

Vaccine efficacy of CD4⁺ T cell responses directed to dominant and subdominant epitopes in ESAT-6 from *Mycobacterium tuberculosis*

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The ESAT-6 (early secretory antigenic target) molecule is a very important target for T cell recognition during infection with *M. tuberculosis*. Although ESAT-6 contains numerous potential T cell epitopes, the immune response during infection is often focused towards a few immuno-dominant epitopes. By immunization with individual overlapping synthetic peptides in cationic liposome's (CAF01™) we demonstrate that the ESAT-6 molecule contain several subdominant epitopes that are not recognized in H-2^{d/b} mice either during TB infection or after immunization with ESAT-6/CAF01™. Immunization with a truncated ESAT-6 molecule (Δ 15ESAT-6) that lacks the immuno-dominant ESAT-6₁₋₁₅ epitope, refocus the response to include T cells directed to subdominant epitopes. After aerosol infection of immunized mice, T cells directed to both dominant (ESAT-6 immunized) and subdominant epitopes (Δ 15ESAT-6 immunized) proliferates and are recruited to the lung. ESAT-6 and Δ 15ESAT-6 both give significant protection against aerosol challenge with TB but the most efficient protection against pulmonary infection is mediated by the subdominant T cell repertoire primed by Δ 15ESAT-6.