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Neutrophil-associated disruption of the granulomatous response in BCG-vaccinated mice exposed to environmental mycobacteria

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Multiple studies over the past 20-30 years have concluded that exposure to mycobacteria widely distributed in the environment [EM] can often subvert the efficacy of the BCG vaccine. A variety of possibilities have been proposed to explain this phenomenon, and here we provide a new hypothesis. In the studies reported here we demonstrate that exposure of mice to *Mycobacterium avium*, given periodically over a prolonged period of time in drinking water can sensitize these animals and establish a low grade infection in the lungs. A consequence of this is the gradual accumulation of certain T cell subsets, principally TH17 cells and a smaller number of -TCR+T cells, in the lungs of these animals. After challenge with a Beijing strain of *M. tuberculosis* acquired protective TH1 immunity developed in a normal manner, but the ability of EM-exposed BCG-vaccinated mice to control the growth of the infection was severely impaired. Examination of the lung pathology indicated that large numbers of neutrophils accumulated in the lungs of the EM-exposed mice, causing substantial “spatial disruption” of the normal granulomatous response. We hypothesize that the establishment of TH17 cells in the lungs of these animals prior to the challenge results in the recruitment of this disruptive neutrophil influx, and studies to directly test this possibility are now underway.

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Construction of a recombinant vaccinia virus expressing E gene of Japanese encephalitis virus and immunogenicity in pigs

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Japanese encephalitis virus (JEV) can infect humans and swine with a high incidence rate in Asia. Consequently, the development of a vaccine that can provide rapid protection with minimal risk is an important research goal. A recombinant vaccinia virus (rVVTK/E3LΔ-E) containing envelope protease coding regions of JEV Yunnan0901 was constructed in this study. With the Tiantan strain of vaccinia virus (E3LΔ), an attenuated vaccine was constructed with TK gene deletion by homologous recombination. After screening and identification with a selectable marker, the recombinant vaccinia virus candidate vaccine was evaluated for its ability to induce humoral and cellular responses in pigs. The animals were vaccinated twice with a 21-day interval, and groups of animals were inoculated with the attenuated vaccine, vaccinia virus or phosphate buffered saline (PBS). All pigs vaccinated with rVVTK/E3LΔ-E developed specific anti-JEV antibodies and neutralizing antibodies. Splenocytes from pigs immunized with rVVTK/E3LΔ-E showed higher levels of T-lymphocyte proliferation, the greatest amounts of interferon-γ and interleukin (IL)-2, and moderate amounts of IL-4 and IL-10 in the presence of JEV. Vaccination with rVVTK/E3LΔ-E provided greater protection than that by the attenuated vaccine against JEV challenge. Moreover, pigs inoculated with the recombinant vaccine rVVTK/E3LΔ-E showed a lower virus load than those given the attenuated vaccine. Our findings indicated that rVVTK/E3LΔ-E might be an attractive candidate vaccine for preventing JEV infection.

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