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LETTERS

Neuroscience at NIH

Regarding the ScienceScope item "Neuroscience tiff at NIH" (6 Nov., p. 879), let me correct any misimpression the reader may have received. Neuroscience was, is, and will continue to be a critical element of the strategic plan for the National Institutes of Health (NIH). It is singled out as a major objective in the critical science and technology area. To quote from the strategic plan, "Two particular areas of extraordinary importance and promise are neuroscience and developmental biology." The plan goes on to identify not only basic neuroscience research but also analysis technologies, such as nuclear magnetic resonance imaging, and positron emission tomography, as areas of emphasis. The notion that neuroscience was left out of the strategic plan is incorrect.

Regarding the issue of space allocation on the NIH campus, as in most major academic and corporate institutions, such allocation is determined on the basis of merit, and merit alone. As in basic research, we must respond with flexibility to opportunities and to areas with promise.

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NIH Expenditures: Extramural Versus Intramural

A letter from Charles A. Gardner (23 Oct., p. 530) suggests that "no one has tried to compare the efficiency of a dollar spent on extramural versus intramural [NIH] research." In fact, in response to that exact question, the intramural National Institutes of Health (NIH) record was documented in congressional testimony on 23 September 1992, before the House Budget Committee Task Force on Human Resources, chaired by Representative James L. Oberstar (D-MN). Even though the intramural program receives only 1 of every 10 NIH dollars, the output per dollar as indicated by citation frequency, publication impact in top journals, and speed of translation of discoveries from the bench to the bed was two to four times greater than that for extramural expenditures. More important, without the intramural NIH program, recent fundamental scientific discoveries, such as the development of gene therapy, of AZT, ddI, and ddC (the only approved drugs for the treatment of AIDS), of taxol treatment of ovarian cancer, and 200 other discoveries listed at the hearing might have been significantly delayed or might not have happened at all.

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Regulations for Genetically Engineered Foods

We appreciated the essay by David A. Kessler *et al.* of the Food and Drug Administration (FDA) elaborating on their reasons for deregulating oversight for genetically engineered foods (Policy Forum, 26 June, p. 1747), but we feel it is important to also present reasoned arguments in favor of stronger regulation than the Bush Administration has offered.

Our concern with the FDA's approach—which allows the industry to decide which products should be evaluated for risks and which do not require any labeling or other consumer information about the presence of genetic modifications in the foodstuffs being consumed—is that the government's approach does not follow what has been called "the precautionary principle." The basis of this approach would be that, unless a novel technological procedure is assuredly free of risk, there ought to be assessment in advance of the impact, including estimation of risk probabilities. In addition, under this approach the burden of proof for demonstrating that the risks are acceptable would fall on the proponents of the new technology.

Underlying the reasoning in the Policy Forum by Kessler *et al.* is a scientifically questionable premise. In this view, if genes from one well-characterized and benign species, say peanuts, are inserted into the genome of another organism that is well characterized and benign, for example, tomatoes, the result is considered to be necessarily well known and benign and need not be assessed in advance. Yet in calculating any risk from a transgenic organism, one should consider four elements: the host organism, the foreign genes, the interaction between the foreign genes and the rest of the genome, and the environment in which the organisms will be used. Although the FDA's proposed policy focuses on the first two elements, the literature contains many examples of genetic ma-

nipulations where inserted genes did not respond in their new environments the way they did in their old ones or where alterations with one part of the genome caused surprising activity in other parts of the genome (*1*). Kessler *et al.* even refer to the possibility that genetically engineered food might "contain high levels of unexpected, acutely toxic substances." The proposed FDA policy does not take this uncertainty into account. It is our belief that regulatory policy must recognize that we are not omniscient about the interactions that occur within and between various parts of a genome.

