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The ins and outs of a new plague vaccine against an old disease

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Although plague has been one of the most notorious diseases that has affected mankind for many millennia, it was not until recently that a vaccine was first developed against the disease. The most recent attempt was a formalin-inactivated, whole-cell vaccine. The vaccine was discontinued because it appeared to protect the vaccinated host only against *Bubonic plague* but not *Pneumonic plague*. We have since found that the whole-cell vaccine only induced antibodies against the capsule F1 protein but not antibodies against the virulence protein (V-antigen) that appears to be required for a robust protection. The new plague vaccine consists of subunits of the F1 capsule protein and V-antigen either as individual subunits or a fusion of the two subunits. The genes for each of these proteins are encoded on two separate virulence plasmids; one of the plasmids is specific for *Y. pestis*. Initially, it was thought that only antibodies against the vaccine subunits were sufficient for protection against an exposure to the pathogen. Part of this reasoning was from studies with immune serum or monoclonal antibodies against the F1 or V-antigen subunits that showed that these sources of antibodies can passively protect an animal against a plague infection. Nevertheless, we have shown that the participation of the host's innate immune system is required for complete protection against a pneumonic plague challenge with *Y. pestis* CO92 a fully virulent strain of plague. Although it is not completely clear how protection is mediated by the new subunit vaccine, the subunit vaccine has been through a Phase IIa human clinical trial. We will present studies to demonstrate the efficacy of the current subunit vaccine in animal models of plague.

Biography

Kei Amemiya is a Principal Investigator in the Bacteriology Division at the US Army Medical Research Institute of Infectious Diseases. He has been at USAMRIID since 1999 and has been involved in developing vaccine candidates against plague, glanders, and melioidosis. His interest has been in studying the host's immune response to the pathogen and vaccines in small and large animal models. Before coming to USAMRIID, he was at the National Institutes of Health and Georgetown University, where he was studying the host response to bacterial and viral pathogens or autoimmune diseases in humans.

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