Retrovirology

Poster presentation

P07-01. The gut mucosal homing receptor integrin α4β7 forms a complex with CD4 and defines a T cell subset that is highly susceptible to infection by HIV-1

C Cicala, E Martinelli, JP Mcnally, M Pascucio, N Patel, K Jelicic, D Wei, D Van Ryk, AS Fauci and J Arthos*

Address: National Institute of Allergy and Infectious Diseases (USA), Bethesda, MD, USA
* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P99 doi:10.1186/1742-4690-6-S3-P99

This abstract is available from: http://www.retrovirology.com/content/6/S3/P99

Background

In the acute phase of HIV infection, following mucosal transmission, the bulk of HIV replication occurs in Peyer's patches and mesenteric lymph nodes. Concurrently, HIV mediates a massive depletion of lamina propria CD4+ T cells. Integrin α4β7 (α4β7) facilitates the migration of lymphocytes from gut inductive sites (Peyer's patches and mesenteric lymph nodes) to the lamina propria. Thus α4β7 is functionally linked to the major sites of HIV replication and CD4+ T cell depletion during acute infection. It is in this context that we described a specific biochemical interaction between the HIV-1 envelope protein gp120 and α4β7 on CD4+ T cells. The explicit linkage between α4β7 and the major sites of HIV replication following mucosal transmission suggests that this interaction plays an important role at an early phase in the HIV infection cycle during sexual transmission.

Methods

HIV replication in α4β7high CD4+ T cells was compared to replication in CD4+ T cells lacking an α4β7high phenotype. Phenotypic characterization of α4β7high CD4+ T cells was carried out on freshly cells isolated from human gut biopsies. FRET and antibody coprecipitation were used to demonstrate CD4/α4β7 complexes.

Results

α4β7 forms a complex with CD4 on α4β7high CD4+ T cells. α4β7high CD4+ T cells are preferentially infected and depleted. These cells are CCR5high and CXCR4low. In gut mucosal tissues metabolically active cells (Ki-67+) are enriched in the α4β7high subset of CD4+ T cells.

Conclusion

The capacity of the HIV envelope to bind to α4β7 represents a strategy whereby HIV is able to more efficiently infect a highly susceptible subpopulation of CD4+ T cells. In this manner the probability of productive infection following sexual/mucosal transmission is increased. Thus strategies aimed at interfering with HIV-α4β7 interactions may reduce the frequency of sexual transmission.