Distinct differences in the expansion and phenotype of TB10.4 specific CD8 and CD4 T cells after infection with *Mycobacterium tuberculosis*

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Recently we and others have identified CD8 and CD4 T cell epitopes within the highly expressed *M. tuberculosis* protein TB10.4. This has enabled, for the first time, a comparative study of the dynamics and function of CD4 and CD8 T cells specific for epitopes within the same protein in various stages of TB infection.

We focused on T cells directed to two epitopes in TB10.4; the MHC class I restricted epitope TB10.4 $_{3\text{-}11}$ (CD8/10.4 T cells) and the MHC class II restricted epitope TB10.4 $_{74\text{-}88}$ (CD4/10.4 T cells). CD4/10.4 and CD8/10.4 T cells displayed marked differences in terms of expansion and contraction in a mouse TB model. CD4/10.4 T cells dominated in the early phase of infection whereas CD8/10.4 T cells were expanded after week 16 and reached 5-8 fold higher numbers in the late phase of infection. In the early phase of infection both CD4/10.4 and CD8/10.4 T cells were characterized by 20-25% polyfunctional cells (IL-2^+, IFN-γ^+, TNF-α^+), but whereas the majority of CD4/10.4 T cells were maintained as polyfunctional T cells throughout infection, CD8/10.4 T cells differentiated almost exclusively into effector cells (IFN-γ^+, TNF-α^+). Both CD4/10.4 and CD8/10.4 T cells exhibited cytotoxicity in vivo in the early phase of infection, but whereas CD4/10.4 cell mediated cytotoxicity waned during the infection, CD8/10.4 T cells exhibited increasing cytotoxic potential throughout the infection.