Retrovirology

BioMed Central

Poster presentation

P19-12. Multimers of llama heavy chain variable domains that bind to the 2F5/4E10 epitope neutralize HIV-1

Y Liu*[1], ME Khatttabi[1], A Forsman[2], MM Asaa-Chapman[2], RA Weiss[2], H Langedijk[3], A Hinz[4], W Weissenhorn[4], H de Haard[1] and T Verrips[1]

Address: [1]Cellular Architecture & Dynamics, Department Biology, Utrecht University, Utrecht, Netherlands, [2]University College London, London, UK, [3]Pepscan Systems BV, Lelystad, Netherlands and [4]European Molecular Biology Laboratory, Grenoble, France

* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P332 doi:10.1186/1742-4690-6-S3-P332

This abstract is available from: http://www.retrovirology.com/content/6/S3/P332

Background

Llamas raise two different types of antibodies against foreign invaders, the conventional antibodies and the heavy chain devoid of light chain antibodies. We have used llama to raise and select the latter class antibodies (VHH) against HIV-1. The advantage of using VHHs is the relative ease to construct large (>10^8) and nearly 100% functional phage libraries. Recently we have succeeded in the selection of VHHs against the CD4 binding site from a CN54 immune library. However, the attempt to select VHHs against gp41 from this library or a gp41 peptide immune library was not successful. Therefore, a recombinant trimeric gp41 was used for immunization and selections in this study.

Methods

To select VHHs that bind to the particular epitopes on gp41, competitive elution with the neutralizing monoclonal antibodies 2F5 and 4E10 was used.

Results

Comparison of the amino acid sequences of the selected VHHs with the *V*-, *D*- and *J*-genes on the chromosome of llamas resulted in the identification of 12 different families of VHHs, which bind to the 2F5/4E10 epitope. Pepscan analysis showed that 5 of the 10 amino acids of the 2F5 epitope were recognized by one of the selected VHHs (2H10). Nevertheless, the selected VHHs did not give favorable results in neutralization assay. As the antigen is a trimer, we reasoned that bi- and/or tri-heads of VHHs with good binding properties may provide neutralization. Indeed the bihead of 2H10 neutralized HIV at nanomolar concentrations.

Conclusion

We selected VHHs that bind to gp41. The amenability of the VHHs to recombine into multivalent peptides enabled the construction of functional bihead of VHHs. The binding affinity of the bihead increased ~ 100-folds, and more importantly, the bihead achieved neutralization of HIV. This shows again that llama VHHs are a versatile tool in targeting the difficult HIV infection mechanism.