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2095, 1994. (Medline: 94322004) Notes: BALB/c mice were immunized with baculovirus expressed gp160 or gp120, and 15 MAbs were generated. No MAbs generated in this study neutralized reference strains, using a tetrazolium-based cytotoxicity assay to test for neutralization. Ten of the Mabs were mapped by peptide ELISA, and seven reacted with the C1 region, one with V2, one with V4, and one with the C-terminal end.

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from 5 ml of bone marrow from an asymptomatic individual who had been HIV-positive for 6 years. These Fab variable regions were sequenced and were found to be diverse. Binding constants were measured and the Fabs generally bound gp120 with high affinity. The methods used to obtain this panel could be used to obtain antibodies to test passive immunization as a therapy for AIDS.

[Burton & Montefiori(1997)] D. R. Burton & D. C. Montefiori. The antibody response in HIV-1 infection. *AIDS* **11 Suppl A**:S87–S98, 1997. (Medline: 98112351) Notes: An excellent review of Ab epitopes and the implications for Envelope structure, neutralization of HIV, the distinction between primary and TCLA strains, ADCC and its role in clearance, and the Ab response during the course of infection.

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In an immunotherapeutic study, administration of a single dose of F105 was non-toxic and the Ab persisted, yet no benefit was observed in 4 individuals. The authors suggest it may be more helpful in other settings, for example, patients with no pre-existing anti-CD4 BS Abs, or in combination with other MAbs.

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monoclonal antibodies produced in each case, were analyzed. The free gp120 and gp120-CD4 complex immunogens stimulated responses were directed mainly toward conformational epitopes, but gp120 immunocomplexed with MAb M77 also produced numerous and varied MAbs directed toward linear epitopes that were presumably inaccessible on the gp120, gp120-CD4 proteins.

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[Ditzel (1997)] H. J. Ditzel, P. W. Parren, J. M. Binley, J. Sodroski, J. P. Moore, C. F. B. 3rd, & D. R. Burton. Mapping the protein surface of human im-

munodeficiency virus type 1 gp120 using human monoclonal antibodies from phage display libraries. *J Mol Biol* **267**:684–95, 1997. (Medline: 97272001) Notes: , (Genbank: U82767 U82768 U82769 U82770 U82771 U82772 U82942 U82943 U82944 U82945 U82946 U82947 U82948 U82949 U82950 U82951 U82952 U82961 U82962) Recombinant monoclonal antibodies from phage display libraries provide a method for Env surface epitope mapping. Diverse epitopes are accessed by presenting gp120 to the library in different forms, such as sequential masking of epitopes with existing MAbs or sCD4 prior to selection or by selection on peptides. Fabs identified by these methods have specificities associated with epitopes presented poorly on native multimeric envelope.

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[Earl (1994)] P. L. Earl, C. C. Broder, D. Long, S. A. Lee, J. Peterson, S. Chakrabarti, R. W. Doms, & B. Moss. Native oligomeric human immunodeficiency virus type 1 Envelope glycoprotein elicits diverse monoclonal antibody reactivities. *J Virol* **68**:3015–3026, 1994. (Medline: 94202289) Notes: In a study of the repertoire of response to oligomeric versus monomeric Env protein, 138 murine MAbs were generated in response to an immunogen that was a gp120/bp41 oligomeric molecule that was not cleaved due

to a mutation in the cleavage site. The oligomeric molecule was found to elicit a response that was very different than the monomer. Most MAbs were conformational, many were to gp41 or if in gp120, to the CD4 BS. Few MAbs to linear V3 epitopes were produced in response to oligomeric protein, though this was a common specificity in response to immunization with gp120 monomeric protein.

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[Moore (1995a)] J. P. Moore, Y. Cao, L. Qing, Q. J. Sattentau, J. Pyati, R. Koduri, J. Robinson, C. F. Barbas III, D. R. Burton, & D. D. Ho. Primary isolates of human immunodeficiency virus type I are relatively resistant to neutralization by monoclonal antibodies to gp120, and their neutralization is not predicted by studies with monomeric gp120. *J Virol* **69**:101–109, 1995a. (Medline: 95074853) Notes: A panel of anti-gp120 MAbs and sera from HIV-1 infected individuals was tested for its ability to neutralize primary isolates. Most MAbs bound with high affinity to gp120 monomers from the various isolates, but were not effective at neutralizing. The MAb IgG1b12, which binds to a discontinuous anti-CD4 binding site epitope, was able to neutralize most of the primary isolates.

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J Virol **67**:863–875, 1993. (Medline: 93124581) Notes: CD4BS antibodies are prevalent in HIV-1-positive sera, while neutralizing MAbs to C4, V2, and V3 and MAbs to linear epitopes are less common. Most linear epitope MAbs in human sera are directed against the V3 region, and cross-reactive MAbs tend to be directed against discontinuous epitopes.

