

HIV-1 Antibody Detection in High Risk Populations Using a Highly Sensitive ELISA with HIV-1 Viral Lysate, Supplemental Envelope Proteins, and Group O Synthetic Peptide for the Solid Phase

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ABSTRACT

Background: Detection of HIV-1 antibodies in individuals at risk for infection remains an important element in understanding evolving epidemiological trends. This study evaluated the utility of a new, highly sensitive ELISA for HIV-1 antibody detection in several at-risk populations.

Methods: Sensitivity of the Vironostika® HIV-1 Plus O Microelisa System (HIVOTEK) was enhanced over the current FDA licensed assay with inclusion of purified viral envelope proteins and a synthetic peptide from an HIV-1 Group O isolate. Assay analytical sensitivity was determined by testing 12 commercially available HIV-1 seroconversion panels and 10 terminal dilution panels. Serum specimens from at-risk individuals from four populations (prison inmates, an HIV outreach clinic, STD clinic, and inner city emergency room) were tested with HIVOTEK and an FDA licensed assay.

Results: With all seroconversion panels tested, the HIVOTEK assay reported a reactive result on average 8 days prior to the FDA licensed assay based on specimen collection interval. In terminal dilution studies, the HIVOTEK assay was found to be 26 times more sensitive than the current assay. Of 1,500 high-risk individuals tested, 116 specimens were reactive with both assays and were confirmed positive by Western blot. The HIVOTEK assay detected an additional 3 specimens, all indeterminate by Western blot with specific glycoprotein bands and one with an IFA positive result.

Conclusion: The improved analytical sensitivity of the HIVOTEK assay should enable earlier detection of HIV-1 antibodies in populations at-risk for acquisition of HIV infection.

INTRODUCTION

Evolution and recombination of HIV-1 has resulted in subtype variants of the main group (Clades A through J) and in localized groups, for example Group O. In vitro recognition of HIV-1 antibodies directed against these different viral variants requires presentation of conserved viral epitopes, which is most efficaciously achieved by incorporating HIV-1 viral lysate as a component of the solid capture phase. Supplementation of the viral lysate with a Group O peptide should enable detection of antibodies from this virus group without affecting sensitivity for detection of other HIV-1 variants.

OBJECTIVE

Evaluate the utility of a new 96 well microelisa plate format, Vironostika® HIV-1 Plus O Microelisa System (HIVOTEK), for HIV-1 antibody detection in at-risk populations.

METHODOLOGY

- Testing performed with HIVOTEK and with current FDA licensed Vironostika® HIV-1 Microelisa System (VirHiV)
- **Analytical Sensitivity:** each member of 12 commercial HIV-1 seroconversion panels (NABI and Boston Biomedica) tested in triplicate and 10 terminal dilution panels from HIV-1 infected individuals tested in duplicate.
- **Clinical Sensitivity:** serum specimens from at-risk individuals from four populations (prison inmates, an HIV outreach clinic, STD clinic, and inner city emergency room) tested using standard CDC algorithm. Repeat reactive specimens confirmed with Western blot.

RESULTS

Table 1 Seroconversion Panels

Seroconversion Panel	First Day Reactive In the Series*		Days Improvement in First Detection with HIVOTEK
	HIVOTEK	VirHiV	
PRB924	33	40	7
PRB927	33	40	7
PRB931	28	33	5
PRB932	34	NR	
PRB940	15	29	14
SV-0071	17	22	5
SV-0111	8	16	8
SV-0241	15	22	7
SV-0321	15	28	13
SV-0341	21	28	7
SV-0351	15	NR	
SV-0361	18	NR	
NR = non-reactive			MEAN = 8 Days

Table 2 Terminal Dilution Panels

Panel	Dilution with Last Reactivity	
	VirHiV	HIVOTEK
5805	1:240	1:1,920
H629	1:8,000	1:64,000
MD-O*	1:400	1:51,200
302-1	<1:50	1:64,000
301-42	1:1,600	1:12,800
302-18	1:1,500	1:12,000
301-24	1:3,000	1:48,000
302-23	1:1,500	1:48,000
302-28	1:1,600	1:12,800
302-17	1:250	1:4,000
Sensitivity Increase Factor, mean		25.8

*HIV-1 Group O

CONCLUSIONS

- HIVOTEK has improved analytical sensitivity over the current licensed FDA HIV-1 antibody comparator test, Vironostika® HIV-1 Microelisa System.
- In high risk populations, the enhanced sensitivity of the HIVOTEK assay resulted in increased detection of glycoprotein specific antibodies.
- The improved analytical sensitivity of the HIVOTEK assay should enable earlier detection of HIV-1 antibodies in populations at risk for acquisition of HIV infection.

Table 3 High Risk Populations

Population	N	HIVOTEK		VirHiV		Western blot
		Initial Reactive	Repeat Reactive	Initial Reactive	Repeat Reactive	
STD Clinic, Houston, TX	251	16 (6.4%)	11 (4.4%)	9 (3.6%)	8 (3.2%)	8 (3.2%)
Colorado Dept. of Corrections, Canon City, CO	513	13 (2.5%)	13 (2.5%)	21 (4.1%)	13 (2.5%)	13 (2.5%)
City Emergency Room Baltimore, MD [†]	500	73 (14.6%)	68 (13.6%)	68 (13.6%)	68 (13.6%)	68 (13.6%)
Outreach Clinic, West Hollywood, CA	250	28 (11.2%)	27 (10.8%)	27 (10.8%)	27 (10.8%)	27 (10.8%)
Totals	1,514	130 (8.6%)	119 (7.9%)	125 (8.3%)	116 (7.7%)	116 (7.7%)

Table 4 High Risk Populations: Analysis of 6 Discordant Specimens

Specimen	HIVOTEK, SCR [†]	VirHiV, SCR [†]	IFA Interpretation	Western blot Interpretation
	Duplicate Repeat Testing	Duplicate Repeat Testing		
1.	4:2; 4:2	0.7; 0.8	Reactive	IND-gp120
2.	1.0 bdr; 1:2	0.6; 0.6	Non-reactive	IND-gp160
3.	2:3; 2:4	0.4; 0.4	Non-reactive	IND-70 kD

SCR = signal to cut-off ratio; nr = borderline non-reactive within 20% of the assay cut-off; bdr = borderline reactive within 20% of the assay cut-off

Western blot Interpretation: IND = Indeterminate (with bands shown); N/A = Not Applicable