primed and nonprimed cells stimulated via the Fc receptor (Immuno beads; Dynal, Oslo, Norway). This experiment, to some extent, mimics part of the in vivo situation of HIV-infected patients with a very high virus load, in agreement with the results of Dios et al. [2]. This does not rule out the possibility of an intrinsic defect acquired by the progenitor cells. Perhaps several regions of the envelope glycoprotein can interact with proteins in the same or different cells and result in cumulative impairment of normal function in general and antimicrobial potential specifically [5]. Multiple regions of several proteins would result in a more effective pathogenesis strategy that would be very hard to block with drugs.

To elucidate the mechanism of this inhibition, we are in the process of characterizing the cell receptor for this envelope region in human neutrophils and other cells. The possibility that the peptide is binding to one of the coreceptors will also be explored. Proteins that are up-regulated and phosphorylated need to be identified in order to understand the molecular details of the cascade that starts with the binding of the peptide to the cell surface receptors and ends by compromising the oxidative-burst capacity of the cell. In our study, we identified a decrease in the expression of a 48-kDa protein and an increase in the expression of a 65-kDa protein after priming with the peptide [3]. These proteins could be the p47phox and p67phox cytosolic components that are essential for the activation of the phagocyte respiratory-burst oxidase and for defense against intracellular pathogens, as illustrated by persons with chronic granulomatous disease [6]. Phosphorylation of p47phox appears to be involved in protein translocation events, and both p47phox and p67phox might help in the translocation by interacting with cytoskeletal elements [6]. Temporal activation or inactivation of these proteins is therefore probably required for releasing the products of oxygen metabolism to the compartments where the intracellular pathogens are located. Together, these findings could provide additional therapeutic targets against HIV. An analog of this peptide could be designed to compete for the receptor with the virus. Furthermore, a peptide representing the virus binding site in the receptor can be prepared in such a way that its affinity for the virus ligand is much greater than that of the cell receptor. Finally, a very small molecule that binds tightly to this domain of gp120 can be a new type of drug against HIV-1 and the development of AIDS.

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Clearance of Cytomegalovirus Viremia after Initiation of Highly Active Antiretroviral Therapy

To the Editor—In a recent report, O’Sullivan et al. [1] showed that immune reconstitution secondary to initiation of highly active antiretroviral therapy (HAART) in 23 human immunodeficiency virus type 1 (HIV)–infected subjects with low CD4 T cell counts (median, 35 cells/mm3) resulted in a progressive decline in cytomegalovirus (CMV) DNAemia (as measured by the Diagnostics, Branchburg, NJ) in an antiretroviral-naive HIV-infected subject in whom HAART was initiated.

A 32-year-old Haitian heterosexual man was diagnosed with an HIV infection at the end of 1997 and initially presented with toxoplasma encephalitis. On stabilization of his condition, antiretroviral therapy was initiated with stavudine (30 mg twice a day), lamivudine (150 mg twice a day), and neflinavir (750 mg 3 times/day). Before therapy, he had a CD4 count of 56 cells/
mm$^3$ and an HIV RNA load of 110,000 copies/mL, or $5.0 \log_{10}$ (Quantiplex HIV RNA 2.0 assay [bDNA]; Chiron, Emeryville, CA; table 1). As part of the patient’s workup, a CMV pp65 antigenemia assay was found to be highly positive (75 positive cells/10$^6$ leukocytes). This was confirmed by use of the Roche PCR test on plasma (1640 copies/mL or $3.2 \log_{10}$) and leukocytes (16,820 copies or $4.2 \log_{10}$) (table 1). A blood viral culture was also positive for CMV after only 7 days of incubation. There were no specific features of symptomatic CMV disease, and the results of an ophthalmologic examination by a trained specialist were entirely normal.