[Moore & Ho(1995)] J. P. Moore & D. D. Ho. HIV-1 neutralization: the consequences of adaptation to growth on transformed T-cells. *AIDS* **9 suppl A**:S117–S136, 1995. (Medline: 96416784) Notes: This review considers the relative importance of a neutralizing antibody response for the development of a vaccine, and for disease progression during the chronic phase of HIV-1 infection. It suggests that T-cell immunity may be more important. The distinction between MAbs that can neutralize primary isolates, and those that are effective at neutralizing only laboratory adapted strains is discussed in detail. Alternative conformations of envelope and non-contiguous interacting domains in gp120 are discussed. The suggestion that soluble monomeric gp120 may serve as a viral decoy that diverts the humoral immune response it in vivo is put forth.

[Moore (1994b)] J. P. Moore, F. E. McCutchan, S.-W. Poon, J. Mascola, J. Liu, Y. Cao, & D. D. Ho. Exploration of antigenic variation in gp120 from clades A through F of human immunodeficiency virus type 1 by using monoclonal antibodies. *J Virol* **68**:8350–8364, 1994b. (Medline: 95056067) Notes: Four of five anti-V3 MAbs were slightly cross-reactive within clade B, but not very reactive outside clade B. Two discontinuous CD4 binding site Mabs appear to be pan-reactive. Anti-V2 MAbs were only sporadically reactive inside and outside of clade B.

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[Moore (1994c)] J. P. Moore, Q. J. Sattentau, R. Wyatt, & J. Sodroski. Probing the Structure of the Human Immunodeficiency Virus Surface Glycoprotein gp120 with a Panel of monoclonal antibodies. *J Virol* **68**:469–484, 1994c. (Medline: 94076440) Notes: . This study compared a large number of MAbs that bind to linear epitopes of gp120, and compared binding affinities for: i) native and SDS-DDT denatured gp120, (clone BH10 of the LAI isolate expressed in CHO cells); ii) recombinant gp120 lacking the V1, V2, V3 loops; iii) a panel of 20 mer peptides; iv) a panel of gp120 mutants; and v) oligomeric versus monomeric gp120. The binding ratio of native versus denatured monomeric gp120 is included in the table in this database. These numbers should be considered with the following points in mind: a continuous epitope may be partially exposed on the surface; and a preparation of rgp120 is not homogeneous and contains fully folded, partly denatured, and some completely unfolded species, so the conformation of what is considered to be a native protein will not only reflect fully folded gp120. The authors suggest that a fivefold increase in the affinity for a MAb binding to denatured versus native gp120 indicates that the epitope is inaccessible in the native form. We also have included here information extracted from Moore et al's list of the gp120 mutations that reduced the binding of a particular MAb. In mapping of exposed regions of gp120, C2, C3, and C5 domain epitopes were found to bind preferentially to denatured gp120. V1, V2 and V3, part of C4, and the extreme carboxy terminus of C5 were exposed on the native monomer. In the oligomeric form of the molecule, only V2, V3 and part of C4 are well exposed as continuous epitopes.

[Moore (1993a)] J. P. Moore, Q. J. Sattentau, H. Yoshiyama, M. Thali, M. Charles, N. Sullivan, S.-W. Poon, M. S. Fung, F. Traincard, M. Pinkus, G. Robey, J. E. Robinson, D. D. Ho, & J. Sodroski. Probing the structure of the V2 domain of human immunodeficiency virus type 1 surface glycoprotein gp120 with a panel of eight monoclonal antibodies: human immune response to the V1 and V2 domains. *J Virol* **67**:6136–6151, 1993a. (Medline: 93381817).

[Moore & Sodroski(1996)] J. P. Moore & J. Sodroski. Antibody cross-competition analysis of the human immunodeficiency virus type 1 gp120 exterior envelope glycoprotein. *J Virol* **70**:1863–1872, 1996. (Medline: 96190589) Notes: 46 anti-gp120 monomer MAbs were used to create a competition matrix, and MAb competition groups were defined. The data suggests that there are two faces of the gp120 glycoprotein: a face occupied by the CD4BS, which is presumably also exposed on the oligomeric envelope glycoprotein complex, and a second face which is presumably inaccessible on the oligomer and interacts with a number of nonneutralizing antibodies.

[Moore (1993b)] J. P. Moore, M. Thali, B. A. Jameson, F. Vignaux, G. K. Lewis, S.-W. Poon, M. S. Fung, P. J. Durda, L. Akerblom, B. Wahren, D. D. Ho, Q. J. Sattentau, & J. Sodroski. Immunochemical analysis of the gp120 surface glycoprotein of human immunodeficiency virus type 1: Probing the structure of the C4 and V4 domains and the interaction of the C4 domain with the V3 loop. *J Virol* **73**:4785–4796, 1993b. (Medline: 93323221) Notes: General observations: C4 and V3 MAbs are sensitive to the way the

epitopes are presented, and this sensitivity cannot be correlated to peptide binding. Some V3-C4 domain interaction was indicated based on mutation and interference studies.

