

Poster presentation

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PI9-21. Sequence variability in the crown of the V3 loop of the HIV-1 envelope is clustered within a small 3D structural zone

D Almond*¹, T Kimura², X Kong¹, J Swetnam¹, S Zolla-Pazner¹ and T Cardozo¹

Address: ¹Sackler Institute, New York University School of Medicine, New York, USA and ²Department of Immunology, Kumamoto University, Kumamoto, Japan

* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, 6(Suppl 3):P341 doi:10.1186/1742-4690-6-S3-P341

This abstract is available from: <http://www.retrovirology.com/content/6/S3/P341>

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Background

The diversity of HIV-1 is a confounding problem for vaccine design, as the human immune response appears to favour strain specific responses to any given HIV-1 virus strain. A significant portion of this diversity is manifested as sequence variability in the loops of HIV-1's surface envelope glycoprotein. The observation of strain specific responses suggests that these loops are structurally (serotypically) variable between strains. However, the existence of cross-strain neutralizing antibodies suggests there may be room for serotypic conservation in the V3 loop.

Methods

6,010 HIV-1 V3 loop sequences were collected from the Los Alamos National Laboratory database and were analyzed for variability at individual positions. Variability was averaged over structurally relevant zones and mapped on to the mAb 2219 bound HIV-1 MN conformation for visualization.

Results

Our results indicate that the most variable sequence positions in the third variable (V3) loop crown cluster to a small zone on the surface of one face of a β -hairpin conformation. These results provide a novel visualization of gp120 variable loops, specifically demonstrating a preponderance of conserved three-dimensional structure in a sequence variable loop.

Conclusion

From a structural point of view, there appears to be plenty of room for serotypic conservation in this region of the major neutralizing determinant of this pathogen.