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LETTERS

Helping Physicists Market Themselves

The News article "Young scientists' network shakes up the establishment" by David H. Freeman (1 Oct., p. 24) points out, accurately in my judgment, the severe oversupply of young physics professionals in relation to the availability of jobs among their traditional research employers—universities and government and corporate laboratories. The Young Scientists' Network, some of whose leaders have been angry at the community of established physicists for "misleading" them about this situation, have taken on the American Physical Society (APS) in order, in some way, to redress the "wrongs" done them and to improve the situation for still younger students. This would be a fine idea if the APS were in a position to alter the attitudes and practices of its senior academic members; unfortunately, it isn't.

The best solution to these serious concerns, in my view, is not to limit the input of students to graduate schools, or to reduce the number of such schools (through such methods as professional accreditation), or to constrain the employment options of non-U.S. citizens. Rather, the solution lies with the tenured faculty of the Ph.D.-granting institutions, as individuals, who each should (i) think more broadly about the kinds of jobs their students could do, outside of the traditional, saturated markets; (ii) set an ethos where seeking these broader classes of jobs is not looked down upon as third-class; (iii) reconsider and modify the standards of training that Ph.D. students receive to better prepare them for the alternative careers available today and in the future (such modifications to include interdisciplinary collaborations with engineering, computer science, and biomedical disciplines); (iv) broaden their own research interests and funding sources and actively explore research collaborations to include the research interests of alternative employers of physicists; and (v) become familiar with, and promote among students, conventional, real-world career assessment and job search techniques, so that all students become confident and capable with these critical skills.

Both students and professors are today sadly unaware of how to market themselves effectively to employers. Although the APS has undertaken to bring workshops on career assessment and job searching to interested campuses, on a cost-sharing basis, such a program cannot succeed without its being institutionalized on campuses as a regular part of students' training.

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Programmed Cell Death and AIDS

The Perspective "Apoptosis in AIDS" by Marie-Lise Gougeon and Luc Montagnier (28 May, p. 1269), although interesting, puts forward several controversial suggestions and does not mention some pertinent points.

First, while there is now a good deal of evidence that in vitro activation of mature T cells from human immunodeficiency virus (HIV)–infected individuals by polyclonal stimuli (such as anti-CD3 monoclonal antibodies or calcium ionophore) induces apoptosis in a fraction of $CD4^+$ and $CD8^+$ T cells (*1, 2*), the impression given in the Perspective is that cells from uninfected individuals do not undergo detectable apoptosis under similar conditions. This is not so. We and others routinely detect "background" apoptosis in as many as 10 to 15% of mature T cells from uninfected individuals after activation for 3 days with polyclonal stimuli (*2, 3*). This background apoptosis is large enough to produce the "DNA ladder" typical of apoptosis when DNA from these cultures is assayed on agarose gels. Thus, although HIV may well accelerate and increase apoptotic cell deaths after in vitro activation, this is not an all-or-nothing phenomenon.

Second, Gougeon and Montagnier also suggest that "the time has come to fight this complex disease by combinations of several treatments including antivirals, antibiotics, and anti-apoptotic drugs." Because the role of apoptosis in HIV-induced T cell depletion in vivo remains to be elucidated, this may or may not be true. However, as apoptosis is the normal physiological cell death mechanism (and as such is vital for the control of proliferating cell populations and for the deletion of autoreactive T and B cells), drugs that can inhibit HIV-induced apoptosis may also interfere with apoptotic cell death in many other cell lineages. This possibility warrants at least a passing mention. In addition, apoptosis-inhibiting drugs may be ineffective on syncytium-inducing (SI) HIV

variants, because although the demise of a syncytium may be delayed by anti-apoptotics, such cells, by virtue of their sheer size alone, would be functionally dead anyway. This is an important consideration, given the observed correlation between accelerated $CD4^+$ T cell depletion and the emergence of SI viral variants in HIV-infected individuals (*4*).

Finally, although indirect mechanisms for apoptosis priming in HIV-infected individuals (such as gp120 crosslinking of CD4) as discussed by Gougeon and Montagnier are attractive, it is important not to lose sight of the fact that direct cell killing (by apoptosis or necrosis) could equally well contribute to the profound $CD4^+$ T cell depletion seen during HIV infection. Recent reports (*5*) reveal a much higher viral load in both peripheral and lymphoid T cell populations during the latent period of HIV infection than was previously thought to exist.

