very complex structural aberrations; (2) the same pattern of chromosome gains and losses, including lack of the Y chromosome, whose supposed presence was quoted by Taoka et al[1] 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,[1] 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.[12,13] 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.[14] 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[1] 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 lymphocytes (CTLs).[2] 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.[3] 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.[3] 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 obtained evaluating peripheral blood CD8 also supports the hypothesis that retroviral infection of CD8 cells may contribute to the functional decline of this subset upon disease progression in HIV-infected individuals.[4] Interestingly, the proviral load of pulmonary $CD8^+$ T cells usually shows an upward trend with respect to the corresponding samples isolated from the peripheral blood of the same patient.[5] 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,[6] 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.[7] 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

follicles where trapped extracellular virions are present in the dendritic network.

In conclusion, on the basis of these data we believe that the retroviral infection of CD8 T cells should be considered as an additional mechanism contributing to the fall of antiviral CD8 T-cell activity during HIV infection. Because it is known that highly active antiretroviral therapy (HAART) leads to a reduction of HIV load, additional studies should be performed to evaluate the ultimate effects of HAART on CD8 T-cell infectivity in relation to their functional activities. On clinical grounds, this information could have an impact on strategies for designing therapeutic intervention in HIV infected patients.

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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 naïve 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.[1,2] Moreover, in vitro CD8 T cells can be productively infected with HIV.[3-8] 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 immunomagnetically 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[9]). 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.[10] 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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