

# Broadly Neutralizing HIV-1 Antibody Reactivity in Diagnostic Tests: Implications for Screening

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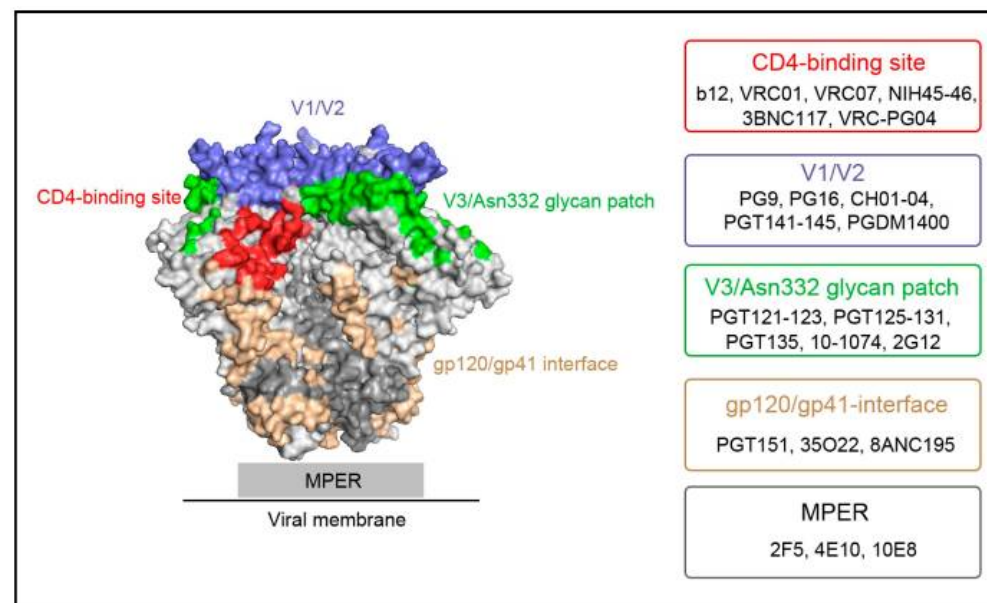
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## Background

### Broadly Neutralizing HIV-1 Antibodies for Prevention

- Passive immunization with long-acting broadly neutralizing antibodies (bNABs) is a novel strategy for HIV prevention
  - Target gp120 (CD4-binding site, V1-V2 and V3 loops) and gp41, two envelope antigens commonly present in diagnostics tests

#### Envelope binding sites for HIV-1 bNABs\*



\*Zhang Z et al Int J Mol Sci 2016

- Possible HIV-1 treatment alternative in cases of multi-drug resistance or ART intolerance or as use as PrEP or PEP
- Depending on bNAb type and dose administered to humans, serum levels can reach ~1 mg/ml and persist for several weeks to months
  - Concentrations as low as 0.08 - 65 µg/ml in serum have been shown to provide protection against SHIV infection, depending on bNAb type
- Most HIV serologic tests contain antigens derived from the HIV envelope

## Objective

We investigated the reactivity of bNABs in several screening and supplemental HIV tests to better inform diagnostic testing during the clinical development of bNABs for prevention.

## Methods

bNABs were acquired from the NIH AIDS Reagent Program:

- Target gp120**
  - VRC01
  - PGT121
  - PGT145
  - 3BNC117
  - 10-1074
  - N6
- Target gp41**
  - 10E8
  - 10E8v4

- bNABs were diluted in phosphate-buffered solution (PBS) pH 7.4 to 1 mg/mL if necessary
  - If reactive at 1 mg/mL, bNAb was diluted to 100 µg/ml or less to estimate minimum concentration detected by the HIV test
    - As SureCheck displayed strong reactivity we further diluted the bNABs to determine their limit of detection in that test
- PBS was used to evaluate reactivity of bNABs with each single-use rapid test to exclude reactivity of blood IgG against the control line

bNABs were tested with the following:

- Screening assays
  - Bio-Rad GS HIV Combo Ag/Ab assay (BRC)
  - Alere Determine HIV 1/2 Ag/Ab Combo test (DC)
  - OraQuick Advance Rapid HIV-1/2 Antibody test (OQ)
  - Medmira Reveal G4 Rapid HIV-1 antibody test (G4)
  - Chembio SURE CHECK HIV 1/2 Assay (SureCheck)
  - Trinity Biotech Uni-Gold Recombigen HIV-1/2 test (Uni-Gold)
  - INSTI HIV-1/2 rapid antibody test (INSTI)
  - Chembio DPP HIV 1/2 Assay (DPP)
- Supplemental assays
  - Bio-Rad Geenius HIV 1/2 Supplemental assay (Geenius)
  - Bio-Rad HIV-1 Western Blot (WB)

## Results

Table 1 shows the results of bNABs at 1 mg/mL, the highest concentration tested, on the HIV tests evaluated

- There was no correlation between the capturing antigen component of the test and bNAb reactivity
- At 100 µg/ml, all bNABs were OQ-non-reactive and yielded no control line reactivity (“invalid”) with G4 and INSTI
- All Geenius HIV-1 indeterminate were gp160 reactive
- The HIV-1 WB positive were gp41/gp160 reactive

	BRC	DC	OQ	G4	SureCheck	Uni-Gold	INSTI	DPP	Geenius	WB
HIV Ags in test	gp160 HIV-2 env	gp41	gp41	gp41 gp120	gp41 gp120	gp41 gp120	gp41 part of gp120	gp41, gp120, gp36	p24, p31, gp41, gp120	gp160, gp120, p65, p55, gp41, p40, p31, p24, p18
VRC01	NR	NR	NR	NR	NR	NR	invalid	NR	HIV-1 IND	Negative
PGT121	NR	NR	NR	R	NR	NR	invalid	NR	Negative	Negative
3BNC117	NR	NR	R	NR	R	NR	invalid	NR	HIV-1 IND	Negative
PGT145	NR	NR	NR	NR	invalid*	NR	invalid	NR	HIV-1 IND	Negative
10-1074	NR	NR	R	NR	R	NR	invalid	NR	HIV-1 IND	Negative
N6	NR	NR	NR	NR	R	NR	R	NR	HIV-1 IND	Negative
10E8	NR	NR	R	R	R	NR	NR	NR	HIV-1 IND	Positive
10E8v4	NR	NR	R	NR	R	NR	NR	NR	HIV-1 IND	Positive

**Table 1.** Test results including targeted epitope for each test. Uni-Gold and DC showed control line reactivity with PBS alone. Ags = antigens, NR = Nonreactive, R = Reactive, IND = Indeterminate. \*Test line was very reactive while nonreactive for the control line.

## Results

**Table 2.** SureCheck reactivity to diluted bNABs.

	1 mg/mL		0.5 mg/mL		0.25 mg/mL		0.125 mg/mL		0.0625 mg/mL	
	CTL	Test	CTL	Test	CTL	Test	CTL	Test	CTL	Test
PGT145	NR	RR	NR	RR	NR	RR	NR	RR	NR	NR
3BNC117	R	R	NR	NR						
10-1074	R	R	R	NR						
N6	R	R	R	R	R	NR				
10E8	R	R	R	R	R	R	NR	NR		
10E8v4	R	R	R	R	NR	NR				

- Three anti-gp120 and two anti-gp41 bNABs were reactive at 1 mg/mL on SureCheck
  - The lowest concentration detected was 0.25 mg/mL with 10E8
- PGT145 was strongly reactive on the antigen-specific line on SureCheck (RR), but it did not bind to the anti-IgG control line (CTL)

## Conclusions

- The widely used screening tests BRC, DC, Uni-gold, and DPP were nonreactive against bNABs, supporting their use to distinguish individuals with true HIV-1 infection from those who have received immunoprophylaxis
- The documented reactivity by some bNABs did not follow any predicted pattern
- Results highlighted the need to establish an appropriate diagnostic strategy to identify HIV infection prior to the clinical use of bNABs

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