Synthetic Peptides Define the Fine Specificity of the Human Immunodeficiency Virus (HIV) gp160 Humoral Immune Response in HIV Type 1-Infected Chimpanzees

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The fine specificities of antibodies produced against human immunodeficiency virus type 1 (HIV-1) gp160 were examined in sera from 23 HIV-1-infected chimpanzees. These animals had been infected with one of six isolates of HIV-1. Sera were screened by enzyme-linked immunosorbent assay for reactivity against seven synthetic peptides corresponding to regions of gp160. Chimpanzees appear to remain healthy after infection with HIV-1, suggesting that these animals may prevent extensive spread of the virus *in vivo* through immunologic mechanisms. Antibody specificity to gp160 epitopes may play a key role in the defense against HIV-1-related disease. Approximately one-half of all chimpanzee sera contained antibodies reactive with peptide 846-860, which corresponds to the carboxyl terminus of gp41. Less than 10% of sera from HIV-1-infected humans that were examined contained antibodies reactive with peptide 846-860, suggesting that this region is not highly immunogenic in humans. Of the human sera containing antibodies reactive with this peptide, all were from individuals classified as Walter Reed stages 1 to 3. No sera from humans with advanced stages of the disease contained antibodies reactive with peptide 846-860. Peptide 600-611, which reportedly reacts with nearly all sera from HIV-infected humans, was reactive with less than one-half of sera from HIV-1-infected chimpanzees. The observed differences in antibody reactivity to gp160 peptides in sera from HIV-1-infected chimpanzees and humans suggest that each may generate antibodies against differing sets of HIV-1 epitopes. These differences may contribute to the lack of disease progression in chimpanzees after infection with HIV-1.

Chimpanzees are currently one of the most widely used animal models for testing potential vaccines against acquired immunodeficiency syndrome (AIDS). Although chimpanzees have been shown to be susceptible to infection with the human immunodeficiency virus (HIV), there have been no reports of an AIDS-like illness developing in these animals (1, 14-16, 27, 37). In addition, levels of chimpanzee circulating CD4⁺ lymphocytes remain within normal ranges after infection with HIV type 1 (HIV-1) (15). The reasons for the lack of disease progression in HIV-1-infected chimpanzees are at present unknown but may involve differences in the humoral and cellular immune response to the virus in comparison with that of humans (11, 46). A recent report suggests that chimpanzees may generate cytotoxic antibodies to HIV-infected cells that are absent in sera from HIV-infected humans (30). By examining the fine specificity of chimpanzee anti-gp160 antibodies, insight may be gained into why these animals show no signs of disease progression after infection with HIV-1.

Our laboratory has used seven synthetic peptides, which correspond to epitopes of HIV-1 envelope glycoprotein gp160, to analyze the antibody specificity of sera from 23 HIV-infected chimpanzees. Synthetic peptides have been shown previously to be useful tools in analyzing the fine specificity of both humoral and cellular immunity to gp160 epitopes (18, 21, 29, 42). This report identifies several regions of gp160 that differ in immunogenicity in chimpanzees and humans infected with HIV-1. A possible association between the presence of antibodies reactive with gp160

peptide 846-860 and disease progression in humans was also examined.

MATERIALS AND METHODS

Chimpanzees. We examined 15 male and 8 female chimpanzees (*Pan troglodytes*) ranging in age from 7 to 15 years. Most of the animals had been used previously in hepatitis vaccine trials. Twelve animals were infected with human T-lymphotropic virus type III (HTLV-III_B), six were infected with lymphadenopathy-associated virus (LAV), four were infected with isolate SF2, and one was infected with human HIV-positive plasma. Productive infection of these animals was confirmed by demonstrating HIV-reactive antibodies by enzyme-linked immunosorbent assay (ELISA) and Western blots (immunoblots). None of the chimpanzees have displayed any signs of an AIDS-like illness. Preimmune sera from eight chimpanzees obtained before HIV infection were used as negative controls. Sera were obtained from the majority of chimpanzees 1 to 4 years after HIV seroconversion.

Human sera. Sera were obtained from 152 HIV-1-infected U.S. Air Force personnel from Wilford Hall USAF Medical Center, San Antonio, Tex. These patients represented all stages of clinical illness according to the Walter Reed (WR) staging of HIV-related disease (35). Control sera were obtained from 23 healthy, HIV-1-seronegative volunteers.

