

## Search Antibody Database

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[MAB ID](#) 2557

[HXB2](#)  
[Location](#) Env

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[Location](#) Env( JR-CSF)

[Research](#)  
[Contact](#) Dr. Zolla-Pazner, Veterans Affairs Center, NY, NY.  
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[Epitope](#)

[Subtype](#) A, CRF02\_AG

[Ab Type](#) gp120 V3 // V3 glycan (V3g)

[Neutralizing](#) tier 1, tier 2 [View neutralization details](#)

[Species](#)  
[\(Isotype\)](#) human

[Patient](#)

[Immunogen](#) HIV-1 infection

[Keywords](#) antibody binding site, antibody generation, antibody lineage, antibody sequence, assay or method development, binding affinity, glycosylation, mimotopes, neutralization, structure, subtype comparisons, vaccine antigen design, vaccine-induced immune responses, variant cross-reactivity

### Notes

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- 2557: The authors selected an optimal panel of diverse HIV-1 envelope glycoproteins to represent the antigenic diversity of HIV globally in order to be used as antigen

candidates. The selection was based on genetic and geographic diversity, and experimentally and computationally evaluated humoral responses. The eligibility of the envelopes as vaccine candidates was evaluated against a panel of antibodies for breadth, affinity, binding and durability of vaccine-elicited responses. The antigen panel was capable of detecting the spectrum of V2-specific antibodies that target epitopes from the V2 strand C (V2p), the integrin binding motif in V2 (V2i), and the quaternary epitope at the apex of the trimer (V2q). [Yates2018](#) (vaccine antigen design, vaccine-induced immune responses, binding affinity)

- 2557: The study compared various factors affecting the accessibility of epitopes for antibodies targeting the V2 integrin (V2i) region, versus the V3 region. CD4 treatment of BaL and JRFL pseudoviruses increased their neutralization sensitivity to V3 MAbs, but not to V2i MAbs. Viruses grown in a glycosidase inhibitor were more sensitive to neutralization by V3, but not V2i, MAbs. Increasing the time of virus-MAb interaction increased virus neutralization by some V2i MAbs and all V3 MAbs. The structural dynamics of V2i and V3 epitopes has important effects in neutralization. The V3 MAbs tested were: 447, 2219, and 2557. [Upadhyay2014](#) (glycosylation, neutralization)
- 2557: Neutralizing and binding activity of 18 anti-V3 MAbs from Cameroonian and Indian patients were compared. The Cameroonian patients had CRF01\_AG (Env corresponding to clade A) and Indian patients had clade C. MAbs from Cameroonian patients were significantly more cross-neutralizing than those from India, suggesting the preference for CRF02\_AG for vaccine design. This MAb was from patient from Cameroon and the subtype of the infecting virus was CRF02\_AG. [Andrabi2013](#) (neutralization)
- 2557: Signature motifs specific for neutralization epitopes present in the V3 loop crown were used to determine the presence or absence of MAb-specific epitopes in vaccine immunogens and in break-through viruses infecting vaccine and placebo recipients in the VAX003 and VAX004 Phase III clinical trials. Of the six epitopes present in the immunogens and targeted by known NAb, only the one targeted by anti-V3 NAb 2219 exhibited a significant reduction in occurrence in vaccinated subjects from VAX003 Thailand cohort compared to the placebo group. The signature motif used for MAb 2557 is K10, [I,V]12, [Y,F]21 in V3-loop position numbers. [Shmelkov2011](#) (vaccine-induced immune responses)
- 2557: VH5-51 gene segment was used by 18 of 51 (35%) anti-V3 MAbs. This study analyzed the crystal structure of 5 Fabs encoded by VH5-51/VL lambda genes. Each Fab interacted with key residues at the same 7 positions in the crown of the V3 loop, although the amino acids could vary, suggesting that while V3 is variable in sequence and structurally flexible, a common structure is retained across strains. MAb 2557 interacted with amino acids K304, K305, I307, A308, I309, L317, Y318 of MN V3 peptide. Most of MAb 2557 contact residues were also present at the corresponding positions of the germline VH5-51 gene. All 18 VH5-51 using MAbs were studied with a constrained peptide mimotope which preserved the 3D of the VH5-51 derived MAbs 2219, 2557, 1006, but did not react with other anti-V3 MAbs that recognize different V3 epitopes. 14/18 (1006 included) were reactive with the mimotope, compared to only 1/30 non-VH5-51 MAbs. [Gorny2011](#) (mimotopes, antibody sequence, structure, antibody lineage)

