Retrovirology

BioMed Central

Oral presentation

OA021-05. Insertion of the HIV-1 gp41 epitopes 2F5 and 4E10 into the membrane-proximal region of the vesicular stomatitis virus glycoprotein

IC Lorenz*, HT Nguyen, SK Phogat, SM Kaminsky, TJ Zamb and CL Parks

Address: International AIDS Vaccine Initiative, Brooklyn, NY, USA
* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):O17 doi:10.1186/1742-4690-6-S3-O17

This abstract is available from: http://www.retrovirology.com/content/6/S3/O17

Background

The membrane-proximal external region (MPER) of HIV-1 gp41, which is thought to be involved in the viral fusion process, is an important target for an HIV vaccine. Two broadly neutralizing monoclonal antibodies, 2F5 and 4E10, bind to adjacent linear epitopes in the gp41 MPER. However, attempts to design immunogens that elicit a neutralizing antibody response against this region have had limited success.

Methods

We inserted the gp41-derived epitope sequences into the envelope glycoprotein G of Vesicular Stomatitis Virus (VSV). VSV G forms homotrimeric spikes on the viral surface, mediates binding of the virus to cells and promotes fusion of the viral and cellular membranes. The membrane-proximal "stem" region of VSV G, which plays a role in VSV fusion, shares sequence similarities with the HIV-1 gp41 MPER. We created chimeric polypeptides by substituting residues in the G stem with the 2F5 and 4E10 epitopes, generated pseudotyped lentiviruses or rescued VSV with the mutant envelope proteins incorporated, and tested the function and antibody reactivity of the recombinant viruses.

Results

VSV-G-2F5 and VSV-G-4E10 formed trimers and were transported to the cell surface, where they were recognized by the 2F5 and 4E10 monoclonal antibodies, respectively. Pseudotyped lentiviruses or recombinant VSV containing G-2F5 or G-4E10 on the viral surface were infectious, and the mutant viruses were neutralized by the 2F5 or 4E10 monoclonal antibodies. We are currently determining if the recombinant viruses are capable of eliciting a neutralizing antibody response in a small animal model.

Conclusion

These results suggest that the 2F5 and 4E10 epitopes inserted into the VSV G stem region, which is likely to be the functional equivalent of the HIV-1 gp41 MPER, adopt a conformation similar to the one in their native context in gp41. Our approach represents a novel strategy to develop a vaccine that induces a humoral immune response against HIV.