Peptides and gp160. Amino acid sequences for gp160 peptides 304-321, 425-448, 503-528, 616-632, 735-752, and 846-860 were derived from the HTLV-III_B (BH10) isolate (34). These regions were selected because of their hydrophilicity, predicted beta-turn secondary structure, and except

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TABLE 1. Amino acid sequences of gp160 synthetic peptides analyzed in this study

Amino acid residues	Sequence ^a
304-321	(C-G-Y)-T-R-P-N-N-N-T-R-K-S-I-R-I-Q-R-G-P-G
425-448	C-R-I-K-Q-I-I-N-M-W-Q-E-V-G-K-A-M-Y-A-P-P-I-S-G
503-528	(C-G-Y)-V-A-P-T-K-A-K-R-R-V-V-Q-R-E-K-R-A-V-G-I-G-A-L-F-L-G
600-611	L-G-I-W-G-C-S-G-K-L-I-C
616-632	(C)-P-W-N-A-S-W-S-N-K-S-L-E-Q-I-W-N-N-(G)
735-752	(Y)-D-R-P-E-G-I-E-E-E-G-G-E-R-D-R-D-R-S-(G-C)
846-860	(C-A-Y)-A-I-R-H-I-P-R-R-I-R-Q-G-L-E-R-(G)

^a Amino acids in parentheses were added to facilitate coupling to carrier proteins for related immunization studies.

for peptide 304-321, conserved sequence homology between isolates (33). The peptides were assembled by solid-phase peptide synthesis on Merrifield polystyrene resin as described previously (7, 8, 23). Protection of amino acid side chains during synthesis and cleavage of the peptide from the solid-phase support by anhydrous hydrogen fluoride has been described elsewhere (24). Peptides were purified by reverse-phase high-performance liquid chromatography, and the composition of each was verified by amino acid analysis and the presence of a single peak by high-performance liquid chromatography. Peptide 600-611, described elsewhere (17), was purchased from Cambridge Research Biochemicals (Valley Stream, N.Y.). The amino acid sequences of the synthetic peptides used in this study are described in Table 1. Recombinant envelope glycoprotein gp160, produced in baculovirus, was the generous gift of Gale Smith (MicroGeneSys, West Haven, Conn.).

ELISA. Because of the insolubility of peptide 600-611 in aqueous buffer, this peptide was solubilized in 35% acetic acid and adhered to wells of microtiter plates (Corning Glass Works, Corning, N.Y.) by overnight incubation at 37°C (250 ng per well). The remaining peptides were dissolved in carbonate buffer (NaHCO₃, pH 9.6) and were adhered to microtiter wells by overnight incubation at 4°C (250 ng per well). The gp160 was coated onto microtiter wells at 20 ng per well overnight at 4°C. Nonspecific sites were blocked with 10% normal goat serum for 1 h at 37°C. The plates were then washed three times with phosphate-buffered saline-0.05% Tween 20 (PBS/T), and chimpanzee or human sera at a dilution of 1/50 in 10% normal goat serum were incubated for 1 h at 37°C in duplicate wells. Rabbit antisera raised against each peptide were used at 1/1,000 as a positive control. To detect binding of the chimpanzee and human antibodies, a 1/1,000 dilution of a horseradish peroxidase-labeled goat anti-human immunoglobulin G (Kirkegaard & Perry Laboratories, Gaithersburg, Md.) was added after three washes with PBS/T and incubated for an additional 1 h at 37°C. Reactivity of the rabbit antisera was similarly detected by using a goat anti-rabbit immunoglobulin G-horseradish peroxidase conjugate (Kirkegaard & Perry Laboratories). After the 1-h incubation at 37°C, the plates were again washed, and 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) (Sigma Chemical Co., St. Louis, Mo.) along with 0.05% hydrogen peroxidase was added as substrate. The enzyme reaction was stopped with 100 µl of 5% sodium dodecyl sulfate per well. Binding was quantitated spectrophotometrically at 405 nm with an automatic plate reader (MR600; Dynatech Laboratories, Inc., Alexandria, Va.). The cutoff for a positive reaction was established for each peptide by multiplying by 3, the mean optical density value obtained with a 1/50 dilution of the 8 preimmune chimpanzee sera or 23 normal human sera. This cutoff value was greater than the optical density value obtained from the mean of the negative con-

trols plus 3 standard deviations and represents greater than a 99% confidence level. Endpoint titers were considered to be the reciprocal of the highest serum dilution that resulted in an optical density at least three times that obtained for a 1/100 dilution of the control sera. All sera were tested for peptide-reactive antibodies in at least three separate ELISAs.

