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INCREASED VIRAL SET POINT FOLLOWING IL-15 TREATMENT OF ACUTE SIV INFECTION

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OBJECTIVES: To test the immunologic, virologic and clinical effect of in vivo treatment of acutely SIV infected non-human primates with the pleiotropic cytokine IL-15.

METHODS: Mamu-A*01+ rhesus macaques were treated during acute SIV infection with IL-15. Animals received 100µg/kg body weight IL-15 (*n*=6) or saline (*n*=6) twice a week for 4 weeks following SIV infection. Peripheral blood and lymph node biopsies were evaluated weekly for SIV-specific CD8+ T cells, lymphocyte subpopulations and viral loads.

RESULTS: Beyond week 3 post-infection IL-15 treated animals exhibited progressively higher blood viremia that reached $43\pm29\times10^6$ SIV RNA molecules/ml blood at week 20 compared to $2.4\pm0.9\times10^4$ SIV RNA molecules/ml in untreated animals. At weeks 25-26, 2 out of 6 IL-15 treated animals developed simian AIDS and were euthanized with one animal exhibiting early ´minimal lesion´ SIV meningoencephalitis. IL-15 treated animals had a 2-fold increase in peripheral blood Gag- and Tat-specific CD8+ T cell and NK cells numbers at day 14 compared to controls with no further differences seen at later time points. CD8+ T cell numbers were also increased by 2-fold in IL-15 treated animals during the course of IL-15 treatment up to week 4. IL-15 treatment significantly decreased the percentage of HLA-DR+Gag-specific CD8+ T cells in blood but increased lymph node numbers of Gag-specific CD8+ T cells by 3 fold at week 30. No differences were found for CD4+ T cells, monocytes and B cells. An increase in percentage of Ki-67+CD4+ T cells was observed at week 1 with 20% in IL-15 treated compared to 10% in untreated animals. CCR5+CD4+ T cells were nearly absent from the blood of IL-15 treated animals after week 3.

CONCLUSIONS: These data show that IL-15 administration during acute SIV infection leads to dramatically increased viral set points and accelerates progression to AIDS.

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