

Poster presentation

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PI9-20. Allogeneic stimulation of the anti-viral APOBEC3G in human CD4⁺ T cells and prevention of SHIV infectivity in macaques immunized with HLA antigens

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Background

APOBEC3G (A3G) is an intracellular anti-viral factor which deaminates cytidine to uridine. The activity of A3G is countered by Vif, which protects the virus by preventing incorporation of A3G into virions. A3G can be upregulated *in vitro* and *in vivo* to overcome Vif activity and inhibit HIV-1 or SIV infection.

Methods

Human CD4⁺ T cells were separated from PBMC of normal HIV-1- subjects and allostimulated by unmatched irradiated PBMC. A3G was assayed before and after allostimulation by RT-PCR, Western blots and immunofluorescence with A3G-specific antibodies. A3G expression in the subsets of memory CD4⁺ T cells was determined by immunofluorescence with antibodies to A3G, CD45RA and CCR7. Allo-immunization with recombinant HLA-class I and class II dextramers, HIVgp140, SIVp27 and the co-adjuvants HSP70 and Titermax (SC x4) was carried out in rhesus monkeys and they were challenged with SHIVSF162.P4.

Results

Allogeneic stimulation of human CD4⁺ T cells *in vitro* upregulated A3G mRNA ($p = 0.01$). The mechanism of

upregulation of A3G mRNA involves interaction between HLA on DC and TCR of CD4⁺ T cells, which is ZAP70 phosphokinase signalling dependent and induces CD40L and A3G mRNA expression in CD4⁺ T cells ($p = 0.001$). *In vivo* significant inhibition in viral load or preventing infection was found against the heterologous viral challenge, when compared with unimmunized control animals. A significant increase in A3G mRNA was found already after the 1st immunization ($p < 0.02$), with upregulation of CD4⁺CD95⁺CCR7⁺ central memory T cells.

Conclusion

In vitro allo-stimulation of human CD4⁺ T cells and *in vivo* immunization with recombinant HLA-class I and II dextramers, trimeric HIVgp140, SIVp27, HSP70 and Titermax elicited significant upregulation of A3G in CD4⁺ memory T cells. A significant inverse correlation between the cumulative viral load and A3G in the central memory T cells suggests that A3G may have contributed to the prevention of SHIV SF162.P4 infection.