CHARACTERIZATION OF THE CD8+ T CELL RESPONSE IN RICKETTSIAL INFECTIONS

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Natural and experimental rickettsial infections provide strong and cross-protective immunity if the individual survives, untreated rickettsial diseases have one of the highest fatality rates know to man (case fatality might be as high as 30%). Although resistance to rickettsial infections is attributed to the induction of antigen-specific T cells, the details of the T cell immune response, as well as the cellular correlates of protection in rickettsiosis have not been systematically defined. Protective immune effector mechanisms have been elucidated using relevant mouse models of rickettsiosis, indicating that the anti-rickettsial immune response is mainly mediated by IFN-γ and by the induction of cytotoxic CD8+ T cells. Furthermore, previously we have demonstrated that T cells can mediate cross-protective immunity between typhus and spotted fever group rickettsiae. However, the systematic characterization of T cell mediated immune response is yet to be addressed. We propose that the systematic analysis of T cell mediated responses, using a larger collection of T cell activation, memory and effector markers, will contribute to the definition of correlates or surrogates of cellular protective immunity against rickettsial infections; which in turn will facilitate the design, identification and testing of post-exposure prophylactic treatments or vaccine candidates with the potential to confer long lasting anti-rickettsial cellular immunity. The objective of the present work is to determine the in vivo phenotype and kinetics of primary CD8+ T cell responses as well as memory rickettsiae-specific CD8+ T cells upon recall. Expression of CD3, CD8, CD25, CD27, CD43, CD44, CD45RA, CD62L, CD69, CD127, CD197, KLRG1, IL-2, IFN-γ, TNF-α, Granzyme B, and perforin will be analyzed ex vivo by multi-color flow cytometry. Here we discuss some preliminary results related to the assessment of anti-rickettsial primary and memory CD8+ T cells.