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Certain HIV-1 infected humans that do not progress to AIDS have been documented to share particular MHC class I alleles that appear to correlate with long-term survival. HIV-1-infected chimpanzees are relatively resistant to progression to AIDS. Out of a group of 10 chimpanzees with CTL activity and nonprogressive HIV-1 infection, 2 animals with prominent cytolytic CD3^+ CD8^+ T cell responses to HIV-1 Ags were studied in detail. Characterization of these CTL revealed that they contained the granzymes A and B, T cell intracellular Ag-1, and perforin and induced calcium-dependent cytolysis that correlated with the presence of apoptotic nuclei in target cells. These CTL responses were directed against two gag peptides, which were found to be identical to previously described epitopes recognized in the context of HLA-B27 and HLA-B57 molecules. The latter two restriction elements occur with increased frequency in human long-term survivor cohorts. Phylogenetic comparisons revealed that the chimpanzee restriction elements, Patr-B^*02 and B^*03, described here do not show any obvious similarity with the HLA-B^*27 and B^*57 alleles, suggesting that CTL responses to HIV-1 in distinct primate species may be controlled by different types of HLA-B-like molecules.

The CTL responses in these two chimpanzees are directed, however, against highly conserved epitopes mapping across the majority of HIV-1 clades. The Journal of Immunology, 1999, 162: 2308–2314.

Most untreated HIV-1-infected humans develop high virus loads and declining CD4^+ T cell numbers within 5–10 yr after infection (1). In contrast to these progressors, a small group of long-term survivors (LTS) do not develop evidence of progression to AIDS despite the fact that they are known to be infected for >17 yr (2–5). In addition, so called exposed seronegative individuals appear to be protected against HIV infection despite several years of unprotected sex with HIV-infected partners (6–9).

As possible mechanisms of resistance to AIDS, several hypotheses have been put forward. In a few defined cases resistance has been documented to be due to defective HIV-1 viruses (10, 11). Similarly, in a small percentage of LTS, mutations in chemokine coreceptors have been identified as genetic factors of host resistance (12–16). In terms of host immune responses, the elimination of infected cells by cytotoxic immune responses is of importance to establish control of the intracellular stages of viral infections (17–19). It has been documented that certain CTL responses may be protective in the case of HIV-1-infected individuals by reducing viral loads (20–23). It has been documented that certain CTL responses may be protective in the case of HIV-1-infected individuals by reducing viral loads (20–23). It has been documented that certain CTL responses may be protective in the case of HIV-1-infected individuals by reducing viral loads (20–23). It has been documented that certain CTL responses may be protective in the case of HIV-1-infected individuals by reducing viral loads (20–23).

Virus-specific Ags have been reported in macaques (30, 31). Similar to humans, CTL responses directed against lentivirus-specific Ags have been reported in macaques (32–35). A particular MHC class I allele has been correlated with long-term survival in SIV-infected rhesus macaques (36, 37). Furthermore a correlation of certain MHC alleles and particular opportunistic infections after the onset of AIDS in macaques has been documented (38). In addition to humans, chimpanzees are one of the few species susceptible to persistent infection with HIV-1. Worldwide, >150 chimpanzees have been infected with divergent HIV-1 isolates including infection by uncultured clinical samples directly from AIDS patients (39). To date there has been only one reported case of a chimpanzee that developed AIDS after infection with several HIV-1 strains (40). In chimpanzees the CCR5 HIV-1 coreceptor is intact and infected animals do not have the mutations associated with resistance to AIDS in humans (41). Additionally, most chimpanzees have been experimentally infected with defined viral inoculums, and deletions in viral genes such as nef have in most cases been ruled out (42). The majority of HIV-1-infected chimpanzees do not show signs of disease progression and in this regard resemble the status in LTS.

Cytotoxic T cell activity has been occasionally observed in chimpanzees after HIV-1 infection or immunizations (43–45). However, to date detailed characterization of HIV-1-specific CTL responses in chimpanzees is lacking. In this study we set out to determine the phenotype and specificity of the CTL responses in two HIV-1-infected chimpanzees in our cohort.

