

Th1 peptide: its immunogenicity and adjuvant activity

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Both mouse models of infection and human patient material have provided evidence that Th1 cells play an important role in the development of resistance to *Mycobacterium (M.) tuberculosis*. One of the major protein antigens secreted from *M. tuberculosis* is Ag85B. Ag85B has been shown to be the most potent antigen species yet purified in humans and in mice and is a promising candidate for inclusion in novel subunit vaccines against tuberculosis. In order to investigate molecular mechanisms of Th1 development by peptide, we have examined immunogenicity of Ag85b for Th1 development in C57BL/6 (I-A^b) mice. We find that Ag85B is immunogenic to induce Th1 development. Peptide-25 (aa240-254) of Ag85B is the major Th1 epitope and is immunogenic in C57BL/6 mice. Active immunization of C57BL/6 mice with Peptide-25 can induce preferential development of CD4⁺ TCRV β 11⁺ Th1 cells that produce IFN- γ and TNF- α , and can protect against subsequent infection with live *M. tuberculosis* H37Rv. Peptide-25 also has a potent adjuvant activity for Th1 development. We would therefore propose to designate Peptide-25 as “Th1-inducing peptide”.

To elucidate cellular and molecular mechanisms of the preferential induction of Th1 cells by Peptide-25, we have isolated cDNA encoding V β 5 and V β 11 chains of TCR from Peptide-25-reactive murine Th1 clones. Analysis of transgenic (Tg) mice expressing TCRV β 5V β 11 revealed that primary stimulation of spleen cells from the TCR-Tg mice with Peptide-25 can induce production of tremendous amounts of IFN- γ . We will discuss cellular and molecular basis of Th1 development in response to Peptide-25.