Impact of IL-15 neutralization on CNS immune and inflammatory responses to acute HIV/SIV infection

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BACKGROUND

Immune responses mounted in the CNS during acute HIV/SIV infection are insufficient to prevent viral seeding and reservoir establishment. The pleiotropic cytokine IL-15 plays a crucial role in anti-viral immune response by stimulating NK and CD8+ T cells to control HIV/SIV infection in blood and tissues. However, the effects of IL-15 on the CNS are largely unknown. Experimental neutralization of IL-15, leading to the depletion of NK and T cells, could significantly influence the viral pathogenesis in the brain, alter reservoir formation, and clarify the role of IL-15 in lentivirus disease. We comprehensively evaluated brain immune and inflammatory responses to acute SIV infection with and without IL-15 neutralization in an established nonhuman primate model.

METHODS

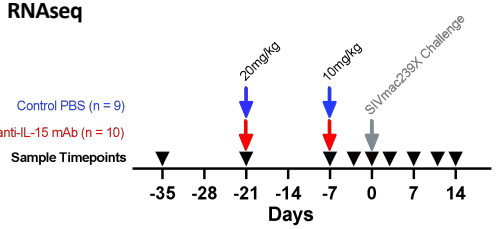
Viral load quantification

Single Genome Amplification (SGA) Analysis

Sequence of integrase gene amplified via PCR -- RNA isolation – cDNA -- RT-PCR

Histology

RNAseq



ADDITIONAL KEY INFORMATION

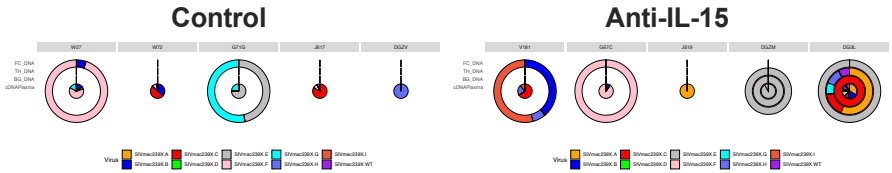
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In rhesus macaques acutely infected with SIV, IL-15 depletion altered the compositions of brain immune response cells and decreased brain inflammatory responses without altering the viral quantities or brain distribution of bar-coded virus.

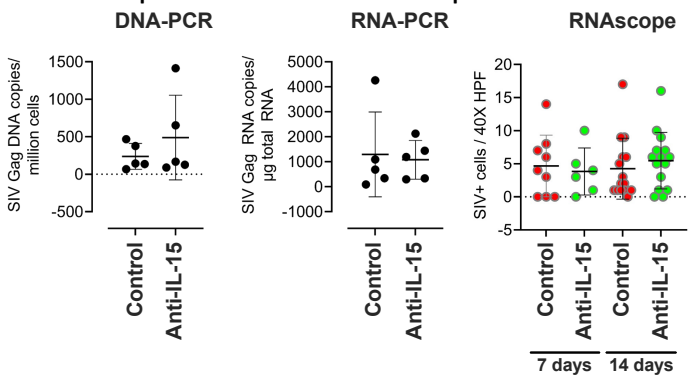
RESULTS

- NK cell depletion resulted in significantly increased acute viral loads in plasma, but did not affect viral loads in the brain
- NK cell depletion only had modest impacts on transmission of barcoded virus variants in all tissues
- NK cell depletion may result in moderate increases in soluble measures of inflammation, and decreases in brain tissue inflammation
- NK cell depletion result in decreased inflammatory response in the brain tissues

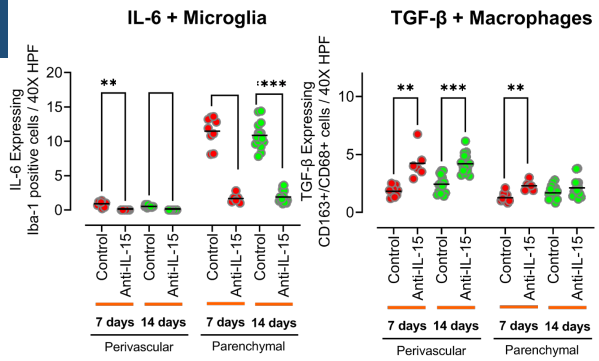
Brain SGA Analysis

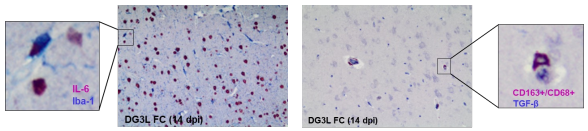


NK cell depletion did not alter SIV viral quantities in the brain



NK cell depletion may be associated with decreased inflammatory response in the brain in acute SIV infection





CONCLUSIONS

IL-15 neutralization altered CNS immune and inflammatory responses to acute SIV infection by decreasing CD8+ T cells and resulting in a tissue environment favoring anti-inflammation, which could overall support the establishment of viral reservoir.

FUNDING

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