Materials and Methods

Animals studied

From a cohort of 10 chronically HIV-1-infected and 3 HIV-1-negative chimpanzees (Pan troglodytes verus), 2 HIV-1-infected chimpanzees (Ch-La and Ch-Ze) were studied in detail. All of the HIV-1-infected chimpanzees in this cohort have been extensively studied in a long-term follow-up...
for evidence of progression to AIDS. None of these infected animals showed signs of lymphadenopathy, a decline in CD4+ T cell numbers, elevated virus load, increased activation or apoptosis markers, anemia, and/or thrombocytopenia (39, 46, 47). The two animals described in detail in this report were part of a group of six chimpanzees who were all infected i.v. on the same day with the same dose and strain of HIV-1 as part of a larger study (48). Ch-La and Ch-Ze had been immunized with rgp120 but subsequently became infected (49). In that study the presence of CTL was not determined. Ch-La and Ch-Ze were tested 5 yr later and were the first animals found in our cohort with positive cytolytic responses and thus chosen for further study. The eight remaining HIV-1-infected animals as well as the three HIV-1 negative chimpanzees served as controls. These animals were MHC typed and lacked the Patr-B*02 or -B*03 molecules.

**Virus-specific CTL activities**

Effector cells were generated from Lymphocyte Separation Medium (Organon Teknika Corporation, Durham, NC) density gradient isolated PBMC. Ag-specific cytotoxic effector cells from PBMC were activated by coculture with autologous PHA (5 µg/ml, Sigma, St. Louis, MO) stimulated, IL-2 (ADP 901, Medical Research Council, Hertfordshire, U.K.) expanded and peptide pulsed T cell blasts as stimulator cells. To prepare stimulator cells the T cell blasts were incubated with overlapping peptide pools (2.5 µg/ml per peptide) spanning the gag protein (22 peptides) for 3 h at 37°C and 5% CO2. Overlapping peptides spanning the gag of HIV-1 SF2 were obtained from MRC AIDS Reagent project (ADP 788, MRC) and consisted of 22 20-mers overlapping by 10 amino acids spanning gag amino acids 10–164. Peptides 1 and 2 covered the residues 135–164 and peptides 13 and 14 covered the residues 252–284. For more detailed epitope mapping, a panel of custom 9-mer peptides overlapping the specific epitopes were used (Quality Control Biochemicals, Hopkinton, MA). After incubation, stimulator cells were irradiated with 30 Gray. Stimulator cells and 15 × 10^6 freshly isolated PBMC were cocultured at a ratio of 0.5:1 in 3 ml RPMI 1640 (Life Technologies, Paisley, Scotland) supplemented with I-glutamine (2 mM, Life Technologies), penicillin (100 U/ml, Biochemie, Vienna, Austria), streptomycin (0.2 mg/ml, Biochemie), and 10% FCS (Life Technologies). After 48 h these cultures were supplemented with IL-2 at a concentration of 20 U/ml. Cultures were regularly fed with culture medium containing IL-2 during the coculture period. After 8 days, cocultures were harvested, enriched for vital cells by lymphocyte separation medium density gradient centrifugation, and restimulated with autologous stimulator cells. After 48 h restimulated cultures were supplemented with IL-2. Cytotoxicity was tested at day 16. Before assaying cytotoxic effector cells, dead cells were removed by lymphocyte separation medium density gradient centrifugation. To enrich cell cultures for CD8+ cells, CD8+ 15 × 10^6 cells were depleted after the first stimulation by incubation with magnetic beads coupled to anti-CD4 Abs (Dynabeads M450, Dynal, Oslo, Norway) for 60 min on ice. Rosette cells were depleted on a magnetic separator (MPC-6, Dynal). The phenotype of cytolytic T cell lines was assessed by triple color flow cytometry analysis (FACSort, Becton Dickinson, Mountain View, CA), using FITC-labeled anti-CD8 (Becton Dickinson); phycoerythrin-labeled anti-CD4 and phycoerythrin Cy5-labeled anti-CD3 (Becton Dickinson). The CD8+ cells were stimulated again after testing in the chromium release assay. Specific cytolytic T cell lines were maintained by periodic restimulation with irradiated autologous stimulator cells and PHA-stimulated human PBMC.

