SIV SPECIFIC IMMUNE RESPONSES AND GENE REGULATIONS IN SIV-INFECTED LONG-TERM NONPROGRESSING RHESUS MACAQUES

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SIVmac infection in Chinese rhesus macaques leads to a high frequency of long-term nonprogressors (LTNP). We compared the cytokine/chemokine profiles, and SIV specific cellular and humoral immune responses between SIV infected Chinese rhesus that are either LTNP or normal progressor. Thus far we have examined levels of cytokines in longitudinal plasma samples of 2 progressors and one LTNP using Bio-Plex Cytokine kit. One progressor had significantly decreased TNF-α and IL-15 at day 28, and increased TNF-α, IL-6 and IL-12 at day 90 post infection. This animal had the highest plasma viral load at set point and developed AIDS in 1.5 years. The LTNP had very stable levels of cytokines except a minor reduction of TNF-α and IL-15 at day 28 p.i. Interestingly, the LTNP consistently displayed significantly higher levels of the chemokine eotaxin (CCL11), a CCR3 ligand, than the progressor. The upregulation of eotaxin mRNA was also observed in another LTNP by microarray assay. The CCAAT/enhancer binding protein delta (C/EBP delta) was also significantly upregulated in CD8+ T cells in the LTNP. All SIV-infected animals elicited variable levels of SIV specific antibody responses to Env and Gag by ELISA. Intracellular cytokine staining showed stronger SIVgag-specific CD4 and CD8+ T cell responses in LTNP than progressors. In addition to SIV-specific CD4 and CD8+ T cells and antibody responses, the role of CCL11 and C/EBP delta merit further investigation in the maintenance of long-term nonprogression in SIV infection.