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LETTERS

Business and Science

As the discoverer of *Thermus aquaticus* (*1*), the organism that is the source of Taq polymerase, I continue to be amazed at what has happened to our science as the result of the "biotechnology" revolution. I refer specifically to the 4 December News & Comment article by Peter Aldhous (p. 1572) stating that Hoffmann–La Roche is taking to court companies who produce and sell this enzyme for use in the polymerase chain reaction (PCR). As I understand it, Cetus took an organism that I freely deposited in the American Type Culture Collection, isolated an enzyme from this organism, and sold the patent to Roche, who now claims a royalty on every use of this enzyme for a particular laboratory procedure. I am not concerned about the money involved, but with how such practices (legitimate or not), stifle the development of scientific research. Where would biology and medicine be today if Walther and Fannie Hesse had patented the use of agar in the plate culture technique that Robert Koch developed in 1882? Agar is a natural product, like Taq polymerase, and the plate culture technique is a laboratory procedure, like PCR. The agar plate technique revolutionized medicine in a manner analogous to the PCR method.

Who do these business types who have sneaked into our scientific research community think they are?

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Measles Vaccine: Titre and Safety

The article "Measles battle loses potent weapon" by Rick Weiss (Research News, 23 Oct., p. 546) discusses the Edmonston-Zagreb (E-Z) measles vaccine, developed by the Institute of Immunology in Zagreb. I would like to comment on some points that may not have been clear. First, the E-Z high-titer vaccine (which contains 10 to 100 times the usual concentration of virus) has been successfully given to Mexican infants (*1*) with no reported death rate that was higher than expected. This contrasts with the puzzling observation that an unusually large percentage of infants given the high-titer E-Z vaccine in Guinea-Bissau died from diseases *other than* measles. Second, Weiss does not mention that another high-titer measles vaccine (Schwarz) has been used with delayed effects similar to those of the high-titer E-Z vaccine used in Guinea-Bissau; thus the problem may be with high titers, not with the E-Z vaccine itself.

Finally, it should be emphasized that the E-Z vaccine has been used in many countries in Europe, Asia, Africa, and Latin America. Millions of vaccinated children have been protected and have not shown side effects. The E-Z vaccine, given in a standard dose, has been approved by the World Health Organization. A recent conference report stated (*2*)

> The evidence examined at this meeting supported the continued use of standard measles vaccinee for all infants in immunization programmes. Standard measles vaccines have been shown to be safe and highly effective and have resulted in significant reduction in morbidity and mortality in numerous countries throughout the world. Measles immunization is generally considered the most cost-effective public health intervention available.

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1. L. E. Markowitz *et al.*, *N. Engl. J. Med.* 332, 580 (1990).
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My colleagues and I spent 4 years studying the Edmonston-Zagreb (E-Z) vaccine while doing field research in a rural area of Senegal. Our conclusions with respect to the safety, immunogenicity, and efficacy of this vaccine given at high titer early in life were different from the results of previous studies. In a clinical efficacy trial (*1*), we found a much higher rate of vaccine failure when the high-titer E-Z live measles vaccine was given to infants 4 to 6 months old than when the standard measles vaccine was given to infants 9 to 10 months old (which was the strategy recommended by the World Health Organization for Africa).

The rationale for the recommended use of the high-titer E-Z vaccine was the higher immunogenicity it provides when given to infants 4 to 6 months old and the hope that it would "pass the barrier of maternal antibodies." However, the study done in Mex-

ico (2) showed there was less seroconversion the higher the concentration of maternal antibodies at the time of vaccination. In our Senegal study (3), we also found no clear evidence of seroconversion among children with high concentrations of maternal antibodies. In fact, most of the clinical vaccine failures occurred in children with high concentrations of maternal antibodies at the time of vaccination. Most other studies did not provide an extensive tabulation of immunogenicity according to concentrations of maternal antibodies.