**Cytotoxicity assay**

Target cells were autologous EBV B-lymphoblastoid cell line labeled with 150 µCi Na2CrO4 (Amersham International, Buckinghamshire, U.K.) for 1 h, followed by 3 washes of pools of peptides at a concentration of 25 µg/ml for 1 h at 37°C, followed by a 16 h incubation period with the same peptides at a concentration of 2.5 µg/ml. Unpulsed B-lymphoblastoid cell lines were used as controls. Subsequently, target cells were washed and plated at 5 × 10^3 cells per well in 96-well U-shaped plates (Costar, Cambridge, MA) together with effector cells at three E:T ratios. After 5 h incubation at 37°C supernatants were harvested and γ counts were performed in a gamma counter (Cobra 5, Packard). Percentages of specific 51Cr release were calculated as 100 × (experimental release – spontaneous release)/(maximum release – spontaneous release). All experimental values were determined in duplicate or triplicate and maximum and spontaneous releases were performed in quadruplicate. Responses of 10% or more above specific lysis of control unpulsed targets, were scored as positive.

**Immunocytochemistry**

The granzymes A and B (GrA and GrB), the RNA binding protein T cell intracellular Ag-1 (TIA-1), and perforin expression on CD8+ and CD4+ T cells was studied using a double-staining technique. Cytosin preparations were fixed in 4% buffered formalin for 9 min, washed in PBS, and preincubated with normal goat serum (10% in PBS). Subsequently, the slides were incubated with anti-GrA (GA11) or -GrB (GB11), both kindly provided by Dr. E. Hack (CLB, Amsterdam, The Netherlands), anti-TIA-1 (Coulter, Hialeah, FL) or antiperforin mAb (T Cell Diagnostics, Woburn, MA). Secondary biotinylated Abs (goat anti-mouse, Dako, Glostrup, Denmark) were used as a secondary Ab. Immunostaining was performed using the avidin-biotin-peroxidase complex (Dako), normal mouse serum (5% in PBS, Jackson Immunoresearch Laboratories, West Grove, PA), FITC-labeled CD8 (DK25) or CD4 (OKT4), peroxidase-labeled rabbit anti-FITC (Dako), and peroxidase-labeled swine anti-rabbit (Dako). All incubation steps were performed at room temperature for 30 min. Endogenous peroxidases were blocked with 0.1% Na2HPO4, plus 0.3% H2O2 in PBS after the incubation with the first Ab AP activity was detected with naphtho-AS-MX phosphate (Sigma), and Fast Blue BB (Sigma) in 0.1 M Tris-HCl, pH 8.5 (20 min in the dark), yielding a blue color. HRP activity was detected using H2O2 (0.03%) and 3-amin-9-ethylcarbazole (Sigma) yielding a red color.

For detection of apoptosis during CTL-mediated killing, cytospin preparations of CTL incubated with peptide pulsed autologous B cell target cells cultured for 5 h were prepared and stained subsequently with anti-CD20 mAb (L26, Dako), FITC-labeled goat anti-mouse Ab (Dako) and ethidium bromide (100 µg/ml in PBS; Sigma).

**MHC class I typing, restriction, and epitope mapping**

Chimpanzees were initially typed for their Patr class I Ags by means of serological methods (50). The corresponding Patr class I nucleotide sequences were determined based on the method described by Ennis et al. (51). The correlation of serotypes and nucleotide sequences was established based on performing extensive segregation studies (52). The Patr class I alleles (Patr-B*02 and -B*03) that are relevant for this study have been published previously (53, 54). These restriction elements were identified by testing cytotoxic reactivity of CTL of Ch-La and Ch-Ze on a panel of allotypic Patr-A, -B, and -C locus-type cells.

**Results**

**Detection of gag-specific CTL in HIV-1-infected chimpanzees**

Of the 10 chimpanzees in our HIV-1-infected cohort, 6 chimpanzees were challenged with HIV-1 in 1990 (49). In that study the presence of CTL were not determined. PBMC from these animals were tested 5 years later for the presence of gag and env-specific CTL responses. Persistent Ag-specific cytotoxic activity was first detected in two animals against different gag epitopes suggesting the existence of at least two CTL epitopes (Fig. 1). The strong gag-specific CTL responses in these two infected animals (Ch-La and Ch-Ze) were selected for further study and characterized in detail. Env-specific CTL were not detected. As controls, cells from chimpanzees lacking the Patr-B*02 and -B*03 molecules were also tested for the ability to recognize the epitopes described in this study in a CTL assay. Cells from three HIV-1 negative control chimpanzees as well as eight HIV-1-infected chimpanzees were stimulated according to the same stimulation protocol with pooled peptides. Taking these 11 animals into account, we have never detected false positive responses in these chimpanzees to the specific epitopes. Cytolytic responses were observed to distinct pooled peptides, but these have not yet been characterized to the epitope level (data not shown).

