Targeting HIV Entry with Broadly Neutralizing Antibodies

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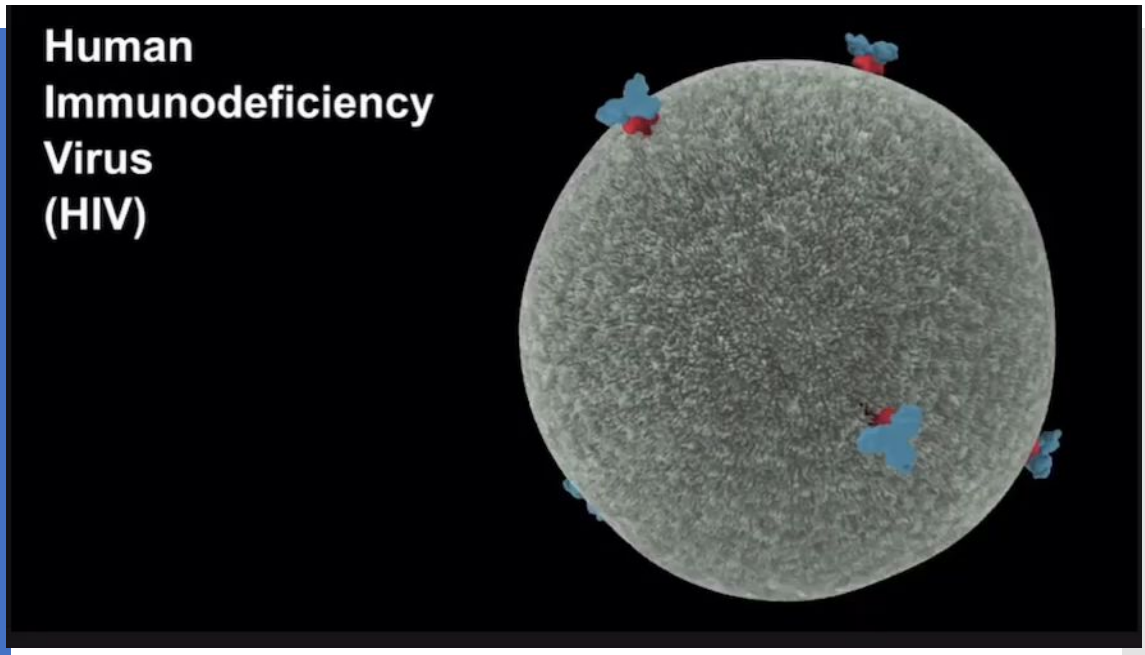
Broadly Neutralizing Antibodies (bNAbs)

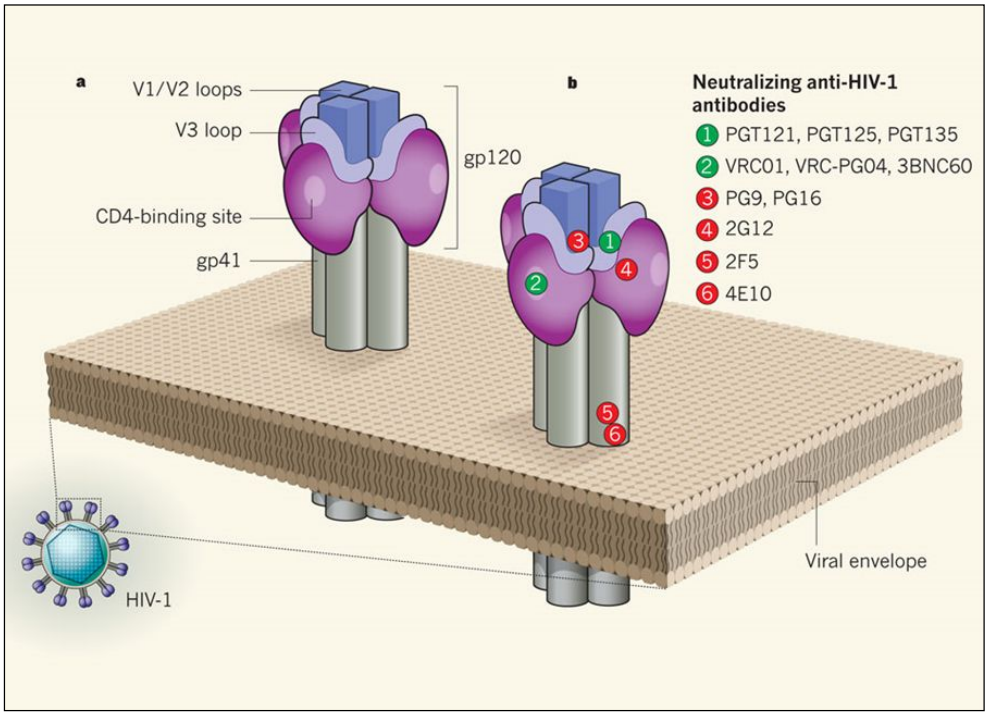
- bNAbs neutralize diverse strains of HIV-1 by targeting different epitopes in the envelope of the virus and combination of bNAbs targeting nonoverlapping epitopes display synergy
- bNAbs have the potential to kill HIV-1-infected cells and to affect the course of HIV-1 infection by directly engaging in the host immunity (activate other immune cells to help destroy HIV-infected cells)
- bNAbs demonstrate important features such as a longer half-life, excellent safety, and engaging host immunity response.
- bNAbs can reduce viral loads and plasma viremia, maintain viral suppression, and control a viral rebound

HIV: Attachment & Fusion



Source: http://scienceofhiv.org/

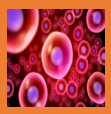
Gp120 is a Key Target for HIV Neutralization



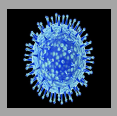
Koff WC. Vaccine. 2012 Jun 19;30(29):4310-5.

