anthrax pathogens. Luminescent bacteria allowed tracking of toxin and capsule expression in emerging strains compared to common laboratory lineages. RNA-seq found global gene expression changes correlated with genomic and phenotypic signatures. The wax worm larvae, mouse, and guinea pig animal models were used to characterize the pathogens. Organ burden, spore burden, and vaccine efficacy against emerging anthrax panels were measured. Toxin neutralizing antibody titers were compared to vaccination responses.
Preliminary results: Several emerging pathogens were more virulent across the small animal models compared to type strains. Sterne vaccination adequately protected against challenge with toxigenic and toxigenic/encapsulated Bacillus cereus in guinea pig and mouse models even though LD50s were lower compared to type strains. Antigenically novel B. anthracis had lower LD50s with incomplete Sterne protection. Single treatments with the previous generation of human vaccine mirrored Sterne observations. Lower LD50s and vaccine protection were correlated with rapid and sustained toxin and capsule production in human serum. These changes were linked to reduced expression of B. anthracis iron acquisition operons.
Preliminary conclusions: B. cereus that acquired B. anthracis virulence factors have increased virulence in small animal models, however, the veterinary Sterne vaccine still protects. B. anthracis with exosporium structural mutations can impact Sterne prime-boost vaccination efficacy. While preliminary, single last-generation human vaccination did not extend mean TTD of mice. Toxin and capsule production and increased binding of immune serum to purified spores indicate a mechanism for decreased efficacy. Depressed siderophore expression can cause iron starvation, increasing consequential virulence factor production.
Impact to the DTRA JSTO mission and the Joint Force: The development of CP216 aligns with the DTRA JSTO mission to enhance the resilience and survivability of the Joint Force by providing effective medical countermeasures against chemical threats, thereby improving operational effectiveness and warfighter safety in environments at high risk for opioid exposure. Emerging anthrax pathogens are potential threats to the nation's agriculture and populace. These organisms are evolving across geographies including Central Asia, Sub-Saharan Africa, and South America. Current vaccination strategies could benefit from comprehensive analysis of alternative approaches or vaccines to ensure sustained defense of the Joint Force against anthrax.