**CTL epitope mapping**

CTL of Ch-La were found to recognize a pool of peptides 1–3 of HIV-1 gag (Fig. 1A). After testing individual peptides it was found that only peptides 1 and 2 were recognized. This suggested that the actual epitope that was recognized was located in the overlapping region of these two peptides (VHQAISPRTL). To test this assumption, two novel peptides were synthesized and target cells were pulsed with these 9-mer peptides. Target cells loaded with VHQAISPRTL were not affected whereas HQAISPRRTL (HIV-1 gag amino acid residues 146–154) loaded target cells were lysed by the effector cells.
CTL of Ch-Ze were found to react with a pool of peptides 11–14 of the same HIV-1 gag preparation mentioned earlier (Fig. 1B). More in detail, only peptides 13 and 14 were recognized mapping to the following 10-mer (KRWIILGLNK). To define the fine specificity of the epitope, target cells were pulsed with the relevant 9-mer peptides. These subsequent studies demonstrated that target cells with KRWIILGLN (HIV-1 gag amino acid residues 265–273) were lysed whereas targets loaded with the RWIILGLNK oligopeptide were not lysed by the effector cells.

Phenotypic characterization of CTL and their killing mechanism

The phenotype of the effector cells was characterized by FACS analysis to determine the cell surface markers. The bulk culture contained CD3⁺CD4⁻T cells, CD3⁻CD8⁺ as an indication of NK cells and CD3⁺CD8⁺ cells as an indication of CTL. After enrichment for CD8⁺ cells using magnetic beads, the CTL culture from Ch-Ze was found to consist of 95% CD3⁺CD8⁺ T cells and 3% CD4⁺ T cells (Fig. 2). These cells were then stimulated again before testing. The cells maintained the same phenotype during the culture period. Similar data were found for the culture of Ch-La and these results were consistent over time.

To establish that these chimpanzee CD3⁺CD8⁺ T cells used the same cytolytic machinery as human CTL, the effector cells were incubated with peptide-labeled target cells according to standardized procedures. The autologous B cell targets were found to have fragmented apoptotic nuclei as was determined by staining the B cells with FITC-labeled anti-CD20 in combination with propidium iodide for detection of B and T cell nuclei. Further analysis revealed that the CD8⁺ T cells were positive for TIA-1 (Fig. 3A). This was in contrast to the CD4⁺ T cells present in the same cultures that were, as expected, negative for these markers (Fig. 3B). The same was seen for the other contents of the cytotoxic granules GrA, GrB, and perforin. Cytolytic responses were also tested for calcium dependency in medium containing 1.5 M EDTA, which was found to completely inhibit these specific chimpanzee CTL responses. Thus, the CTL activity observed in these chimpanzees is caused by CD3⁺CD8⁺ T cells carrying GrA, GrB, TIA-1, and perforin that use a calcium-dependent pathway resulting in apoptosis of target cells and therefore resembles human CTL (55).

Characterization of MHC restriction elements

The involvement of MHC class I restriction elements was determined for both chimpanzees using a mAb W6/32 (anti-MHC class I molecules). By FACS analysis the binding of the Ab W6/32 on the surface of the target cells was found to be optimal in the 1:100
dilution. As can be seen in the dose-response curve, a 1:100 dilution of the supernatant stock of Ab W6/32 resulted in complete inhibition of the Ag-specific functional cytolytic response (Fig. 4).

