HIV: Current Research

Extended Abstract

# Conformational Epitope-Specific Broadly Neutralizing Plasma Antibodies Obtained from an HIV-1 Clade C-Infected Elite Neutralizer Mediate Autologous Virus Escape through Mutations in the V1 Loop

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## Abstract

Broadly neutralizing antibodies isolated from infected patients who are elite neutralizers have identified targets on HIV-1 envelope (Env) glycoprotein that are vulnerable to antibody neutralization; however, it is not known whether infection established by the majority of the circulating clade C strains in Indian patients elicit neutralizing antibody responses against any of the known targets. In the present study, we examined the specificity of a broad and potent cross-neutralizing plasma obtained from an Indian elite neutralizer infected with HIV-1 clade C. This plasma neutralized 53/57 (93%) HIV pseudoviruses prepared with Env from distinct HIV clades of different geographical origins. Mapping studies using gp120 core protein, single-residue knockout mutants, and chimeric viruses revealed that G37080 broadly cross-neutralizing (BCN) plasma lacks specificities to the CD4 binding site, gp41 membrane-proximal external region, N160 and N332 glycans, and R166 and K169 in the V1-V3 region and are known predominant targets for BCN antibodies. Depletion of G37080 plasma with soluble trimeric BG505-SOSIP.664 Env (but with neither monomeric gp120 nor clade C membrane-proximal external region peptides) resulted in significant reduction of virus neutralization, suggesting that G37080 BCN antibodies mainly target epitopes on cleaved trimeric Env. Further examination of autologous circulating Envs revealed the association of mutation of residues in the V1 loop that contributed to neutralization resistance. In summary, we report the identification of plasma antibodies from a clade C-infected elite neutralizer that mediate neutralization breadth via epitopes on trimeric gp120 not yet reported and confer autologous neutralization escape via mutation of residues in the V1 loop.

**IMPORTANCE:** A preventive vaccine to protect against HIV-1 is urgently needed. HIV-1 envelope glycoproteins are targets of neutralizing antibodies and represent a key component for immunogen design. The mapping of epitopes on viral envelopes vulnerable to immune evasion will aid in defining targets of vaccine immunogens. We identified novel conformational epitopes on the viral envelope targeted by broadly cross-neutralizing antibodies elicited in natural infection in an elite neutralizer infected with HIV-1 clade C. Our data extend our knowledge on neutralizing epitopes associated with virus escape and potentially contribute to immunogen design and antibody-based prophylactic therapy.

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