

Oral presentation

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OA07-02. Adenovirus vectors induce expansion of memory CD4 T cells with a mucosal homing phenotype that are readily susceptible to HIV-1 infection

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Background

In the recently halted human immunodeficiency virus type 1 (HIV-1) vaccine STEP trial individuals that were seropositive for adenovirus serotype 5 (Ad5) showed increased rates of HIV-1 infection on vaccination with an Ad5 vaccine. We undertook a series of *ex vivo* strategies to address the hypothesis that immunisation of Ad5 seropositive individuals with adenoviral vectors may result in activation, expansion, and trafficking of Ad5-specific memory CD4 T cells to mucosal tissues thereby increasing the number of HIV-1 susceptible targets at the initial sites of infection.

Methods

Ad5 and Ad11 antibody titers were measured in 20 healthy volunteers. Dendritic cells (DC) were generated from these individuals, pulsed with replication defective Ad5 or Ad11 and co-cultured with autologous lymphocytes. Cytokine profiles, proliferative capacity and the migration potential of the adenovirus-stimulated memory T cells were measured. The susceptibility of re-stimulated memory Ad-specific T cells to infection with a CCR5-utilising HIV-1 was also assessed by multi-colour flow cytometric analysis and p24 ELISA assays.

Results

Stimulation of T cells from Ad5 seropositive but Ad11 seronegative individuals with Ad5, or serologically distinct Ad11 vectors induced expansion of adenovirus memory CD4 T cells expressing alpha 4 beta 7 and CCR9, indicating a mucosal-homing phenotype. CD4 T cell proliferation and IFN-gamma production in response to Ad stimulation correlated with Ad5 antibody titers. In contrast, Ad5 serostatus did not correlate with total cytokine production upon re-challenge with Ad5 or Ad11. Expanded Ad5 and Ad11 memory CD4 T cells showed an increase in CCR5 expression and higher susceptibility to infection by R5 tropic HIV-1.

Conclusion

Adenoviral-based vaccination against HIV-1 in individuals with pre-existing immunity against Ad5 may result in preferential expansion of HIV-susceptible activated CD4 T cells that home to mucosal tissues, increase the number of virus targets and lead to a higher susceptibility to HIV infection.