RESULTS

Of the 23 animals studied, 12 (52%) were infected with the HTLV-IIIB isolate and 6 (26%) were infected with the LAV isolate. These two HIV isolates have nearly identical amino acid sequences for gp160.

Sera from HIV-infected chimpanzees were initially screened by ELISA for antibodies reactive with recombinant gp160 (data not shown). Only animals with significant levels of gp160-reactive antibodies were studied further. The epitope specificities of these antibodies were then determined by screening these sera for reactivity against a panel of seven synthetic peptides. The amino acid sequence for each peptide (Table 1) was based on that of the HTLV-IIIB (BH10) isolate.

Sera at a 1/50 dilution from HIV-infected chimpanzees were screened for reactivity to each peptide by ELISA. The reactivities of sera from 14 unvaccinated animals were compared with those of sera from all 23 HIV-infected chimpanzees (Table 2). No clear differences in percentages of reactive sera were observed between the two groups. A high percentage of chimpanzee sera reacted with synthetic peptide 846-860 (11 of 23; 48%). Of the 11 chimpanzee sera that contained antibodies reactive with this peptide, 6 were from animals infected with LAV, 2 were from animals infected with HTLV-IIIB, 2 were from animals infected with SF2, and 1 was from an animal infected with human plasma from an HIV-infected patient.

The synthetic peptide corresponding to amino acid sequences 304 to 321 encompasses a portion of a loop region of gp120. The amino acid sequence of this loop region is highly variable among HIV isolates and has been reported to induce type-specific neutralizing antibodies (20, 40). Of 23 sera from HIV-infected chimpanzees, 7 (30%) contained antibodies reactive with peptide 304-321. Six of the seven positive animals had been infected with either HTLV-IIIB or LAV. These two isolates have identical amino acid sequences at the 304 to 321 region of gp160. An additional chimpanzee, which had been infected with the SF2 isolate, also possessed antibodies reactive with this peptide. The SF2 isolate is 83% homologous with the HTLV-IIIB isolate at the 304 to 321 region of gp160.

Peptide 600-611 has been previously reported to represent an immunodominant epitope in humans in which greater than 95% of HIV-1-seropositive individuals possess antibod-

TABLE 2. Reactivity of sera from HIV-seropositive chimpanzees to synthetic peptides as determined by ELISA

Synthetic peptide (amino acid residues)	No. (%) of reactive sera		HIV isolates used to infect (no. of animals)
	Unvaccinated animals (n = 14)	All animals ^a (n = 23)	
304-321	5 (35)	7 (30)	LAV (4), IIIB (2), SF2 (1)
425-448	3 (21)	3 (13)	LAV (1), IIIB (1), SF2 (1)
503-528	4 (28)	5 (22)	LAV (2), SF2 (2), plasma (1)
600-611	7 (50)	9 (39)	LAV (4), IIIB (3), SF2 (1), plasma (1)
616-632	1 (7)	1 (4)	SF2 (1)
735-752	3 (21)	5 (22)	LAV (3), SF2 (1), plasma (1)
846-860	7 (50)	11 (48)	LAV (6), IIIB (2), SF2 (2), plasma (1)

^a Includes both unvaccinated chimpanzees and chimpanzees immunized with several HIV-1 vaccine candidates before challenge with infectious HIV-1. Sera were obtained 1 to 4 years postchallenge.

ies recognizing this region (18, 19, 31, 38, 39, 41, 45). Reactivity to this peptide was observed in 9 (39%) of 23 sera from HIV-infected chimpanzees. This peptide corresponds to a highly conserved region of gp41 and is the target for group-specific antibodies in humans. Of the nine chimpanzees that generated antibodies to this peptide, four were infected with LAV, three were infected with HTLV-IIIB, one was infected with SF2, and one was infected with plasma from an AIDS-infected patient.

Since approximately one-half of all sera from HIV-infected chimpanzees contained antibodies reactive with peptide 846-860, we then tested the reactivities of 152 sera from HIV-infected humans to this peptide. Figure 1 shows a representative ELISA that compares the reactivities of sera from chimpanzees and humans to peptide 846-860. We found that sera from HIV-infected humans were generally unreactive, with only 13 (9%) of 152 sera containing significant levels of antibodies recognizing peptide 846-860.

