Retrovirology

BioMed Central

Oral presentation

Coreceptor Dependent Signaling in Individual Primary Resting CD4+ T-cells Mediated by Low Levels of HIV Binding

Marta Melar[1], David Ott[2] and Thomas J Hope*‡[1]

Address: [1]Department of Microbiology and Immunology, University of Illinois at Chicago, Chicago, IL and [2]Basic Research Program, SAIC-Frederick, Inc. NCI Frederick, Frederick, Maryland

Email: Thomas J Hope* - thope@northwestern.edu

* Corresponding author ‡Presenting author

from 2005 International Meeting of The Institute of Human Virology
Baltimore, USA, 29 August – 2 September 2005

Published: 8 December 2005

Retrovirology 2005, **2**(Suppl 1):S3 doi:10.1186/1742-4690-2-S1-S3

In order to enter into the target cell, HIV requires functional contact with CD4 and CCR5 or CXCR4. The last two are G-protein coupled receptors that when activated with chemokines, or HIV envelope can initiate a wide range of biological responses, including Ca^{2+} mobilization, cytoskeletal rearrangements and cell migration. To determine the specificity of X4-tropic gp120-mediated signaling through CXCR4, we have chosen a microscopy-based approach to observe the response at the level of individual cells providing greater sensitivity. Target cells were able to activate a signaling cascade in response to both monomeric recombinant gp120 and virion-bound trimeric gp120. C^{2+} elevation was a direct measurement of CXCR4 engagement because it was dependent on the tropism of the envelope, engagement of CD4, and sensitive to the CXCR4 antagonist AMD-3100. Signaling required much lower levels of envelope when virion associated. Imaging analysis allowed the correlation of the pattern of virion-mediated C^{2+} fluxing with the exact number of viral particles bound to cells. This analysis revealed that an average of four virions, and as few as two virions associating with a primary resting T cell could mediate C^{2+} mobilization. The ability of several virions to stimulate signaling in primary resting T cells is physiologically relevant and has important implications for AIDS pathogenesis. Funded in part by DHHS NO1-CO-12400 and RO1-AI052051.