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Potent Neutralization Activity against a Primary Viral Isolate

Author(s): Narayan, KM (Narayan, Kristin M.)[1,2] ; Agrawal, N (Agrawal, Nitish)[3] ; Du, SX (Du, Sean X.)[1,2] ; Muranaka, JE (Muranaka, Janelle E.)[1,2] ; Bauer, K (Bauer, Katherine)[3] ; Leaman, DP (Leaman, Daniel P.)[3] ; Phung, P (Pham Phung)[4] ; Limoli, K (Limoli, Kay)[4] ; Chen, HL (Chen, Helen)[1] ; Boenig, RI (Boenig, Rebecca I.)[1,2] ; Wrin, T (Wrin, Terri)[4] ; Zwick, MB (Zwick, Michael B.)[3] ; Whalen, RG (Whalen, Robert G.)[1,2]

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Abstract: Development of a vaccine for HIV-1 requires a detailed understanding of the neutralizing antibody responses that can be experimentally elicited to difficult-to-neutralize primary isolates.

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
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Rabbits were immunized with the gp120 subunit of HIV-1 JR-CSF envelope (Env) using a DNA-prime protein-boost regimen. We analyzed five sera that showed potent autologous neutralizing activity (IC50s at similar to 10(3) to 10(4) serum dilution) against pseudoviruses containing Env from the primary isolate JR-CSF but not from the related isolate JR-FL. Pseudoviruses were created by exchanging each variable and constant domain of JR-CSF gp120 with that of JR-FL or with mutations in putative N-glycosylation sites. The sera contained different neutralizing activities dependent on C3 and V5, C3 and V4, or V4 regions located on the glycan-rich outer domain of gp120. All sera showed enhanced neutralizing activity toward an Env variant that lacked a glycosylation site in V4. The JR-CSF gp120 epitopes recognized by the sera are generally distinct from those of several well characterized mAbs (targeting conserved sites on Env) or other type-specific responses (targeting V1, V2, or V3 variable regions). The activity of one serum requires specific glycans that are also important for 2G12 neutralization and this serum blocked the binding of 2G12 to gp120. Our findings show that different fine specificities can achieve potent neutralization of HIV-1, yet this strong activity does not result in improved breadth.


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Reprint Address: Zwick, MB (reprint author)


 Scripps Res Inst, Dept Immunol & Microbial Sci, La Jolla, CA 92037 USA.

Organization-Enhanced Name(s)
Scripps Research Institute

Addresses:

[1] Maxygen Inc, Dept Infect Dis, Redwood City, CA USA

[2] Altravax Inc, Sunnyvale, CA USA

 [3] Scripps Res Inst, Dept Immunol & Microbial Sci, La Jolla,

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Organization-Enhanced Name(s)
Scripps Research Institute

[4] Monogram Biosci Inc, San Francisco, CA USA

E-mail Addresses: zwick@scripps.edu;
robert.whalen@altravax.com

Author Identifiers: Author Identifiers:

Author	ResearcherID Number [?]	ORCID Number [?]
AGRAWAL, NITISH	E-3468-2013 [View profile at ResearcherID.com]	
AGRAWAL, NITISH	H-6186-2011 [View profile at ResearcherID.com]	0000-0003-0823- 7355 [View profile at Orcid.org]

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