LETTERS

Letters to the Editor

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Retraction of an Interpretation

WE WRITE TO RETRACT AN INTERPRETATION IN our Report, "Contribution of human α-defensin 1, 2, and 3 to the anti–HIV-1 activity of CD8 antiviral factor" (*1*), wherein we demonstrated that human α-defensin 1, 2, and 3 account for much of the anti–HIV-1 activity of the CD8 antiviral factor (CAF) that is not attributable to β-chemokines. Although the antiviral activity of human α-defensin has not been called into question, the cellular source of these α-defensins has been reinterpreted in light of more recent experiments. Our experiments were done using purified CD8 T cells from long-term nonprogressors or normal persons that were stimulated with anti-CD3 and anti-CD28 antibodies, recombinant interleukin-2, phytohemagglutinin, and irradiated allogeneic peripheral blood mononuclear cells (PBMC). This method of stimulating CD8 T cells had been commonly used by many groups working on CAF (*2*–*7*). However, in a follow-up attempt to define the specific subpopulation of CD8 T cells that produce α-defensins, we have found that in the absence of allogeneic irradiated PBMC (feeders), stimulated CD8 T cell supernatants do not contain α-defensins. Although it could be argued that an allogeneic stimulus is a prerequisite for α-defensin production by CD8 T cells, it is more likely that they are derived from a cell population residing within allogeneic feeders.

To pursue the exact source of α-defensins in allogeneic feeders, we positively selected individual cell populations from irradiated PBMC and subjected them to the aforementioned stimulation conditions in the absence of allogeneic exposure. α-Defensins were detected in the supernatants of CD4 and CD8 T cells and CD19 B cells. However, if the allogeneic PBMC feeders were first treated with an anti-CD15 monoclonal antibody to eliminate residual neutrophils before being subjected to irradiation, then α-defensins were no longer detectable in the supernatants of stimulated T or B cells. These findings suggest that under our experimental conditions, even minor degrees of neutrophil contamination could result in the detection of α-defensins in the culture supernatant of other cell populations.

In a different set of experiments using antibody staining in flow cytometry or immunofluorescence, we also detected α-defensins within several freshly isolated mononuclear cell populations, including CD8 T cells, as we have reported (*1*). But, in stark contrast, no α-defensin mRNA could be detected in CD8 T cells using a sensitive RT-PCR assay. This discrepancy prompted a series of in vitro cell-mixing experiments, which led us to the conclusion that during the steps of cell processing, fixation, and permeabilization, α-defensins readily leaked from neutrophils into other cells that are not natively producing these proteins. In preliminary experiments, we also find that the release of α-defensins into the supernatant becomes more striking when activated CD8 T cells are present, perhaps because they release cytokines that facilitate degranulation of α-defensins from contaminating neutrophils. Taken together, these new findings convinced us that α-defensins cannot account for the CAF activity in experimental systems that do not use allogeneic feeders (*8*–*11*).

We wish to emphasize that the experimental findings in our Report (*1*) are repeatable. In particular, we have solidified the results shown in figs. 3 and 4 of our paper (*1*). The removal or neutralization of α-defensins by specific antibodies again resulted in the loss of anti–HIV-1 activity in the supernatant of CD8 T cells stimulated by allogeneic feeders. It should be pointed out that there is, in fact, very little residual anti–HIV-1 activity remaining once α-defensins and β-chemokines are eliminated. More importantly, we have also tested human neutrophil-derived α-defensins from independent sources and found their antiviral potency to be equivalent to those previously described (*1*), irrespective of the viral strain or target cell used in the experiment. Other investigators have confirmed this observation (*12*, *13*). Thus, the anti–HIV-1 activity of α-defensins we have described (*1*) is not in doubt, and the mechanism of their antiviral effect should be pursued.

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Brightening Depression

CONSTANCE HOLDEN'S OVERVIEW "FUTURE brightening for depression treatments" (Special Issue on Brain Disease, News, 31 Oct., p. 810) explored the current exciting approaches for creating novel antidepressants. Absent from this discussion were two major nonpharmacological, biological antidepressant treatments that have been clearly demonstrated to be highly efficacious and fast.

> **"Given the psychological suffering that depression inflicts..., it is surprising how little notice is taken of these remarkable chronobiological interventions [sleep deprivation and light therapy]."**
>
> –*WIRZ-JUSTICE* ET AL.

A single night of total or partial sleep deprivation—"wake therapy"—induces rapid and dramatic, albeit usually short-lasting, improvement of mood in about 60% of all depressed patients, independent of diagnostic subgroup (*1*). A positive response to sleep deprivation predicts and hastens the response to antidepressant medication (*1*). Sleep deprivation can be combined with a variety of drugs to maintain the response attained within hours (*2*–*4*)—theoretically, a perfect combination (*5*).

Light therapy is the only treatment in psychiatry that evolved directly out of neurobiological models of behavior (*6*, *7*). It is the treatment of choice for seasonal affective disorder, or winter depression (*6*), but is

also efficacious in nonseasonal depression (*8–10*). Light therapy is characterized by a fast onset of antidepressant action—within days—and it can prevent the depressive relapse after recovery sleep following sleep deprivation (*4*, *11*). Furthermore, light and medication can be combined (*8–12*).

Sleep deprivation and light therapy cannot be patented, and they will not bring profits to the conventional psychopharmacology industry, but they can help the patient in a shorter time and with fewer side effects than drugs—and can be easily and successfully combined with medication (*3*, *4*, *11*, *12*). Given the psychological suffering that depression inflicts—including the danger of suicide—and the financial pressures to minimize the duration of hospitalization, it is surprising how little notice is taken of these remarkable chronobiological interventions. We must include them in the therapeutic armamentarium. For light therapy, an American Psychiatric Association task force recently has concluded the same (*13*).

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The Difficulties of Testing for SARS

WE READ WITH INTEREST THE ARTICLE "SEARCH for SARS origins stalls" (M. Enserink, D. Normile, News Focus, 31 Oct., p. 766). The experience of the Canadian National Microbiology Laboratory, stemming from a positive SARS test that was later found to be a false alarm (Sidebar, "Unexplained false alarm may hold lessons," M. Enserink, p. 767), struck a particularly resonant chord, as it mirrored almost exactly our own experience in Hong Kong, one of the places most affected by SARS.

As the provider of the only private test service for the SARS coronavirus (CoV) in Hong Kong, we had been contracted by a local private hospital to test patient samples from cases of atypical pneumonia. The majority of tests were conducted after Hong Kong had been declared free from SARS. After testing many samples with our enhanced real-time PCR method, which we developed in-house, one sample gave a preliminary positive result with our