Sera from two representative chimpanzees and humans that contained antibodies reactive to peptide 846-860 were then analyzed by ELISA to determine endpoint titers. Chimpanzee serum 1 had an endpoint titer of 1/800, whereas serum 2 had an endpoint titer of 1/400 (Fig. 2A). Endpoint titers of two human sera were 1/3,200 and 1/1,600 against peptide 846-860 (Fig. 2B).

To ensure the immunologic specificity of these antibodies, a representative human antiserum containing antibodies reactive with peptide 846-860 was absorbed to an affinity column containing peptide 846-860. The eluted antibodies were then tested for reactivity against HIV-1 proteins by Western blot. The affinity-purified antibodies reacted to bands corresponding to gp41 and gp160 while demonstrating no reactivity toward gp120 (data not shown). These data indicate that antibodies reactive with peptide 846-860 could be removed on a peptide-containing immunosorbent column.

The human sera that contained antibodies reactive with peptide 846-860 were then grouped according to the WR staging of HIV-related clinical illness (Table 3). All reactive humans were classified as WR 1 to 3, which corresponded to individuals with normal cellular immunity, as determined by delayed hypersensitivity. Sera from individuals classified as WR 4 to 6 were not found to contain antibodies reactive with peptide 846-860. Individuals classified as WR 4 to 6 have defective cellular immune responses and have fewer than 400 CD4⁺ cells per mm³ in the peripheral blood.

The region of gp41 encompassing amino acids 846 to 860 is generally conserved among isolates of HIV-1 (Table 4). When the peptide sequence was compared with sequences of nine other HIV-1 isolates, the degree of sequence homology ranged from 80 to 100%, with the average level of amino acid sequence conservation being 89%.

Since the 600 to 611 region of gp41 has been shown to be immunodominant in humans, we compared the endpoint titers of reactive human sera with those of chimpanzee sera. Chimpanzee serum 3 had an endpoint titer of 1/3,200, whereas serum 4 had an endpoint titer of 1/400 (Fig. 3A). Titration of two positive human sera indicated that serum 3 had an endpoint titer of 1/1,600 and that serum 4 had an endpoint titer of 1/800 (Fig. 3B).

Little reactivity was observed between the chimpanzee sera and peptides 425-448, 503-528, 616-632, and 735-752.

FIG. 1. Reactivities of chimpanzee and human sera to peptide 846-860. Each point represents the optical density (O.D.) at 405 nm obtained with a 1/50 dilution of serum binding to peptide 846-860. The dashed line represents the cutoff for positive reactivity and is three times the mean optical density value obtained with control sera. Each point represents the mean of duplicate values.

FIG. 2. Binding curves of sera from HIV-1-infected chimpanzees and humans to peptide 846-860. Two representative HIV-1-infected sera and an uninfected control were tested for binding to peptide 846-860 as measured by ELISA. The sera were diluted in 10% normal goat serum. Each point represents the mean of triplicate values. The vertical range bars represent the mean optical density (O.D.) plus 1 standard deviation.

Reactivity for the 23 HIV-infected chimpanzee sera ranged from 4 to 22% against these four peptides (Table 2). The reactivities of HIV-1-infected chimpanzee sera to each gp160 peptide are summarized in Table 5. Individual animals demonstrated a wide range of antibody reactivity to these peptides. Only one chimpanzee infected with an SF2 isolate of HIV-1 demonstrated reactivity to all seven gp160 peptides.

DISCUSSION

Our laboratories have been examining the chimpanzee as a potential animal model for HIV infection (1, 10, 37). As part of these studies, a variety of HIV-1 isolates were used in infectivity studies. The sera used in this study were obtained

TABLE 3. WR staging of HIV-infected humans with antibodies reactive to gp160 peptide 846-860

WR stage	No. reactive/total no. examined
1	9/92
2	3/18
3	1/17
4-6	0/25

FIG. 3. Binding curves of sera from HIV-infected chimpanzees and humans to peptide 600-611. Details are as given in the legend to Fig. 2.

from animals infected with one of six isolates of HIV-1. This report describes the fine specificity of the anti-gp160 humoral immune response in sera from 23 HIV-1-infected chimpanzees.

