Expanding the binding ability and specificity of anti-HIV antibody KD-247

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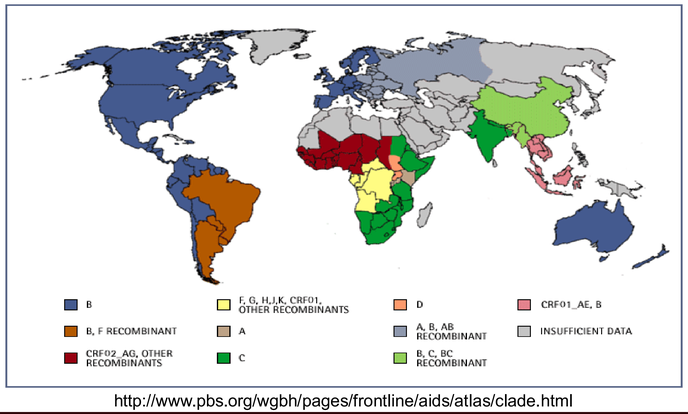
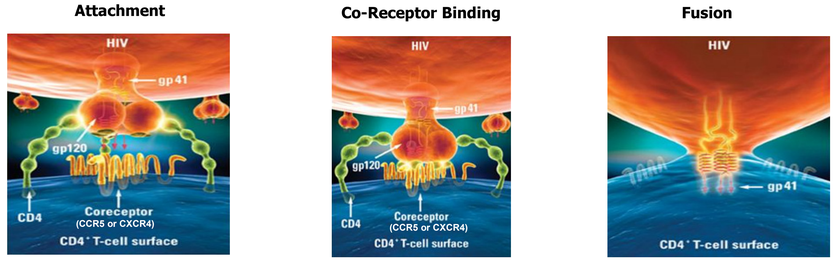
Introduction

HIV-1, which has many different clades, has claimed more than 25 million lives in the last thirty years. Clade B is most common in the United States and Europe, while non-clade B is more common in other parts of the world, especially sub-Saharan Africa. Non-clade B strains are responsible for >80% of HIV infections.

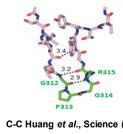


http://www.pbs.org/wgbh/pages/frontline/aids/atlas/clade.html

HIV Entry and the 3rd Hypervariable (V3) Loop



M. Westby and E. van der Ryst, Antivir. Chem. Chemother. (2005) 16, 339



C-C Huang *et al.*, Science (2005) 310, 1025

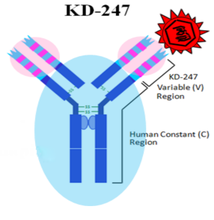
Clade B: GPGR

Non-clade B: GPGQ

During binding of HIV-1, the third hypervariable loop of the gp120 protein is expressed. This loop has different amino acids in clade B and non-clade B.

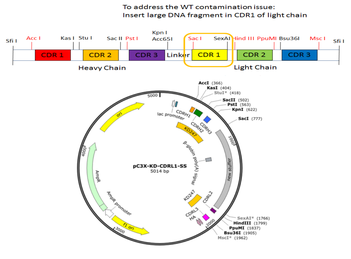
KD-247 and pC3X-KD-V1

KD-247 is a humanized monoclonal antibody against the V3 (third hypervariable loop) of gp120.



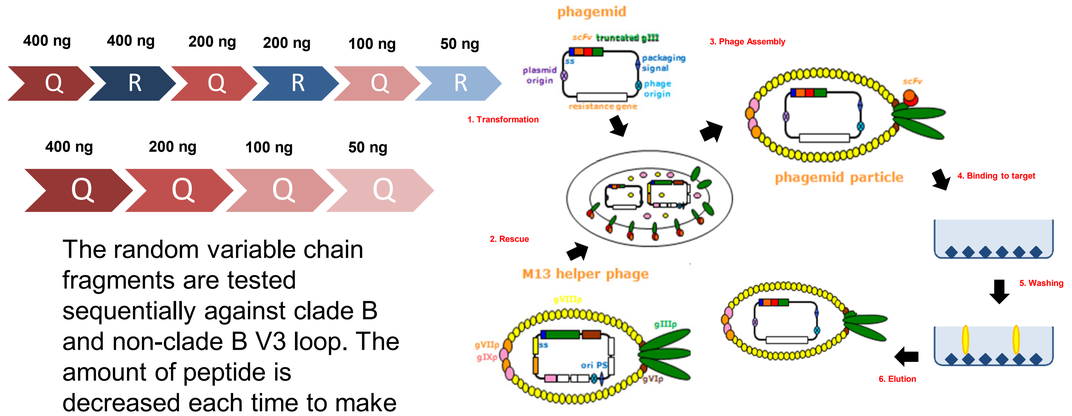
Y. Eda et al. J. Virol. (2006) 80, 5552

pC3X-KD-V1 is a phagemid that contains the DNA sequences for the CDR region of KD-247.



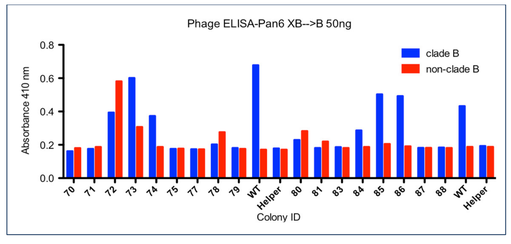
Phage panning and selection

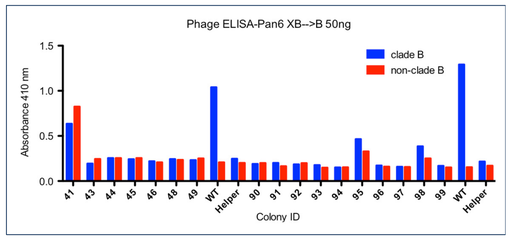
Phage display was chosen to allow a large number of variants of the library.



The random variable chain fragments are tested sequentially against clade B and non-clade B V3 loop. The amount of peptide is decreased each time to make the process more selective.

Results of library variant binding





ID	Pan #	Peptide	Sequence
WT			VTMSCKSSQSLLNSGDQKNYLTWYQQ
41	6	XB-->B	VTMSCKSSQSGPTTVERLLPLTWYQQ
72	6	XB-->B	VTMSCKSSQSVPSPPTRPRRLTWYQQ
73	6	XB-->B	VTMSCKSSQSYPFLPPRTQPLTWYQQ
85	6	XB-->B	VTMSCKSSQSAARPRHRPPALTWYQQ
86	6	XB-->B	VTMSCKSSQSSPSVSLLLRALTWYQQ
95	6	XB-->B	VTMSCKSSQSPPWQPAPQAALTWYQQ
98	6	XB-->B	VTMSCKSSQSPPPRPLLQPTLTWYQQ

Phage variants were tested for clade B and non-clade B V3 loop binding using ELISA. Those colonies that bound well were sequenced to determine the amino acid sequence.

Conclusion

- This technique did yield single chain variable fragments of antibodies that seem to bind better than the wild-type KD-247 to non-clade B.
- Neutralization and other CDR regions should be tested.

Acknowledgments

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