stemming the HIV epidemic. With the limited resources in hand, we can do at least two things: stand back until enough funds become available (to afford ACTG 076) or do the best we can with what we have (trials of short-course AZT alone or in combination).

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Notes

1. *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Council for International Organizations of Medical Sciences, Geneva, 1993).

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Helper CD4⁺ T Cells and HIV-1

The study "Vigorous HIV [human immunodeficiency virus]-1–specific $CD4^+$ T cell responses associated with control of viremia" by Eric S. Rosenberg *et al.* (Reports, 21 Nov., p. 1447) suggests a possible mode of immuno-intervention in AIDS patients. However, the frequencies (1/10,000 and 1/19,000, respectively) of the T cell precursors that reacted against p24 antigen detected in the two long-term, nonprogressor patients described in the study could be an underestimation of the real frequencies because, in the regular T cell proliferation assay (figure 3 in the report), Rosenberg *et al.* say they used 105 cells per well and detected a stimulation index of 100 on day 3. It is unlikely that only 10 cells at the start of culture (105 divided by the calculated frequency of 104) would give such strong proliferation; with a doubling time of 18 hours, those initial 10 cells would result, after four doublings, in 160 cells; such a small number of cells is not likely to reflect the brisk proliferation detected. This relatively low frequency could be a result of the assay conditions: Rosenberg *et al.* do not report adding interleukin-2, which is known to affect the detected frequency. In our experience, interleukin-2 can increase the detected frequency 10-fold (*2*), an effect also noted by others (*3*, *4*). In addition, Rosenberg *et al.* do not report examining the cell frequency below 103. Because limiting dilution assays may have multiple-hit patterns (*4*), the authors could have missed the detection of high-frequency cells.

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Response: We agree with Mor that the precursor frequency analysis likely is an underestimation of the true frequency of HIV-1–specific helper cells, for the reasons he outlines. We had initially not included these data in the manuscript, but were requested by the reviewers to add them. The type of functional assay used can be anticipated to underestimate the true frequency because the frequency calculation is based on the assumption that a single HIV-1–specific helper cell in a well will result in a positive readout (the single-hit hypothesis). We are in the process of trying to develop a more sensitive assay system.

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