Retrovirology

BioMed Central

Oral presentation

Open Access

HIV Entry and Its Inhibition: How Do Chemokines Fit In?

Oliver Hartley*‡

Address: Department of Structural Biology and Bioinformatics, University of Geneva, Geneva 1211, Switzerland

Email: Oliver Hartley* - oliver.hartley@medecine.unige.ch

* 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):S7 doi:10.1186/1742-4690-2-S1-S7

HIV entry. HIV requires a chemokine coreceptor, either CCR5 or CXCR4, in addition to CD4 to enter target cells. A recently proposed model, based on apparent structural homology between the V3 region of the envelope glycoprotein and chemokine beta-hairpin loops, suggests that the V3 region may direct coreceptor choice through structural mimicry of the chemokines that bind to either coreceptor. Some of our recent research based on available chemokine structure-activity data has produced evidence that challenges this model.

HIV entry inhibition. The native ligands of HIV coreceptors prevent viral entry via a combination of steric blockade and removal of receptors from the cell surface (receptor sequestration). Our work on synthetic and semisynthetic chemokine analogues has led to the discovery of potent HIV entry inhibitors such as PSC-RANTES, which owe their activity to a greatly enhanced capacity to sequester CCR5. PSC-RANTES has shown promise as a microbicide candidate, but as a totally synthetic protein it is likely to be too expensive for use in the developing world. We are now focused on discovering similarly potent molecules that are either partly or wholly accessible by biosynthesis and thus much cheaper to produce.