PALADINS: PROTECTIVE APPROACHES LEVERAGING AD-APTIVE AND IN-NATE SYSTEMS

Longitudinal Study Of Immune Responses To Q-vax In Young Healthy Adults To Support The Development Of Novel Vaccines For Q Fever And Tests For Exposure Surveillance

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Coxiella burnetii (Cb), a highly infectious and resilient intracellular bacterial pathogen, is the cause of Q fever, and has biothreat potential due to stability and aerosol transmission. Q-VAX vaccine prevents Q fever but requires pre-screening for prior Cb exposure to avoid side effects and is only licensed in Australia. Need exists for new, non-reactogenic Q fever vaccines. We have previously used mass cytometry to define anti-Cb immune responses associated with vaccine efficacy in murine models. Quantitation of immune responses in humans infected during a Dutch Q fever outbreak provided insights into long-lived T cell memory against Cb. The current project characterizes Q-VAX-induced immune responses in Australian veterinary students. The study also seeks to extend an exploratory study demonstrating that an interferon-γ release assay (IGRA) for cell-mediated responses to Cb could outperform standard immunoassays and the intradermal skin test for detecting prior exposure.

Methods: Vaccine responses were evaluated in students receiving Q□VAX upon matriculation to the University of Queensland Veterinary School. Antibody responses were quantified with established clinical immunoassays. Cellular immune responses were measured using a Cb-specific IGRA. The breadth of the immune response is being assessed using mass cytometry. Immunological assays were complemented by online surveys to document self-reported vaccine reactions. Vaccine responses were assessed in two cohorts in consecutive years to define robust and reproducible immune response profiles.
Results: Vaccination was judged appropriate for all participants based on screening test results. No participants experienced clinically significant reactions to Q□VAX. Pre- and post-vaccination immune responses were evaluated in 140 study participants over two cohorts. Both study cohorts exhibited significant increases in circulating anti-Cb antibodies at 4-8 weeks post-vaccination. Cell-mediated immune responses in the IGRA also increased post-vaccination.

Conclusions: Patterns of humoral and cellular responses to Q-VAX vaccination were highly similar between the two study cohorts. Study results confirmed IGRA sensitivity for measuring Cb-specific responses to vaccination. Both study cohorts lacked individuals with prior Cb exposure confirmed by clinical record or clinical assays, limiting evaluation of IGRA specificity for use in pre-vaccination screening. Initial analysis of mass cytometry data from Cohort 1 identified immune cell populations associated with clinical vaccine responses, including a subpopulation of mature B cells and populations indicating an effector memory T cell response. Curation of the associations among cell populations and clinical vaccine responses is ongoing. Evaluation of the reproducibility of these correlations in Cohort 2 is pending, with a focus on identifying novel correlates of immune protection against Q fever.
Impact to the Mission and Warfighter: Q fever is of concern to the US Department of Defense because of high seroconversion rates detected among military personnel serving in endemic regions, motivating interest in improved vaccines and diagnostic assays for Cb exposure. Data from this study will help define human-relevant immune markers of protection from Cb infection and inform testing of novel Q fever vaccines. Additionally, confirmation of IGRA performance will support further development of a rapid, sensitive Cb-exposure assay for use in austere settings, which would have application both in vaccine development and in exposure surveillance.

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