very complex structural aberrations; (2) the same pattern of chromo-
some gains and losses, including lack of the Y chromosome, whose
supposed presence was quoted by Taoka et al as an important feature
distinguishing TI-1 cells from the K-562 cells; and (3) identical CGH
profiles and chromosomal locations of amplified BCR/ABL in TI-1 and
K-562 cells. Because our G-banded karyotype is the same as the
karyotype published by Taoka et al., the cross-contamination most
likely occurred at the original source.

Importantly, Drexler and colleagues have estimated that 18% of
human tumor cell lines have intraspecies cross-contamination that
occurred at the source of cell line establishment, including other
cases in which K-562 was the contaminating culprit. It has
recently been recommended that short tandem repeat profiling be
used as an international reference standard for human cell lines
used in research settings. We wish to notify the scientific
community that the TI-1 cell line is a cross-contaminant of K-562
and should no longer be used for research on AML.

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To the editor:

Why antiviral CD8 T lymphocytes fail to prevent progressive immunodeficiency
in HIV-1 infection

We would like to comment on the recent review by Lieberman et al by offering an additional interpretation on the mechanisms that
contribute to lack of protection by antiviral CD8 T cells in HIV
infection. In the last few years we have been able to demonstrate that, since the early phases of HIV infection, the pulmonary
microenvironment can be infected by the etiologic agent of AIDS and that the intra-alveolar presence of HIV evokes a discrete
immune response mediated by antiviral CD8+ cytotoxic T lympho-
cytes (CTLs). In asymptomatic patients the appearance of pulmonary
CD8 T cells is associated with the clearance of the virus from the
lung microenvironment. But with the progression of HIV
disease, the cytotoxic activity of pulmonary CTLs declines. Our
data published in 1995 emphasize the role of HIV infection in the
progressive functional impairment of CD8 T cells. Although
lymphocytes expressing the CD4 receptor are the principal cell
target for HIV, lung CD8+ T cells of most patients with AIDS show
an unexpected in vivo HIV infectivity. When proviral load on pulmonary T-cell subsets is assessed using the DNA–polymerase
chain reaction (PCR) technique, most of the bronchoalveolar
lavage (BAL) proviral DNA can be found in the underrepresented
CD4 T-cell subset, but PCR analysis directly performed on highly
enriched CD8+ T cells shows that this population also carries
detectable amounts of HIV DNA. Circumstantial evidence ob-
tained evaluating peripheral blood CD8 also supports the hypothe-
thesis that retroviral infection of CD8 cells may contribute to the
functional decline of this subset upon disease progression in
HIV-infected individuals. Interestingly, the proviral load of pulmo-
nary CD8+ T cells usually shows an upward trend with respect to the
corresponding samples isolated from the peripheral blood of
the same patient. Because we demonstrated that CD8+ T cells
accumulating in the lungs of HIV-infected patients are preactivated
Tc1 cells prone to spontaneous and activation-induced apoptosis, it
is tempting to relate the productive infection to the increased
apoptosis rate of CD8+ T cells.

Concerning the mechanisms that account for the infection of CD8+ CTL, at least 2 hypotheses can be proposed. The repeated
contacts occurring in the lung microenvironment between activated
HIV-specific CTLs and relevant targets might lead to the infection of
CD8 cells. This hypothesis is supported by in vitro studies showing that HIV may be transmitted through cell-to-cell contact
between persistently infected CD4 cells and CD8 CTLs. An
additional, though not necessarily alternative, hypothesis is that
lung CD8+ CTLs derive from T-cell precursors that transiently
coexpress both CD4 and CD8 determinants in secondary
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Response:

HIV infection of CD8 T cells: a factor in progressive immunodeficiency?

Agostini and Semenzato suggest that an important factor in the lack of protection by antiviral CD8 T cells in HIV infection is infection of CD8 T cells by HIV. A number of studies have indicated that, when naive CD8 T cells are activated via the T-cell receptor (TCR), they express CD4, although at reduced levels compared to that on CD4 T cells. Moreover, in vitro CD8 T cells can be productively infected with HIV. The real question is how significant HIV infection of CD8 T cells is in vivo, whether it is productive, and whether it contributes to the lack of CD8 T cell function. The studies of HIV infection in vivo have relied on polymerase chain reaction (PCR) amplification of proviral DNA from immunologically separated or sorted cell populations. The majority have studied advanced patient samples. Although it is unlikely that the PCR results are all due to contaminating CD4-expressing T cells or monocytes, none of the published studies use quantitative or even semiquantitative assays to give an accurate assessment of the rates of infection of CD8 T cells in vivo. There is also little evidence that the infection is productive in vivo. Moreover, in early and moderately advanced disease the number of CD8 T cells is expanded above normal levels, and HIV-specific CD8 T cells represent a sizable proportion of the expanded population (see references in Lieberman et al). Therefore, because HIV infection of CD8 T cells would be expected to deplete CD8 T cells, as it does CD4 T cells, it is unlikely that HIV infection of CD8 T cells contributes in any substantial way to CD8 T cell dysfunction in less advanced stages of disease. In more advanced patients with AIDS, however, HIV infection might well contribute to the late decline in CD8 T cells and loss of HIV-specific immunity. This merits further study. Quantitative assessment of HIV proviral DNA and mRNA in highly purified CD8 T cells or simultaneous measurement of CD8 and CD3 with intracellular HIV p24 protein or in situ hybridization of HIV RNA would help establish that this is an important contributing factor to antiviral CD8 T cell dysfunction. In vitro studies that demonstrate functional effects of selected in vitro infected HIV-specific CD8 T cells would also help build a case.

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References


Why antiviral CD8 T lymphocytes fail to prevent progressive immunodeficiency in HIV-1 infection

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