

STATUS OF NON-HUMAN PRIMATE MODELS OF *FRANCISELLA* INFECTION

S 11-1

**Humoral immunity to *Francisella tularensis* strain LVS fails to uniformly protect *Cynomolgus* macaques from disease induced by aerosol infection with strain Schu S4**J. A. Wilder<sup>1</sup>, M. Valderas<sup>1</sup>, A. Monier<sup>1</sup>, T. Brasel<sup>1</sup>, R. Sherwood<sup>1</sup>, C. R. Lyons<sup>2</sup><sup>1</sup>Lovelace Respiratory Research Institute, Albuquerque, United States, <sup>2</sup>University of New Mexico, Albuquerque, United States

Vaccination with *Francisella tularensis* strain LVS has been shown to protect non-human primates from the mortality induced by aerosol exposure to *F. tularensis* Schu S4.

**Aims:** Determine the mechanism(s) of protection induced by the LVS vaccine in *Cynomolgus* macaques.

**Methods:** Macaques were vaccinated with  $10^4$  –  $10^7$  LVS via the intradermal or sub-cutaneous route or by scarification. Five weeks to 27 months later, vaccinated animals and non-vaccinated controls were challenged with 27 – 1780 Schu S4 CFU by aerosol. The immune response was characterized by measuring plasma IgG anti-LVS levels, as well as the ability of peripheral blood mononuclear cells to secrete IFN $\gamma$  in response to LVS.

**Results:** Although all the animals produced IgG specific to LVS (titers  $> 1 \times 10^5$ ), only 2 of 9 vaccinated primates survived to day 21 post-aerosol challenge and none remained disease free. Seven vaccinated animals succumbed to the Schu S4 aerosol between day 4 and 16, whereas two of three non-vaccinated controls succumbed on days 5 and 6 and one was euthanized on day 21. LVS-induced IFN $\gamma$  production was variable, with a trend toward higher responsiveness being correlated with a protracted time to death. Schu S4 organisms were recovered from the lungs and tracheobronchial lymph nodes despite vaccination status but dissemination to the liver and spleen appeared diminished in LVS-vaccinated animals.

**Conclusions:** Data suggest that LVS vaccination induces a uniformly strong humoral immune response and a variable cellular immune response, the former of which is unable to predict protection of macaques from mortality induced by Schu S4 aerosol challenge.

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