- 2557: Masking signatures were developed and analyzed for 4 anti-HIV V3 loop MABs, 2219, 3074, 2557, 447-52D. The epitopes were classified as "masked" if their signature motifs were present in a virus, but there was no detectable neutralization by the MAb of the same virus in vitro. The signature motif for MAb 2219 used in the study was R9+K10+[L,V]12+[Y,F]21. Of the 4 MABs, 2219 neutralized the largest number of pseudoviruses containing its epitope. The 2219 neutralization epitope is unmasked in 25/68 (36.8%) of the viruses containing the 2219 epitope. [Agarwal2011](#) (neutralization)
- 2557: Structure of 2557 bound to a peptide containing the sequence of the V3 loop was used to derive sensitive and specific signature motifs for its neutralization epitope. 2557 epitope ( $^{10}\text{Kx}[\text{I},\text{V}]xxxxxxx\text{Y}^{21}$ ) was found conserved in 52% of circulating HIV-1 strains belonging to all major subtypes. 2557 neutralized 18% of subtype A pseudovirions, 47% of subtype B, 21% of subtype C, 10% of subtype D and 100% of CRF02\_AG. [Swetnam2010](#) (antibody binding site, neutralization, variant cross-reactivity, subtype comparisons, structure)
- 2557: 2557 neutralizing activity was assessed against pseudoviruses expressing Envs of diverse HIV-1 subtypes from subjects with acute and chronic infection. IC50 neutralization activity was also statistically assessed based on the area under the neutralization curves (AUC). 2557 was able to neutralize 5/57 viruses in U87-based assay and 13/41 viruses in TZM-based assay, including Tier 1 and Tier 2 viruses, viruses of subtypes B, C, D, AG, and viruses from both chronic and acute infections. AUC analysis revealed that 22/57 viruses in the U87-based assay, and 12/41 viruses in the TZM-based assay, were significantly neutralized by this Ab. Thus, the AUC method has the ability to detect low levels of neutralizing activity that otherwise may be missed. [Hioe2010](#) (assay or method development, neutralization, variant cross-reactivity)
- 2557: Two V3-scaffold immunogen constructs were designed and expressed using 3D structures of cholera toxin B (CTB), V3 in the gp120 context, and V3 bound to 447-52D MAB. The construct (V3-CTB) presenting the complete V3 was recognized by 2557 MAB and by the large majority of other MABs (18/24), indicating correctly folded and exposed MAB epitopes. V3-CTB induced V3-binding Abs and Abs displaying cross-clade neutralizing activity in immunized rabbits. Short V3-CTB construct, presenting a V3 fragment in conformation observed in complex with 447-52D, was recognized by 2557 and by 9/24 other MABs. [Totrov2010](#) (vaccine antigen design, binding affinity, structure)
- 2557: Crystal structures of 2557 Fab in complex with different V3 peptides revealed that 2557 interactions can be divided into three regions: the arch, the circlet, and the band. 2557 CDR L3 was unusually long (19 residues), but it pointed away from the V3 binding site. Crystal analyses of 2219 and 1006-15D Ab-V3 complexes revealed that they interact with V3 in similar manner as 2557, indicating that these Abs recognize V3 using similar modes of binding. It is shown that broadly-reactive Abs can bind to conserved elements in four regions of the V3: the arch, the circlet, the band, and the V3 peptide main chain backbone. These conserved elements are either unaffected by or are subjected to minimal sequence variation. A mimotope that preserved the key structural elements in the circlet and band regions, but with GPG of the arch replaced by a disulfide bond, interacted with broadly reactive MABs 2557, 1006 and 2219. It did not react with 447-

52D nor 268-D, which are dependent on the Arg in the arch. Thus, mimotopes can be constructed that may focus the immune response on structurally conserved elements.

