Retrovirology

Poster presentation

P19-34. Formal breaking of B cell tolerance to induce HIV blocking CCR5 specific antibodies in mouse model

L Lopalco*, L Diomede and C Pastori

Address: Division of Immunology, Infectious Diseases and Transplantation, San Raffaele Scientific Institute, Milan, Italy
* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P354 doi:10.1186/1742-4690-6-S3-P354

This abstract is available from: http://www.retrovirology.com/content/6/S3/P354

Background

Since its discovery the chemokines receptor CCR5 that acts as a required co-receptor for HIV-1 (R5) infection and represents a key target for antivirals aiming at inhibiting the HIV-1 entry process such as CCR5 specific antibodies that have been shown to internalize the receptor and efficiently block HIV entry. These antibodies been elicited in mice upon specific antigen presentation of human CCR5 specific regions.

Methods

The aim of this study is to formal breaking tolerance and to inducing infection-protecting anti-CCR5 auto-antibodies in mice without signs of pathologic phenomenon. For this purpose, we generated chimeric immunogens containing the relevant autologous mouse CCR5 peptide in the context of the capsid protein of Flock House Virus (FHV), a molecular system particularly suitable for containing looped peptide.

Results

Administered by intra-peritoneal or intra-nasal routes, the immunogens elicited anti-CCR5 IgG and IgA (in serum and vaginal fluids). In analogy with previous studies, mice producing anti-CCR5 autoantibodies express significantly reduced levels of CCR5 on the surface of CD4+ cells from peripheral blood and vaginal washes. No signs of immunopathology have been found in immunized mice. *In vitro* studies have shown that murine IgG and IgA: i) specifically bind human and mouse CD4+ lymphocytes and the CCR5-transfected U87 cell line; ii) down-modulate CCR5 expression of cultured CD4+ cells from both humans and untreated mice.

Conclusion

Results from these studies have been providing novel direction for the development of durable HIV infection prevention measures not restricted to specific HIV isolates.