The induction and kinetics of antigen-specific CD8 T cells are defined by the stage specificity and compartmentalization of the antigen in murine toxoplasmosis.

Abstract:
Toxoplasma gondii forms different life stages, fast-replicating tachyzoites and slow-growing bradyzoites, in mammalian hosts. CD8 T cells are of crucial importance in toxoplasmosis, but it is unknown which parasite stage is recognized by CD8 T cells. To analyze stage-specific CD8 T cell responses, we generated various recombinant Toxoplasma gondii expressing the heterologous Ag beta-galactosidase (beta-gal) and studied whether 1) secreted or cytoplasmic Ags and 2) tachyzoites or bradyzoites, which persist intracerebrally, induce CD8 T cells. We monitored the frequencies and kinetics of beta-gal-specific CD8 T cells in infected mice by MHC class I tetramer staining. Upon oral infection of B6C (H-2(bxd)) mice, only beta-gal-secreting tachyzoites induced beta-gal-specific CD8 T cells. However, upon secondary infection of mice that had received a primary infection with tachyzoites secreting beta-gal, beta-gal-secreting tachyzoites and bradyzoites transiently increased the frequency of intracerebral beta-gal-specific CD8 T cells. Frequencies of splenic and cerebral beta-gal-specific CD8 T cells peaked at day 23 after infection, thereafter persisting at high levels in the brain but declining in the spleen. Splenic and cerebral beta-gal-specific CD8 T cells produced IFN-gamma and were cytolytic upon specific
restimulation. Thus, compartmentalization and stage specificity of an Ag determine the induction of CD8 T cells in toxoplasmosis.