Within a month of starting HAART, the patient’s CD4 T cell count increased to 190 cells/mm$^3$, with an important decrease in the HIV RNA load ($-2.3 \log_{10}$) and moderate decrease in the CMV load in leukocytes, as determined by PCR ($-0.7 \log_{10}$) and pp65 antigenemia assays (table 1). After 2 months of HAART, the HIV RNA load became undetectable (<500 copies/mL), as did the CMV PCR test on plasma (<400 copies/mL), the CMV pp65 antigenemia assay, and the CMV blood culture. The PCR test on leukocytes was the last CMV assay to become negative after ~3 months of HAART. After 5 months of antiretroviral therapy, the HIV RNA load increased to 17,290 copies/mL ($4.2 \log_{10}$), and the CD4 T cell count dropped slightly to 139 cells/mm$^3$ because of poor compliance. However, CMV remained undetectable in the blood by all methods (table 1). The patient was counseled and reevaluated 1 month later. The HIV load then decreased to 3899 copies/mL ($3.6 \log_{10}$) and the CD4 T cell count rose to 227 cells/mm$^3$. Again, all assays showed no signs of active CMV replication in the blood, and the patient remained asymptomatic during this period.

In agreement with the study by O’Sullivan et al. [1], our data confirm the decline in the CMV load following initiation of HAART, probably through restoration of a functional CMV-specific CD4 repertoire [2]. The decline in the CMV DNA load in leukocytes of our patient was progressive over 3 months (from 4.2 to $2.0 \log_{10}$). Of interest, we noted a more rapid clearance of CMV-mediated cytopathic effect, CMV pp65 antigens, and CMV DNA in plasma. Absence of CMV replication was continually maintained after 3 months of HAART in the presence of a CD4 T cell count $\geq 139$ cells/mm$^3$, despite a rebound in HIV load because of poor compliance. This could suggest that the CD4 T cell count or function is more important than the HIV load for protection against opportunistic infections. It is noteworthy that the CMV DNA load decline after HAART was considerably less rapid than that seen in patients treated with ganciclovir, as reported in our previous study [3]. In the latter case, the mean CMV DNA load in leukocytes decreased by $\sim 1.5 \log_{10}$ after only 10 days of induction therapy. Thus, although potent anti-HIV therapy with sustained immune response can permit safe withdrawal of maintenance therapy for CMV [4], we suggest that specific anti-CMV therapy is still needed in the presence of active CMV disease to rapidly inhibit CMV replication.

### Table 1. HIV and CMV loads in a patient who received HAART.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Days of HAART</th>
<th>CD4 cells/mm$^3$</th>
<th>HIV RNA load in plasma $\log_{10}$</th>
<th>CMV DNA load in plasma $\log_{10}$</th>
<th>CMV DNA load in leukocytes $\log_{10}$</th>
<th>CMV pp65 antigenemia (positive cells/10$^6$ cells)</th>
<th>CMV blood culture (days to positivity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>56</td>
<td>5.0</td>
<td>110,000</td>
<td>3.2</td>
<td>1640</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>190</td>
<td>2.7</td>
<td>550</td>
<td>2.9</td>
<td>725</td>
<td>3.5</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>190</td>
<td>&lt;2.7</td>
<td>&lt;500$^a$</td>
<td>&lt;2.6</td>
<td>&lt;400$^a$</td>
<td>2.8</td>
</tr>
<tr>
<td>4</td>
<td>85</td>
<td>180</td>
<td>&lt;2.7</td>
<td>&lt;500$^a$</td>
<td>&lt;2.6</td>
<td>&lt;400$^a$</td>
<td>2.0</td>
</tr>
<tr>
<td>5</td>
<td>154</td>
<td>139</td>
<td>4.2</td>
<td>17,290</td>
<td>&lt;2.6</td>
<td>&lt;400$^a$</td>
<td>&lt;2.0</td>
</tr>
<tr>
<td>6</td>
<td>188</td>
<td>227</td>
<td>3.6</td>
<td>3899</td>
<td>&lt;2.6</td>
<td>&lt;400$^a$</td>
<td>&lt;2.0</td>
</tr>
</tbody>
</table>

*NOTE.: HIV, human immunodeficiency virus; CMV, cytomegalovirus; HAART, highly active antiretroviral therapy.

$^a$ Lower limit of detection of assay.

### References


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