

Poster presentation

Open Access

P09-13. Structure of HIV-1 gp41 interactive region: layered architecture and basis of conformational mobility

M Pancera^{*1}, S Majeed¹, Y Ban², L Chen¹, C Huang¹, L Kong¹, Y Kwon¹, J Stuckey¹, T Zhou¹, J Robinson³, W Schief², J Sodroski⁴, R Wyatt¹ and P Kwong¹

Address: ¹NIH/NIAID/VRC, Bethesda, MD, USA, ²University of Washington, Seattle, WA, USA, ³Department of Pediatrics, Tulane University Medical Center, New Orleans, LA, USA and ⁴Department of Cancer Immunology and AIDS, Dana-Farber Cancer Institute, Boston, MA, USA

* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, 6(Suppl 3):P126 doi:10.1186/1742-4690-6-S3-P126

This abstract is available from: <http://www.retrovirology.com/content/6/S3/P126>

© 2009 Pancera et al; licensee BioMed Central Ltd.

Background

Crystal structures of unliganded, CD4-bound, and antibody-bound gp120 core show large conformational rearrangements upon ligand binding. Moreover, cryo-EM tomograms of the HIV-1 viral spike (gp120/gp41) also show large ligand-induced shifts in gp120 orientation. Conformational change is one mechanism that HIV-1 has developed to evade the host immune response. We hypothesized that the key to understanding this mobility resided in the critical gp41-interactive region of gp120. However, previously determined core structures all contained deletions of the gp41-interactive region.

Methods

We determined the structure at 3 Å resolution for an HXBc2 gp120 core with intact gp41-interactive region, bound to two-domain CD4, and the antigen-binding fragment of 48 d.

Results

The new structure revealed that most of the N terminus packs intimately against the previously determined core, adding three β-strands and one α-helix to the inner domain. The tips of the newly defined termini form two anti-parallel β-strands, which extend away from gp120. Meanwhile, the gp41-interactive region consists of a single surface composed of at least four different sequence segments, and includes the N and C tips and a central

seven-stranded β-sandwich. The more complete inner domain is centered about this seven-stranded β-sandwich, from which three structural excursions emanate. Each of these excursions packs as a separate topological layer. Comparison to other gp120 structures indicates that these layers are structurally plastic with weak interlayer interactions.

Conclusion

Structural analysis and cryo-EM tomograms were consistent with a model in which the layers in the inner domain of gp120 act as a shape-changing spacer between structurally invariant outer domain and gp41-associated β-sandwich to allow movement within the viral spike. Thus, we define a layered gp120 architecture that allows for extraordinary conformational change while retaining gp41 interaction through an invariant β-sandwich and associated termini. The mechanism of gp120 mobility revealed here assists HIV-1 in both immune evasion and entry.