The region of gp41 encompassing amino acids 600 to 611 has been previously reported to be highly immunogenic in humans, being reactive with nearly all sera from HIV-infected individuals. Our study indicates that less than one-half of the HIV-1-infected chimpanzees examined produced antibodies reactive with this peptide. Titers of chimpanzee antibodies to peptide 600 to 611 appeared to be similar in both chimpanzee and human sera. Whereas this epitope is immunodominant in humans, it appears to be less immunogenic in HIV-1-infected chimpanzees. The reported presence of antibodies to the 600-611 epitope in nearly all sera from HIV-infected humans (representing the entire spectrum of HIV-related illness) suggests that these antibodies do not significantly alter disease progression.

Peptide 304-321 corresponds to a highly variable loop region of gp120 (12). This area is reportedly involved in the fusion of HIV-infected cells to uninfected CD4⁺ lymphocytes (36). Of the chimpanzee sera containing reactive antibodies, six of seven were from animals infected with isolates with amino acid homology to peptide 304-321. These results suggest that this highly variable epitope stimulates production of isolate-specific antibodies. Others have also reported that chimpanzee antibodies to this region of gp120

TABLE 4. Amino acid sequence homology of synthetic peptide 846-860 to other HIV-1 isolates^a

HIV isolate	Sequence	% Homology
Peptide 846-860	AlaIleArgHisIleProArgArgIleArgGlnGlyLeuGluArg	
LAV	-----	100
MN	-----Leu-----Thr-----	87
SC	-----Leu-----Thr-----	87
SF2	-----Leu-----His-----	87
CDC4	---PheLeu-----Phe-----	80
WMJ2	-----Ile-----	93
RF	---PheLeu-----	87
JH3	-----Leu-----Thr-----	87
BRVA	-----Leu-----	93

^a Amino acid sequences are according to references 28 and 44. Overall homology was 89%.

are isolate specific and capable of neutralizing HIV in vitro (20, 40).

Fewer sera from HIV-infected chimpanzees contained antibodies reactive with peptide 425-448, 503-528, 616-632, or 735-752. Peptide 425-448 was examined in this study because an earlier report had suggested that this region of gp120 was involved in binding to the CD4 molecule (26). This region has also been reported to be recognized by human cytotoxic T cells (4). The 425 to 448 region of gp120 appeared to be poorly immunogenic in HIV-1-infected chimpanzees.

Nearly one-fourth of all sera from HIV-infected chimpanzees contained antibodies reactive with peptide 503-528. This finding contrasts with reports that nearly one-half of all sera from HIV-infected humans contain antibodies reactive with this region of gp160 (32, 39). Sera from chimpanzees infected with four HIV-1 isolates produced antibodies reactive with peptide 503-528, suggesting that this epitope stimulates group-specific antibodies. Our laboratories have reported previously that a peptide corresponding to amino acid sequences 503 to 532 stimulated production of HIV-1-neutralizing antibodies in rabbits (22).

The 616 to 632 and 735 to 752 regions of gp160 have both been previously reported to induce antibodies that neutralize HIV-1 in vitro (7, 9, 21, 23). The lack of reactivity of nearly all (22 of 23) chimpanzee sera to peptide 616-632 demonstrates that reactivity of sera to other gp160 peptides was not the result of nonspecific binding. Approximately one-fourth of the sera from HIV-1-infected chimpanzees contained antibodies reactive with peptide 735-752. Our laboratories have previously shown that this peptide can suppress normal human lymphocyte proliferation and natural killer cell activity in vitro (6, 8).

The region of gp160 encompassing amino acids 846 to 860

appears to be a major target for antibodies in HIV-1-infected chimpanzees. Approximately one-half of all chimpanzee sera examined contained antibodies reactive with this peptide. Reactive animals had been infected with five isolates of HIV-1, suggesting that the 846-860 epitope of gp160 stimulated group-specific antibodies. This peptide corresponds to the carboxyl terminus of gp41 and is relatively conserved among HIV-1 isolates. We found few (13 of 152) sera from HIV-infected humans that contained antibodies reactive with peptide 846-860. Interestingly, of those humans producing antibodies to peptide 846-860, all were classified as WR stages 1 to 3. No sera from individuals with advanced stages of illness (WR 4 to 6) contained detectable levels of peptide 846-860-reactive antibodies. The low level of reactivity of HIV-infected human sera to peptide 846-860 contradicts an earlier report by Klasse and co-workers (25). This difference in reactivity may reflect slight differences in peptide composition used in the two studies. Our laboratories have previously demonstrated that peptides corresponding to this region of gp41 can inhibit normal human lymphocyte proliferation and natural killer cell activity in vitro (6, 8).