[Moore (1995b)] J. P. Moore, A. Trkola, B. Korber, L. J. Boots, J. A. Kessler II, F. E. McCutchan, J. Mascola, D. D. Ho, J. Robinson, & A. J. Conley. A human monoclonal antibody to a complex epitope in the V3 region of gp120 of human immunodeficiency virus type 1 has broad reactivity within and outside clade B. *J Virol* **69**:122–130, 1995b. (Medline: 95074855) Notes: The epitope was defined as including amino acids on both sides of the loop of the V3 loop: -I—-G–FY-T, where the G is the second G of the GPGR tip of the loop. This antibody bound well to gp120 molecules from clades A,B,C,E, and F, when the critical amino acids were present. Binding did not parallel neutralization however; 19b could produce a 50-fold reduction of infectivity in some primary B isolates, and in C clade isolates at low virus input concentrations, but not in isolates from all clades where binding could occur (A,E, and F).

[Moore (1994d)] J. P. Moore, R. L. Willey, G. K. Lewis, J. Robinson, & J. Sodroski. Immunological evidence for interactions between the first, second and fifth conserved domains of the gp120 surface glycoprotein of human immunodeficiency virus type 1. *J Virol* **68**:6836–6847, 1994d. (Medline: 95018590) Notes: Mutation 267N/Q in C2 region results in exposing the carboxy-terminal end gp120.

[Moore (1993c)] J. P. Moore, H. Yoshiyama, D. D. Ho, J. E. Robinson, & J. Sodroski. Antigenic variation in gp120s from molecular clones of HIV-1 LAI. *AIDS Res Hum Retroviruses* **9**:1185–1193, 1993c. (Medline: 94190623) Notes: The binding of MAbs to four molecular clones of HIV-1 LAI: HxB2, HxB3, Hx10, and NL4-3, was measured. Despite the close relationship between these clones, there is considerable variation in their antigenic structure, judged by MAb reactivities to the V2, V3, and C4 domains and to discontinuous epitopes. Small variations in sequence can profoundly affect recognition of gp120 by all five groups of defined anti-gp120 neutralizing antibodies.

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monoclonal antibodies to the C4 domain of gp120 from human immunodeficiency virus type 1. *J Virol* **67**:6179–6191, 1993. (Medline: 93381821) Notes: Multiple CD4 binding domain antibodies are described; only one has a linear peptide reactivity (13H8). A V3 loop binding antibody is also described (1026).

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MAbs recognized an epitope present in SIVagmTYO-7, SIVagmTYO-5, and HIV-2/SIVmac. The anti-p17 recognized an epitope present in SIVagmTYO-7, SIVagmTYO-5, HIV-2/SIVmac, SIVagmTYO-1, HIV-1, and SIVmnd. This study shows that the matrix protein expresses at least one highly conserved epitope.

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of virus to cells expressing CCR5 in the presence of sCD4. Preincubaton with MAb 17b blocks binding, as did the natural ligand for CCR5, MIP-1$beta$ and anti-CCR5 MAb 2D7. Mutations 437 P/A and 442 Q/L increased CCR5 binding affinity. The region of gp120 CCR5 binding is shown to be the highly conserved $beta$-sheet bridging structure, located proximal to the V3 loop.

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[Wyatt (1992)] R. Wyatt, M. Thali, S. Tilley, A. Pinter, M. Posner, D. Ho, J. Robinson, & J. Sodroski. Relationship of the human immunodeficiency virus type 1 gp120 third variable loop to elements of the CD4 binding site. *J Virol* **66**:6997–7004, 1992. (Medline: 93059644) Notes: This paper examines mutations which alter MAb binding and neutralization. Anti-V3 MAb 9284 has enhanced binding due to a mutation in the C4 region that is also important for CD4 binding, and anti-CD4 binding MAbs F105, 1.5e and 1125H show increased precipitation of a gp120 from which the V3 loop was deleted, relative to wild type, in RIPA buffer containing non-ionic detergents.

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[Zolla-Pazner (1999b)] S. Zolla-Pazner, M. K. Gorny, P. N. Nyambi, T. C. VanCott, & A. Nadas. Immunotyping of human immunodeficiency virus type 1 (HIV): an approach to immunologic classification of HIV. *J Virol* **73**:4042–51, 1999b. (Medline: 99214343) Notes: 21 human anti-V3 MAbs were studied with respect to cross-clade reactivity and immunological relationship to other human anti-V3 MAbs. Broad cross-reactivities were observed, and V3 peptides were grouped into immunotypes that contained peptides from several clades.

[Zolla-Pazner (1995)] S. Zolla-Pazner, J. O'Leary, S. Burda, M. K. Gorny, M. Kim, J. Mascola, & F. McCutchan. Serotyping of primary human immunodeficiency virus type 1 isolates from diverse geographic locations by flow cytometry. *J Virol* **69**:3807–3815, 1995. (Medline: 95264474) Notes: A set of 13 human MAbs to a variety of epitopes were tested against a panel of primary isolates of HIV-1, representing different genetic clades. The V3 loop tended to be B clade restricted, and a single gp120 C-terminus binding antibody was clade specific. Two other gp120 C-terminus binding antibodies were group specific.

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