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Response: We did not say that apoptosis in HIV infection was an all-or-nothing phenomenon, but we stressed the significance of observing increased apoptosis in lymphocytes of HIV-infected patients under two different conditions: (i) in culture in medium deprived of activating factors and cytokines and (ii) upon in vitro activation. The first phenomenon, "spontaneous" apoptosis, may reflect an abnormal activation of a large fraction of T lymphocytes during HIV infection. In a recent study (*1*), we observed that most of the $CD4^+$ and $CD8^+$ cells dying spontaneously after up to 24 hours of incubation in culture had the phenotype of activated cells and expressed the CD45R0 antigen, an activation marker. This apoptosis, which involved about 2 to 10% of peripheral T cells in healthy (control individuals) and 5 to 40% of T cells in HIV-infected individuals, was also found during the acute phase of Epstein-Barr virus (EBV) infection (infectious mononucleosis) (*2*) and, as we described for HIV-infection (*3*), it concerned both $CD4^+$ and $CD8^+$ T cells which harbored the CD45R0 phenotype. Thus this in vitro–induced spontaneous apoptosis could be a more general process occurring in the course of many infections, and such in vitro cell death may be only the consequence of cytokine deprivation of activated cells outside their natural environment. What is striking in HIV infection is that such abnormal activation is continuous and lasts during the whole course of the preclinical and clinical stages of the disease.

This "spontaneous" apoptosis must be distinguished from the apoptosis induced by in vitro activation. Indeed, mature peripheral T cells generally respond to T cell receptor stimulation by cell proliferation and cytokine secretion, and a background rate of apoptosis can be observed after several days of culture, as mentioned by Martin, possibly resulting from decreased amounts of cytokines in the culture or from some negative regulation. However, the mechanism of this late-occurring apoptosis is probably different from the one we and others (*3*, *4*) observed after activation of patients' lymphocytes: less than 24 hours after T cell receptor stimulation, rates of apoptosis significantly higher than background (spontaneous) apoptosis were observed. The rapidity of this phenomenon indicates that the cell death is a direct consequence of the activation process and suggests that a cell death program has been

previously induced in these cells that can be triggered by specific cell activation. In this respect, a body of evidence has shown that, after stimulation, the secretion of lymphokines (such as IL-2) actually predisposes T cells to apoptosis when there is further antigen receptor stimulation.

Another point discussed by Martin concerns our views on the mechanisms of CD4 cell depletion in AIDS pathogenesis. We are convinced that direct cell killing must contribute to CD4 cell depletion, especially in light of a recent analysis of viral load in lymphoid organs (5). We believe that continuous and profound CD4 cell depletion is the result of multiple mechanisms, as we mentioned in the first paragraph of our Perspective. In addition, we believe that the possible impairment in T cell renewal may contribute, to some extent, to the CD4 cell depletion.

Finally, Martin argues that combinations of antivirals, antibiotics, and anti-apoptotic drugs may interfere with apoptotic cell death in other cell lineages. Actually the goal is not to suppress apoptosis (which might be almost impossible to achieve and might be dangerous in that it could induce autoimmunity and favor cancers), but to reduce apoptosis to a normal rate in lymphocytes of HIV-infected patients. This could be accomplished by acting on the causal agents that lead to apoptosis (virus, microbial factors, free radicals) or during the many steps of the apoptotic process.

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NSF: A New Name?

The ScienceScope item "NSF: What's in a name?" (3 Sept., p. 1263) about the reaction to a proposal by the American Association of Engineering Societies (AAES) to rename the National Science Foundation (NSF) the National Science and Engineering Foundation is not an accurate reflection of the full picture. Many engineering professionals and at least 14 other engineering and technical societies, with more than one million members support this proposal.

In 1985, Congress broadened the NSF Organic Act to provide a statutory emphasis for engineering research and education equivalent to that of science. The name change would highlight this broadened emphasis and would foster greater recognition of the co-equal role that engineering plays with science in the research enterprise. This proposed change seems consistent with the spirit of the report of the National Science Board's Commission on the Future of NSF (*1*), which called for the allocation of NSF's resources with two goals in mind: "support of first-rate research *at many points on the frontiers of knowledge . . .*" (emphasis added) and a "balanced allocation of resources in strategic research areas. . . ."

Changing the name of NSF would not require Congress to redirect the Foundation's mission away from fundamental research. The engineering community vigorously supports the NSF programs that provide grants for fundamental science and engineering research to individual investigators and university research centers as vital to maintaining the research base at academic institutions. The engineering profession is a beneficiary of the results of