Whether antibodies reactive with the 846-860 epitope contribute to a disease-free state in chimpanzees is not known. However, studies examining virus variants of the HTLV-III_B isolate have suggested that changes in the 3' region of the *env* gene result in a mutant virus that does not kill normal human T cells in vitro (13). These authors suggest that the carboxyl terminus of gp41 may have a direct role in killing T cells. The possibility therefore exists that antibodies to this region of gp41 may inhibit the destruction of T cells, thereby preventing disease progression. In time, if chimpanzees should develop an AIDS-like illness, it will be interesting to follow their immune response to this and other epitopes of HIV-1. Although the number of human sera containing antibodies to peptide 846-860 was low, each of these sera was from an individual classified as WR stages 1 to 3. Our results suggest that there may be an association between the presence of these antibodies and the absence of severe illness in HIV-1-infected humans.

Analysis of sera from unvaccinated chimpanzees suggested that antibody specificity to the peptides was comparable to that in the group of all HIV-infected animals. In particular, the percentage of reactive sera among unvaccinated animals was nearly the same as that for all animals studied for peptides 304-321, 503-528, 616-632, 735-752, and 846-860. Therefore, vaccination of some of the chimpanzees before challenge with HIV-1 did not seem to significantly alter the fine specificity of the anti-HIV antibodies.

The apparent absence of an AIDS-like illness developing

TABLE 5. Summary of reactivities of chimpanzee antisera to gp160 synthetic peptides

No. of chimpanzees	Reactivity to given peptide						
	304-321	425-448	503-528	600-611	616-632	735-752	846-860
11	-	-	-	-	-	-	-
2	+	-	-	+	-	-	+
1	-	-	-	-	-	-	+
1	-	-	-	+	-	-	-
1	-	-	+	-	-	-	+
1	-	-	-	+	-	-	+
1	-	-	+	+	-	+	+
1	+	+	-	+	-	-	+
1	+	-	+	+	-	+	+
1	+	+	+	+	-	+	+
1	+	+	+	+	+	+	+

in HIV-1-infected chimpanzees may be due to several factors. Our results suggest that chimpanzee antibodies to gp160 may be directed toward viral epitopes that are infrequently recognized by humans infected with HIV. In addition, sera from HIV-1-infected chimpanzees have been reported to contain cytotoxic antibodies capable of lysing HIV-infected cells while being absent in human sera (30). Cellular immunity to HIV-1 appears to be stronger in infected chimpanzees than in humans. Peripheral blood lymphocytes from HIV-1-infected chimpanzees have been shown to proliferate in response to HIV antigen in vitro, whereas similar responses are generally weak or absent in HIV-infected humans (11, 27, 43, 47). Even after several years, cellular immunity to HIV-1 appears to persist in infected chimpanzees.

The ideal AIDS vaccine would be one that prevented infection with HIV. However, the fact that as few as four tissue culture infective doses at 50% of HIV-1 can infect a chimpanzee (2) indicates that no vaccine may be capable of preventing infection. A vaccine that stimulates an immune response which suppresses the spread of HIV-1 in vivo and allows an infected individual to remain disease free would obviously be beneficial. Examples of lifelong viral infections in which the majority of individuals remain disease free include Epstein-Barr virus and cytomegalovirus (3). In these cases, suppression of the existing immune response can lead to a reappearance of the disease state (5). Chimpanzees may provide a useful model for studying how an infected animal can apparently inhibit HIV-1 activity in vivo and remain clinically healthy.

Our study suggests that although they are close relatives of humans, chimpanzees may produce antibodies against epitopes on HIV-1 gp160 that are not immunogenic to most humans (e.g., 846–860). In addition, epitopes that are immunodominant in humans, such as that defined by peptide 600–611, may not be highly immunogenic to chimpanzees. If chimpanzees and humans recognize different sets of gp160 epitopes, this fact may help explain the differences in clinical outcome between the two species after infection with HIV-1.

The chimpanzee model allows one to examine the immune response of an animal that, although susceptible to infection with HIV-1, appears to remain disease free. Identifying differences in anti-HIV-1 antibody specificity between chimpanzees and humans may lead to more effective HIV-1 vaccine candidates and immunotherapeutic strategies.

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