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NOTES

1. See, for example, D. MacKenzie, *New Sci.* **128**, 18 (15 December 1990); *Economist* **315**, 83 (14 July 1990); J. Jenkins *et al.*, "Field test of transgenic cottons containing a *Bacillus thuringiensis* gene" (Technical Bulletin 174, Mississippi Agricultural and Forestry Experiment Station, Mississippi State University, Starkville, MS, 1991); V. G. Pursel *et al. Science* **244**, 1281 (1989); J. L. Marx, *ibid.* **242**, 32 (1988); N. Danhash *et al.*, *Bio/Technology* **9**, 179 (1991).

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IL-1β and *Escherichia coli*

The report "Enhancement of growth of virulent strains of *Escherichia coli* by interleukin-1" by R. Porat *et al.* (18 Oct. 1991, p.430) (*1*) was praised by many scientists and was reported in the *New York Times* (*2*). Nearly 20 years ago, one of us (K.S.K.) performed similar experiments in which the actions of interferons on strains of pathogenic bacteria were tested, and no reproducible effect was seen (*3*). We set up the experiment performed by Porat *et al.* (*1*) in order to study the properties of *E. coli* that affect bacterial resistance to host defense mechanisms. The report (*1*) indicates that all six "virulent" strains resistant to human serum were enhanced in growth when 100 nanograms per milliliter of interleukin 1β (IL-1β) were added in culture and that growth was enhanced by as much as tenfold after 3 to 4 hours of incubation [figure 1 of (*1*)]. In contrast, four "avirulent" human serum–sensitive strains were not responsive. Growth enhancement was reported (*1*) to be specifically blocked by the IL-1 receptor antagonist. Porat *et al.* calculated 20,000 to 40,000 IL-1β binding sites per cell on the basis of studies of radiolabeled IL-1 binding.

We examined three human serum–resistant strains of *E. coli*, including one freshly isolated from the blood of a bacteremic patient. We used an *E. coli* K12 strain as a control. The experimental conditions used were identical to those in (*1*), including the two culture media (BH1 and RMPI 1640). We used recombinant human IL-1β from BioSource International (Westlake Village, California) with a specific activity of 10^7 units per milligram. Three attempts to reproduce the findings reported in (*1*) were unsuccessful. IL-1β had no growth stimulatory effect on the tested strains. Although the strains grew much better in BH1 than in RPMI medium, the growth rate and final yield of cells after 10 hours of cultivation varied, which apparently reflected the characteristics of each strain.

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REFERENCES

1. R. Porat, B. D. Clark, S. M. Wolff, C. A. Dinarello, *Science* **254**, 430 (1991).
2. G. Kolata, *New York Times*, 18 October 1991, p. A18.
3. K. S. Kim, L. Gobel, J. Vilćek, unpublished data.

Response: We reported (*1*) a two- to tenfold increase in bacterial log phase growth when virulent bacteria were freshly obtained from the blood of bacteremic patients and exposed to IL-1; avirulent bacteria did not respond to IL-1. However, we subsequently reported that when the bacteria were passaged in serum or broth, or kept at −20°C for several weeks, they lost their responsiveness to IL-1 (*2*). This result has also been observed by other investigators (*3*). We did not appreciate these phenomena at the time of our initial report (*1*).

We have since tested IL-1–induced growth-enhancing effects on 64 *E. coli* strains. We have not found responses to IL-1 as high as those we originally reported in (*1*). We have isolated strains that respond to IL-1 significantly ($P < 0.05$), but growth was enhanced by a factor of only 1.5 to 2 (Fig. 1). These strains represent approximately one-fifth of the isolates. However, we believe that growth factors derived in vivo may contribute to the responsiveness to IL-1 and other cytokines.

Other investigators have observed increased growth of different microorganisms with the use of human cytokines (including IL-1, IL-2, and IL-6) or granulocyte-macrophage colony-stimulating factor and have found specific receptors for human cytokines on bacteria and fungi (*4*). Moreover, there are many reports of receptors for various mammalian proteins on bacteria (*5*).