Deletion of Antigen-Specific CD4+ T Cells is a Strategy of Immune Evasion and Persistence of *Anaplasma marginale*

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Previously we showed that calves immunized with outer membrane protein or peptides of *A. marginale* had rapid and permanent loss of antigen-specific $CD4^+$ T cell activity in the peripheral blood upon challenged with live *A. marginale,* concurrent with peak rickettsemia that occurred 2 to 4 weeks post-infection. Using novel bovine MHC class II tetramers we determined that loss of antigen-specific proliferation and IFN- γ secretion was due to physical deletion of these cells from PBMC, with no evidence of sequestration in tissues or anergy of specific T cell clones. (Han S, J Norimine, WC Brown. Rapid deletion of *Anaplasma marginale*-specific $CD4^+$ T cells following infection represents a novel strategy of immune evasion in bacterial persistence. *The Journal of Immunology*, 2008 Dec; 181: 7759-7769). We hypothesize that this rapid loss of antigen-specific $CD4^+$ T cells is due to apoptosis from direct antigenic stimulation of primed $CD4^+$ T cells, as opposed to a mere bystander effect of acute phase anaplasmosis. To test this hypothesis we will immunize cattle to prime strong antigen-specific $CD4^+$ T cell memory responses to *A. marginale* outer membrane proteins MSP1a and MSP2. We will then challenge cattle with *A. centrale,* a subspecies that lacks expression of key T cell epitopes of MSP1a, but which fully expresses conserved MSP2 epitopes. If rapid deletion of specific $CD4^+$ T cell clones is driven by activation induced cell death (AICD), we expect to see retention of MSP1a-specific $CD4^+$ T activity and cell frequency and deletion of MSP2-specific $CD4^+$ T cells in the PBMC. Additionally we will be monitoring the frequency of apoptosis of antigen-specific $CD4^+$ T cells in the spleen near the peak of infection. Activation induced cell death likely represents a mechanism of immune evasion by the organism that may facilitate persistent infection, a hallmark of this disease.