[Jiang2010](#) (antibody binding site, mimotopes, structure)

- 2557: The Ig usage for variable heavy chain of this Ab was as follows:IGHV:5-51\*01,IGHD:3-22, D-RF:2, IGHJ:3. There was a preferential usage of the VH5-51 gene segment for V3 Abs. The usage of the VH4 family for the V3 Abs was restricted to only one gene segment, VH4-59, and the VH3 gene family was used at a significantly lower level by these Abs. The V3 Abs preferentially used the JH3 and D2-15 gene segments. [Gorny2009](#) (antibody sequence)
- 2557: This Ab was shown to neutralize SF162 and the neutralization sensitivity increased in the SF162 variant with a JR-FL V3 loop, SF162(JR-FL V3). In contrast, a great reduction in sensitivity to neutralization was observed in the SF162(JR-FL V1/V2) variant and was somewhat restored in the SF162(JR-FL V1/V2/V3) variant, indicating that the masking of the V1/V2 loop plays a much greater role in restricting neutralization sensitivity than the variations in V3. This Ab was shown to neutralize viruses with V3 sequences from several different subtypes (B, F, A1, H, C, CRF02\_AG and CRF01\_AE). This Ab failed to neutralize SF162(JR-FL V1/V2) with V3 derived from different HIV-1 clades except A1, indicating effective V1/V2-mediated masking of several HIV-1 clades. The effect on the neutralization sensitivity of the residue at the crown of the V3 loop (position 18) was shown to be low for this Ab. [Krachmarov2006](#) (neutralization, variant cross-reactivity, subtype comparisons)
- 2557: This MAb was derived from plasma from a patient with env clade A virus with the GPGQ V3 motif. When cross-reactivity was tested, this Ab bound to both the V3subtypeB-fusion protein containing GPGR motif and V3subtypeA-fusion protein containing GPGQ motif. This Ab was also shown to be able to neutralize both clade B psSF162 (GPGR) and clade C psMW965 (GPGQ) virus and the majority of subtype B and non-B primary isolates. [Gorny2006](#) (neutralization, variant cross-reactivity, binding affinity, subtype comparisons)
- 2557: Sera from subtype A infected individuals from Cameroon have antibodies that react strongly with subtype A and subtype B V3 loops in fusion proteins, and neutralize SF162 pseudotypes, while sera from 47 subtype B infected individuals reacted only with subtype B V3s. Sera from Cameroon did not neutralize primary A or B isolates, due to indirect masking by the V1/V2 domain rather than due to loss of the target epitope. 2557 was derived from a person infected with a clade A or CRF02 virus, and binds to A and B V3 loops. Neutralization of JR-FL and SF162(UG V3) by anti-V3 MAbs 2557, 2558, 2601, but not subtype A primary isolates despite binding to the subtype A V3 loops, suggested masking by V1V2 blocking of neutralization by these antibodies. [Krachmarov2005](#) (antibody binding site, variant cross-reactivity, subtype comparisons)
- 2557: MAbs 2557 and 2558 were produced from individuals who were infected with the CRF02AG virus subtype and living in Cameroon. V3 MAb neutralization is influenced by retaining the epitope, exposure on the intact virion, mobility during CD4-induced conformational change, and affinity. Anti-V3 MAbs selected using V3 peptides neutralize less effectively than V3 MAbs selected using fusion proteins or gp120, suggesting

antigenic conformation is important. This antibody was selected using a JRCSF fusion protein. [Gorny2004](#) (antibody generation)

## References

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### Isolation Paper

**Gorny2004** Mirosław K. Gorny, Kathy Revesz, Constance Williams, Barbara Volsky, Mark K. Louder, Christopher A. Anyangwe, Chavdar Krachmarov, Samuel C. Kayman, Abraham Pinter, Arthur Nadas, Phillipe N. Nyambi, John R. Mascola, and Susan Zolla-Pazner. The V3 Loop is Accessible on the Surface of Most Human Immunodeficiency Virus Type 1 Primary Isolates and Serves as a Neutralization Epitope. *J. Virol.*, 78(5):2394-2404, Mar 2004. PubMed ID: [14963135](#). [Show all entries for this paper.](#)

