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*).

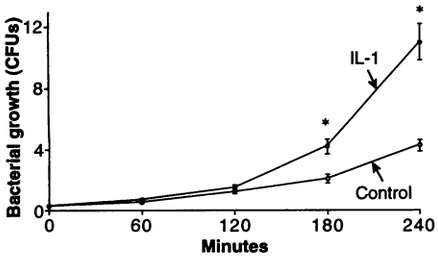


**Fig. 1.** Growth of a virulent *E. coli* strain incubated in RPMI, with and without recombinant human IL-1β at 100 nanograms per milliliter, determined by direct colony counts. Results are expressed in mean colony forming units (CFUs) × $10^5$ ± SEM with four experiments. *, $P < 0.05$, Student's *t* test.

We sent one of the newly isolated IL-1–responsive *E. coli* strains to Kim and Le, who did not confirm the growth-promoting effect in their laboratory. The strain was returned to us, and we again observed a growth-promoting effect of IL-1, using direct colony counts. We invited Kim and Le to come to Boston to observe our methods, but they declined our invitations. Therefore, we cannot explain this discrepancy.

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## REFERENCES

1. R. Porat, B. D. Clark, S. M. Wolff, C. A. Dinarello, *Science* **254**, 430 (1991).
2. ———, in *Cytokines and Regulation of Disease*, A. Mantovani and P. Ghezzi, Eds. (Liss, New York, in press).
3. M. Denis, personal communication.
4. H. Shiratsuchi, J. L. Johnson, J. J. Ellner, *J. Immunol.* **146**, 3165 (1991); M. Denis, *Cell. Immunol.* **141**, 182 (1992); C. B. Treseler, R. T. Maziarz, S. M. Levitz, *Infect. Immun.* **60**, 183 (1992); M. Denis, D. Campbell, E. O. Gregg, *ibid.* **59**, 1853 (1991).
5. L. Visai, P. Speziale, S. Bozzini, *Infect. Immun.* **58**, 449 (1990); M. Ullberg, G. Kronvall, I. Karlsson, B. Wiman, *ibid.*, p. 21; J. S. Padda and A. B. Schryvers, *ibid.*, p. 2972.

## Corrections and Clarifications

In the letter of 23 October by Charles A. Gardner (p. 530), Dr. Gardner's address was incorrectly given as the Subcommittee on Human Resources and Intergovernmental Relations of the House Committee on Government Operations. Dr. Gardner was a AAAS Congressional Science Fellow assigned to that subcommittee through August 1992, but the views expressed in his letter were his own and not those of the subcommittee.