CAMO (COMPARING ANIMAL MODELS TO ORGANOIDS) - TESTING MEDICAL COUNTERMEASURES WITH MICROPHYSIOLOGICAL SYSTEMS AND COMPARING TO TRADITIONAL ANIMAL MODELS AND CLINICAL TRAILS

Sex Differences In Protection Conferred By Heterologous Vaccines For Pneumonic Plague In An Aerosol Challenge Model

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Pneumonic plague, caused by the gram-negative bacterium Yersinia pestis, is a severe and rapidly progressing illness transmitted via aerosol, which can only be successfully treated if appropriate antibiotics are initiated early after infection. There are no FDA-approved vaccines for plague, and candidate vaccines may be less effective against pneumonic plague than bubonic plague. Y. pestis is not known to impact males and females differently in mechanism of pathogenesis or severity of infection. However, a recent study reported sex-biased vaccine effectiveness after intranasal challenge. In this study we observed that when male BALB/c mice were given a heterologous prime-boost vaccine that is largely protective in females challenged with aerosolized virulent Y. pestis C12, males were not protected. We then gave male and female BALB/c mice a recently developed heterologous vaccine strategy and monitored their survival, bacterial burden (CFU), and immunological factors before and after aerosol challenge with Y. pestis C12. This strategy consisted of two subcutaneous injections: one of Y. pestis live attenuated vaccine (LAV) strain pgm-pPst-Δcaf1 or pgm-pPst-ΔyopD/Δcaf1, and one of rF1-V protein subunit combined with adjuvants CpG and Alhydrogel. When primed with rF1-V followed by boost with pgm-pPst-Δcaf1 LAV, 100% of females and 50% of males survived challenge. This sex difference was observed to a lesser extent with three other vaccine regimens. Males had higher CFU titers and showed differing patterns of serum antibodies, cytokines in lungs, and splenic memory T cells. These data provide new knowledge about sex differences in vaccine efficacy and the immunological factors that differ between males and females.

The opinions, interpretations, conclusions, and recommendations presented are those of the authors and are not necessarily endorsed by the U.S. Army or the Department of Defense Health Agency.
Research was conducted in compliance with the Animal Welfare Act and other federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the Guide for the Care and Use of Laboratory Animals, National Research Council, 2011. The facility where this research was conducted is fully Accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.