Hypothesis

Our bNAbs have a broad antiviral spectrum against HIV-1



293T cells were transfected with ten different full-length Transmitted/Founder (T/F) HIV-1 infectious molecular clones (clades B and C) using Lipofectamine 2000

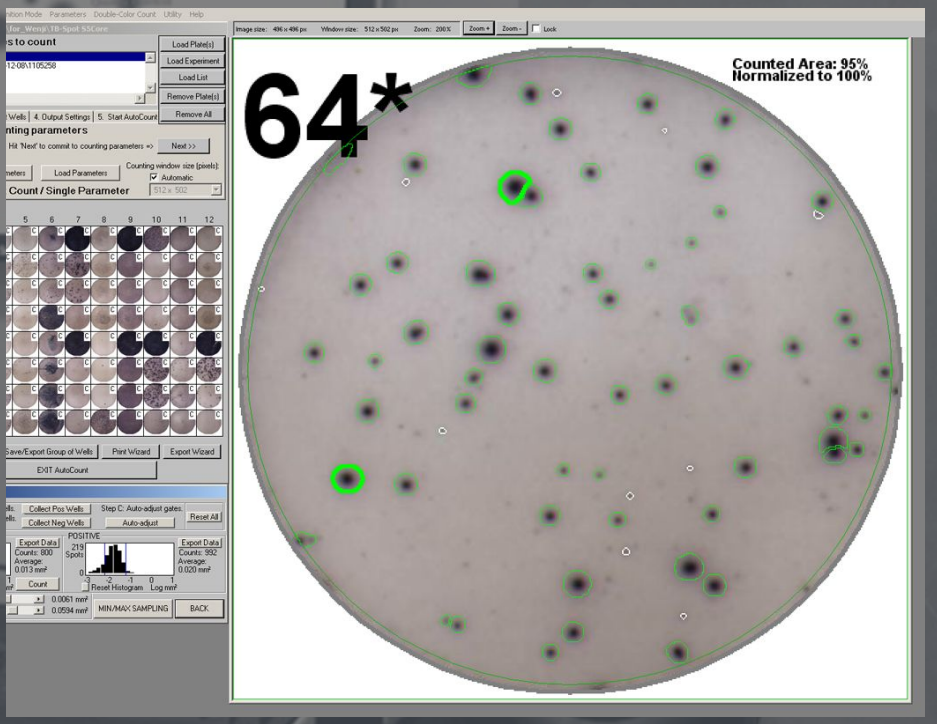


HIV-1 T/F viruses were harvested from the 293T cells supernatant 72 hours after transfection and tittered using the TZM-bl assay

XTT assay was used to test cytotoxicity (CC_{50}, half-maximal toxic concentration) while the TZM-bl assay (using C.T.L. Immunospot) was used to determine antiviral activity (EC_{50}, half-maximal inhibitory concentration)

CC_{50} and EC_{50} values were calculated using a dose–response–inhibition analysis on GraphPad Prism v8.3.1 software

C.T.L. Immunospot to Count Infected Cells



Viruses	EC_{50} nM (95% CI)		
	*hIgG1 Control	§ hIgG1-A	† hIgG1-B
11740	>140.6	>20.6	>20.6
11742	>140.6	0.3 (0.17 to 0.85)	0.25 (0.08 to 0.85)
11743	>140.6	4.5 (2.6 to 8.6)	0.08 (0.04 to 0.3)
11745	>140.6	2.9 (0.85 to 10.3)	0.43 (0.08 to 2.40)
11747	>140.6	6.7 (2.9 to 18.6)	1.3 (0.9 to 1.8)
11748	>140.6	2.0 (0.9 to 4.4)	2.3 (0.7 to 7.03)
11856	>140.6	0.3 (0.08 to 0.9)	0.08 (0.02 to 0.26)
12649	>140.6	1.3 (0.43 to 3.4)	0.43 (0.08 to 0.85)
13262	>140.6	1.8 (1.0 to 3.5)	0.43 (0.17 to 1.02)
13277	>140.6	~20.6	14.6 (3.4 to 27.4)

*CC_{50} > 140.6 nM; §CC_{50} > 20.6 nM; †CC_{50} > 20.6 nM.

Both bNAbs Show Broad Anti-HIV-1 Spectrum

Conclusions & Future Steps

hIgG1B is more potent than hIgG1A (mean EC_{50} of 0.43 nM versus 2nM)

Both bNAbs have similar broad spectrum (9 out of 10 HIV-1 T/F viruses were inhibited)

Additional preclinical studies need to explore the potential of these molecules to prevent/treat HIV infection

Acknowledgments

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