To elucidate which MHC class I molecules were functioning as restriction elements, an allogeneic B cell panel typed for the different Patr molecules was used as target cells. This panel of chimpanzee cells was selected based on the presence of known MHC class I and II nucleotide sequences. The autologous and (partly) matched allogeneic target cells were pulsed with the relevant gag peptides and subsequently tested with the effector cells of Ch-La and Ch-Ze (Table I). The target cells that are lysed are expected to share the same Patr allele that functions as restriction element. As expected, CTL from Ch-La effectively lysed autologous target cells and also cells from Ch-Ro, Ch-Wo, and Ch-Ka (Table I). All these cells share the Patr-B*02 and -C*05 molecules. To distinguish which of these two restriction elements are used, Ch-Su and Ch-Pe were selected that are positive for the Patr-C*05 molecules and lack Patr-B*02 Ags. These target cells were not lysed, indicating that the selected CTL from Ch-La recognize the gag epitope HQAISPRTL in the context of Patr-B*02 molecules. The same procedure was used to elucidate the restriction element of the CTL from Ch-Ze. The CTL from Ch-Ze recognized its autologous target cells as well as the allogeneic target cells from Ch-Fr, Ch-Qu, Ch-Na, and Ch-Ph (Table I). Apart from Ch-Ph, all these animals share Patr-A*06, -B*03, and -C*03 molecules. Ch-Ph, however, only shares the Patr-B*03 and -C*03 molecules with the previously mentioned cells. Cells of Ch-Pea were not lysed confirming that the Patr-A*06 molecules were not able to present the peptide. To further differentiate between the Patr-B*03 and -C*03 molecules, cells of Ch-Yv were selected that are positive for the Patr-C*03 molecules. These target cells were not lysed. This indicates that CTL from Ch-Ze, that are described in this study, recognize the HIV-1 gag epitope KRWIILGLN in the context of Patr-B*03 molecules.

![FIGURE 3.](image)

**FIGURE 3.** Analysis of Ch-La PBMC in culture after two rounds of stimulation. The cells were double stained for (A) CD8 and TIA-1 and (B) CD4 and TIA-1. Original magnification was ×60.

![FIGURE 4.](image)

**FIGURE 4.** Inhibition of the cytolytic response of CTL from Ch-Ze at an E:T ratio of 2.5:1. Several dilutions of the anti-MHC class I Ab W6/32 were added to the peptide-pulsed autologous target cells for 30 min at 37°C. Then the target cells were added to the effector cells of Ch-Ze in a ⁵¹Cr release assay.

<table>
<thead>
<tr>
<th>Patr</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>CTLⁿ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectors Cells from Ch-La</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ch-La</td>
<td>A<em>03, A</em>09</td>
<td>B<em>02, B</em>10</td>
<td>C<em>05, C</em>02</td>
<td>+ (86)</td>
</tr>
<tr>
<td>Ch-Ro</td>
<td>A<em>03, A</em>09</td>
<td>B<em>02, B</em>10</td>
<td>C<em>05, C</em>02</td>
<td>+ (65)</td>
</tr>
<tr>
<td>Ch-Wo</td>
<td>A*01, ??</td>
<td>B<em>02, B</em>14</td>
<td>C<em>05, C</em>01</td>
<td>+ (73)</td>
</tr>
<tr>
<td>Ch-Ka</td>
<td>A<em>07, A</em>11</td>
<td>B<em>02, B</em>13</td>
<td>C*05, ??</td>
<td>+ (40)</td>
</tr>
<tr>
<td>Ch-Su</td>
<td>A<em>03, A</em>09</td>
<td>B*25, ??</td>
<td>C<em>05, C</em>03</td>
<td>− (0)</td>
</tr>
<tr>
<td>Ch-Pe</td>
<td>A<em>12, A</em>15</td>
<td>B<em>11, B</em>13</td>
<td>C<em>05, C</em>06</td>
<td>− (0)</td>
</tr>
<tr>
<td>Ch-Jo</td>
<td>A<em>03, A</em>09</td>
<td>B<em>10, B</em>26</td>
<td>C<em>01, C</em>02</td>
<td>− (7)</td>
</tr>
<tr>
<td>Ch-So</td>
<td>A<em>09, A</em>15</td>
<td>B<em>10, B</em>13</td>
<td>C<em>02, C</em>07</td>
<td>− (0)</td>
</tr>
<tr>
<td>Ch-Fr</td>
<td>A<em>04, A</em>06</td>
<td>B<em>14, B</em>03</td>
<td>C<em>01, C</em>03</td>
<td>− (0)</td>
</tr>
<tr>
<td>Ch-Ag</td>
<td>A<em>09, A</em>15</td>
<td>B<em>10, B</em>13</td>
<td>C<em>02, C</em>07</td>
<td>− (0)</td>
</tr>
</tbody>
</table>

