Retrovirology

BioMed Central

Poster presentation

P19-20. Allogeneic stimulation of the anti-viral APOBEC3G in human CD4+ T cells and prevention of SHIV infectivity in macaques immunized with HLA antigens

Y Wang*[1], T Whittall[1], J Scholler[2], R Wyatt[3], M Singh[4], LA Bergmeier[1], E Bunnik[5], H Schuitemaker[5], O Shaw[1], R Vaughan[1], J Pido-Lopez[1], T Seidl[1], K Babaahmady[1], G Yang[6], R Thorstensson[7], G Biberfeld[7] and T Lehner[1]

Address: [1]Mucosal Immunology Unit, Kings College London, London, UK, [2]Immunodex, Copenhagen, Denmark, [3]National Institute of Health, Bethesda, MD, USA, [4]Lionex Diagnostics & Therapeutics, Braunschweig, Germany, [5]Academic Medical Center, Amsterdam, Netherlands, [6]Chinese Centre for Disease Control and Prevention, Beijing, PR China and [7]Swedish Institute for Infectious Disease Control, Stockholm, Sweden

* Corresponding author

from AIDS Vaccine 2009
Paris, France. 19–22 October 2009

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P340 doi:10.1186/1742-4690-6-S3-P340

This abstract is available from: http://www.retrovirology.com/content/6/S3/P340

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.