Scientists who have worked with the E-Z vaccine have observed that the virus infects cells in a different way from the Schwarz vaccine virus. This has complicated the definition of the titer of the vaccines, which is based on evidence of cell infection. There is still a wide variation in the estimates of vaccine titer between laboratories; these estimates span the threshold that distinguishes high-titer vaccines from medium-titer vaccines (4). The excess mortality associated with the high-titer E-Z vaccine was an unexpected development for investigators; there was early enthusiasm for it, and negative findings tended to be ignored.

To solve the problem of early measles mortality, more effort could be devoted to case management, which reduced the measles case-fatality rate by 73% in Senegal, a result similar to that produced by vaccination (1). Although more costly than vaccination, case management is an important complement to immunization.

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Research in Japan

The article "Japanese academics bemoan the cost of years of neglect" by Alun Anderson in the special issue devoted to science in Japan (23 Oct., p. 564) discusses the problem of practices in Japan that "are not exactly welcoming" to foreigners. I believe that the Japanese research community is making great efforts to overcome this problem. Over the past 2 years, as an American living in Japan, I have seen the Department of Public Health in the Faculty of Medicine at the University of Tokyo reach out to the international community. They hosted the Fourth International Symposium on Neurobehavioral Methods and Effects in Occupational and Environmental Health, sponsored by the World Health Organization and the International Commission on Occupational Health in 1991, and offered me and a visiting industrial health physician scholar from Belgium the opportunity to collaborate together on a public health study. In our case at least, there has been no lack of opportunity.

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The special issue on science in Japan did not mention one of Japan's most impressive recent accomplishments—a demonstration of the utility of fuzzy logic in industrial applications. Fuzzy controllers, for example, have been shown to be competitive in performance and cost. Their early use gave Japanese industries a technological advantage and impressive revenues. Moreover, fuzzy controllers have been designed for some control tasks that are beyond the capabilities of classical controllers: Michio Sugeno of the Tokyo Institute of Technology successfully tested one that controlled a pilotless helicopter by simple vocal commands (1). Other applications in knowledge engineering, robotics, medicine, and economics are opening ever greater opportunities for innovations in fuzzy logic.

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Brain Research in Europe

In the article "An uncertain start for a brain decade" by Peter Aldhous (News & Comment, 2 Oct., p. 23), it is stated that the ad hoc task force implemented by the Commission of the European Community (CEC) for preparing a "Plan of Action" for the European Decade of Brain Research is being dominated by neuropsychiatrists and that the scientific program is mainly focused on clinical research and not enough on basic neuroscience. As president of the task force, I would like to clarify these issues. First, the task force is composed of experts from preclinical neuroscience, including executive members from the European Neuroscience Association and other European societies, and experts from clinical neuroscience. The composition of the task force is balanced. As reported in the article, some parts of the scientific program are still being developed. The task force is guided by the principles of balance between basic and clinical neurosciences, interdisciplinarity, and communication among all neuroscientists. The introduction of the scientific program states

> An understanding of the functions of the brain represents one of the greatest intellectual and scientific challenges to mankind, and at the same time will bring far-reaching practical applications which may contribute to solve the major brain-related medical and psychosocial problems. Science has just reached the point where the enabling technologies for this long-dreamt-of goal have been developed: neuroscience has undergone a major revolution in the last few years, on the basis of the new capabilities created by molecular biology and genetics, by space-age instrumentation, and by information technology.

Encouraging collaboration with the industry is important for both applied and basic research. The final version of the "Plan of Action" will have contributions from the relevant societies and the scientific leaders from Europe representing both basic and clinical neuroscience. It is essential that this program be approved and funded at an appropriate level without further delay.

If these objectives are achieved, all neuroscientists in Europe will benefit.

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Fetal Transplant Update

I would like to clarify some of the information in the article by Larry Thompson "Fetal transplants show promise" (News & Comment, 14 Aug., p. 868). We have now performed transplants on 54 patients at the University of Birmingham in the United Kingdom, 48 of which were reported (36 in detail) at the Fourth International Symposium on Neural Transplantation (held from 12 to 16 July 1992 at the George Washington University School of Medicine in Washington, D.C.). None of our patients has died as a result of the transplant oper-