| Effectors Cells from Ch-Ze |
| Ch-Ze | A*01, A*06 | B*10, B*03 | C*02, C*03 | + (30) |
| Ch-Fr | A*04, A*06 | B*14, B*03 | C*01, C*03 | + (26) |
| Ch-Qu | A*01, A*06 | B*10, B*03 | C*02, C*03 | + (42) |
| Ch-Na | A*04, A*06 | B*10, B*03 | C*03, C*03 | + (27) |
| Ch-Ph | A*04, A*07 | B*10, B*03 | C*02, C*03 | + (94) |
| Ch-Re | A*02, A*04 | B*10, B*14 | C*01, C*02 | − (3)  |
| Ch-Pe | A*06, ??  | B*10, B*13 | C*02, C*07 | − (4)  |
| Ch-Wo | A*01, ??  | B*02, B*14 | C*05, C*01 | − (4)  |
| Ch-Lo | A*01, A*16 | B*09, B*10 | C*02, C*07 | − (0)  |
| Ch-Ma | A*01, A*04 | B*10, B*14 | C*01, C*02 | − (3)  |
| Ch-Yv | A*03, ??  | B*25, ??  | C*03, ??  | − (0)  |

ᵃ MHC class I restriction for the epitopes recognized by CTL of Ch-La and Ch-Ze. CTL of Ch-La and Ch-Ze were tested on a B cell panel of matched and mismatched targets. Shown are the typings of the Patr-A, -B and -C molecules. In italics are the restricting Patr molecules shared by the targets recognized.

ᵇ “+”, Targets presenting the specific 9-mer epitope were recognized and lysed by CTL; “−”, targets presenting the specific 9-mer epitope were not recognized and lysed by CTL.

ᶜ A homozygous or blank specificity.
The cytolytic activities in the two chimpanzees, Ch-La and Ch-Ze, were found to be directed against two distinct 9-mer sequences in HIV-1 gag. CTL of Ch-La and Ch-Ze recognize the epitope HQAISPRTL and KRWIIGLLN, respectively. At least two research groups reported independently, that in humans the CTL epitope HQAISPRTL is also recognized in the context of HLA-B*57 molecules (29). Likewise the 9-mer KRWIIGLLN is recognized by human that are restricted by HLA-B*2705 gene products (56). Both the HLA-B*57 and -B*27 specificities are observed more frequently in LTS than in rapid progressors to AIDS (3, 24, 26). Based on these reports evidence suggests that these HLA specificities may be involved in protective immune responses against AIDS.

It is known that humans and chimpanzees share as much as 98% genetic similarity as determined at the DNA level. For that reason, it is possible that humans and chimpanzees share highly identical MHC molecules that have the capacity to bind the same peptide. That this possibility may reflect reality has been demonstrated for HLA-DR3-like molecules in humans and chimpanzees that were reported to bind the same peptide from the heat shock protein 65 of Mycobacterium tuberculosis (57). With regard to the A locus in humans and chimpanzees a similar observation was made for the relevant nucleotide sequences (54). Thus, the same HIV-1 gag peptides are bound by totally different types of HLA-B and Patr-B molecules, which group into distinct lineages. Due to promiscuity the same MHC molecule may bind a large set of peptides. As a consequence the same epitope may be bound by different MHC molecules. This has been described for a HCV CTL epitope (59) and for two HIV-1 nef/CTL epitopes (60–62). Human individuals, especially LTS, and chimpanzees that are relatively resistant to AIDS, recognize the same epitopes for mounting CTL responses. One may wonder whether there is a biological relevance to this phenomenon. Scanning of HIV-1 clades shows that particular regions are highly conserved. This appears to be the case for the two epitopes described here that map to such highly conserved regions (Fig. 6). In this light, the hypothesis would be that protective CTL responses are preferentially mounted against highly conserved epitopes. In other words, some individuals in the human population may have the right type of HLA molecules that can bind such peptides. In the case that a mutation in such an epitope occurs, progression to disease may follow. This is illustrated by a study of Goulder et al. (63) demonstrating that a mutation in the KRWIIGLLNK epitope, which took place 12 years after infection, correlated with subsequent progression to AIDS.

It is too early to conclude on the basis of only these two chimpanzees that CTL-mediated protection may solely explain why chimpanzees are relatively resistant to AIDS. It is likely that multiple immunological mechanisms are responsible for this resistance. Further studies are underway to investigate whether other conserved HIV-1 epitopes are recognized by chimpanzee CTL. Studies of the immune responses mounted by chimpanzees to HIV-1 infection may further elucidate the role of CTL in protection from progression to AIDS and provide insight for the development of effective HIV-1 vaccines or immunotherapeutic strategies.

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CONSERVED HIV-1 CTL EPITOPES IN CHIMPANZEES