**Agarwal2011** Alpana Agarwal, Catarina E. Hioe, James Swetnam, Susan Zolla-Pazner, and Timothy Cardozo. Quantitative Assessment of Masking of Neutralization Epitopes in HIV-1. *Vaccine*, 29(39):6736-41, 9 Sep 2011. PubMed ID: [21216319](#). [Show all entries for this paper.](#)

**Andrabi2013** Raiees Andrabi, Constance Williams, Xiao-Hong Wang, Liuzhe Li, Alok K. Choudhary, Naveet Wig, Ashutosh Biswas, Kalpana Luthra, Arthur Nadas, Michael S. Seaman, Phillipe Nyambi, Susan Zolla-Pazner, and Mirosław K. Gorny. Cross-Neutralizing Activity of Human Anti-V3 Monoclonal Antibodies Derived from Non-B Clade HIV-1 Infected Individuals. *Virology*, 439(2):81-88, 10 May 2013. PubMed ID: [23466102](#). [Show all entries for this paper.](#)

**Gorny2006** Mirosław K. Gorny, Constance Williams, Barbara Volsky, Kathy Revesz, Xiao-Hong Wang, Sherri Burda, Tetsuya Kimura, Frank A. J. Konings, Arthur Nadas, Christopher A. Anyangwe, Phillipe Nyambi, Chavdar Krachmarov, Abraham Pinter, and Susan Zolla-Pazner. Cross-Clade Neutralizing Activity of Human Anti-V3 Monoclonal Antibodies Derived from the Cells of Individuals Infected with Non-B Clades of Human Immunodeficiency Virus Type 1. *J. Virol.*, 80(14):6865-6872, Jul 2006. PubMed ID: [16809292](#). [Show all entries for this paper.](#)

**Gorny2009** Mirosław K. Gorny, Xiao-Hong Wang, Constance Williams, Barbara Volsky, Kathy Revesz, Bradley Witover, Sherri Burda, Mateusz Urbanski, Phillipe Nyambi, Chavdar Krachmarov, Abraham Pinter, Susan Zolla-Pazner, and Arthur Nadas. Preferential Use of the VH5-51 Gene Segment by the Human Immune Response to Code for Antibodies against the V3 Domain of HIV-1. *Mol. Immunol.*, 46(5):917-926, Feb 2009. PubMed ID: [18952295](#). [Show all entries for this paper.](#)

**Gorny2011** Mirosław K. Gorny, Jared Sampson, Huiguang Li, Xunqing Jiang, Maxim Totrov, Xiao-Hong Wang, Constance Williams, Timothy O'Neal, Barbara Volsky, Liuzhe Li, Timothy Cardozo, Phillipe Nyambi, Susan Zolla-Pazner, and Xiang-Peng Kong. Human Anti-V3 HIV-1 Monoclonal Antibodies Encoded by the VH5-51/VL Lambda Genes Define a Conserved Antigenic Structure. *PLoS One*, 6(12):e27780, 2011. PubMed ID: [22164215](#). [Show all entries for this paper.](#)

**Hioe2010** Catarina E. Hioe, Terri Wrin, Michael S. Seaman, Xuesong Yu, Blake Wood, Steve Self, Constance Williams, Mirosław K. Gorny, and Susan Zolla-Pazner. Anti-V3 Monoclonal Antibodies Display Broad Neutralizing Activities against Multiple HIV-1 Subtypes. *PLoS One*, 5(4):e10254, 2010. PubMed ID: [20421997](#). [Show all entries for this paper.](#)

**Jiang2010** Xunqing Jiang, Valicia Burke, Maxim Totrov, Constance Williams, Timothy Cardozo, Mirosław K. Gorny, Susan Zolla-Pazner, and Xiang-Peng Kong. Conserved Structural Elements in the V3 Crown of HIV-1 gp120. *Nat. Struct. Mol. Biol.*, 17(8):955-961, Aug 2010. PubMed ID: [20622876](#). [Show all entries for this paper.](#)

