

P006 Vaccination with mycobacterial heat shock protein complexes induces interferon gamma and provides protection in the murine aerosol challenge model of TB

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The re-emergence of TB and, in particular, the emergence of antibiotic-resistant strains, has refocused attention on the development of more effective vaccines for this major global disease. The current BCG vaccine has been shown to be ineffective in a number of field trials and it is generally accepted that this is due to prior exposure to environmental mycobacteria. The use of a sub-unit vaccine would be expected to override these problems of prior exposure and may also be of utility in HIV patients who cannot be vaccinated with live vaccines but provide the greatest threat of a possible multi-drug resistant TB pandemic. We originally proposed that the integration of innate and acquired immunity was mediated by the interaction of antigen-presenting cells, in particular dendritic cells, with stress protein complexes. These complexes would provide not just the non-specific stimuli for the innate immune response, but also the pathogen-specific antigens for the acquired immune response. This hypothesis suggested that pathogen-derived stress protein complexes could provide universal, multi-subunit vaccine candidates for the prevention and treatment of infectious diseases.

We have investigated this in the mouse aerosol challenge model for TB. We show that mycobacterial heat shock protein complexes induce a Th1 type cell mediated response with the production of interferon gamma. Most importantly vaccination of mice with these complexes provides protection against aerosol challenge with live TB. These results provide a simple approach to the development of an effective TB vaccine.