**Krachmarov2005** Chavdar Krachmarov, Abraham Pinter, William J. Honnen, Mirosław K. Gorny, Phillippe N. Nyambi, Susan Zolla-Pazner, and Samuel C. Kayman. Antibodies That Are Cross-Reactive for Human Immunodeficiency Virus Type 1 Clade A and Clade B V3 Domains Are Common in Patient Sera from Cameroon, but Their Neutralization Activity Is Usually Restricted by Epitope Masking. *J. Virol.*, 79(2):780-790, Jan 2005. PubMed ID: [15613306](#). [Show all entries for this paper.](#)

**Krachmarov2006** C. P. Krachmarov, W. J. Honnen, S. C. Kayman, M. K. Gorny, S. Zolla-Pazner, and Abraham Pinter. Factors Determining the Breadth and Potency of Neutralization by V3-Specific Human Monoclonal Antibodies Derived from Subjects Infected with Clade A or Clade B Strains of Human Immunodeficiency Virus Type 1. *J. Virol.*, 80(14):7127-7135, Jul 2006. PubMed ID: [16809318](#). [Show all entries for this paper.](#)

**Shmelkov2011** Evgeny Shmelkov, Arthur Nadas, James Swetnam, Susan Zolla-Pazner, and Timothy Cardozo. Indirect Detection of an Epitope-Specific Response to HIV-1 gp120 Immunization in Human Subjects. *PLoS One*, 6(11):e27279, 2011. PubMed ID: [22076145](#). [Show all entries for this paper.](#)

**Swetnam2010** James Swetnam, Evgeny Shmelkov, Susan Zolla-Pazner, and Timothy Cardozo. Comparative Magnitude of Cross-Strain Conservation of HIV Variable Loop Neutralization Epitopes. *PLoS One*, 5(12):e15994, 2010. PubMed ID: [21209919](#). [Show all entries for this paper.](#)

**Totrov2010** Maxim Totrov, Xunqing Jiang, Xiang-Peng Kong, Sandra Cohen, Chavdar Krachmarov, Aidy Salomon, Constance Williams, Michael S. Seaman, Ruben Abagyan, Timothy Cardozo, Mirosław K. Gorny, Shixia Wang, Shan Lu, Abraham Pinter, and Susan Zolla-Pazner. Structure-Guided Design and Immunological Characterization of Immunogens Presenting the HIV-1 gp120 V3 Loop on a CTB Scaffold. *Virology*, 405(2):513-523, 30 Sep 2010. PubMed ID: [20663531](#). [Show all entries for this paper.](#)

**Upadhyay2014** Chitra Upadhyay, Luzia M. Mayr, Jing Zhang, Rajnish Kumar, Mirosław K. Gorny, Arthur Nadas, Susan Zolla-Pazner, and Catarina E. Hioe. Distinct Mechanisms Regulate Exposure of Neutralizing Epitopes in the V2 and V3 Loops of HIV-1 Envelope. *J. Virol.*, 88(21):12853-12865, Nov 2014. PubMed ID: [25165106](#). [Show all entries for this paper.](#)

**Yates2018** Nicole L. Yates, Allan C. deCamp, Bette T. Korber, Hua-Xin Liao, Carmela Irene, Abraham Pinter, James Peacock, Linda J. Harris, Sheetal Sawant, Peter Hraber, Xiaoying Shen,

Supachai Rerks-Ngarm, Punnee Pitisuttithum, Sorachai Nitayapan, Phillip W. Berman, Merlin L. Robb, Giuseppe Pantaleo, Susan Zolla-Pazner, Barton F. Haynes, S. Munir Alam, David C. Montefiori, and Georgia D. Tomaras. HIV-1 Envelope Glycoproteins from Diverse Clades Differentiate Antibody Responses and Durability among Vaccinees. *J. Virol.*, 92(8), 15 Apr 2018. PubMed ID: [29386288](#). [Show all entries for this paper.](#)

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