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LETTERS

NIH R&D Priorities

I must object to the way Jeffrey Mervis, in his 3 June News & Comment article (p. 1395), portrays my views about the 6 May memorandum on fiscal year (FY) 1996 research and development priorities signed by John Gibbons and Leon Panetta. In an interview with Mervis specifically related to the memorandum, I strongly supported the effort to lay out principles, goals, and priorities for development of FY 1996 agency budgets. I also told Mervis that I agreed with the specific principles and priorities that were selected and said that the scientific community would applaud an emphasis on peer review, investment in human resources, and fundamental science. The comments Mervis attributes to me were drawn from a talk I gave on 24 May at a public policy meeting of the American Society for Biochemistry and Molecular Biology; that talk did *not* relate to the memorandum by Gibbons and Panetta, but was aimed at explaining the specific hard choices that have to be made in today's difficult climate as we shape budgets for the National Institutes of Health and distribute funds among the institutes.

Harold Varmus
Director, National Institutes of Health, Bethesda, MD 20892

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Risks in Using Transgenic Plants?

The recent report by Ann E. Greene and Richard F. Allison, "Recombination between viral RNA and transgenic plant transcripts" (11 Mar., p. 1423), raises safety issues about the field release of transgenic plants. In their Perspective in the same issue (p. 1395), Bryce Falk and George Bruening come to the conclusion that there is probably no greater chance of recombination producing a dangerous new virus than of two viruses jointly infecting a nontransgenic plant. What was not brought out in the Perspective was that recombination is just one of the potential risks of using transgenic crops and that there are ways of minimizing undesirable effects.

The expression of viral sequences in transgenic plants is designed to confer protection against the donor virus and related strains. The major question that arises is, what is the possibility of an interaction between the products of a transgene and an unrelated superinfecting virus? There is a wide range of approaches to this nonconventional protection strategy (*1*) and at least one of them, that of inducing crop plants to express viral coat proteins to give viral protection, will be commercialized soon. The coat protein of many viruses confers the specificity of interaction with the vector (for example, insect, nematode, or fungus) that naturally transmits the virus. This raises the possibility of a transgenically produced coat protein encapsidating the genome of a superinfecting virus, thus changing its vector specificity. There are examples of this heteroencapsidation between related and even unrelated viruses occurring in transgenic plants (*2, 3*).

The argument that these interactions rarely happen in natural joint infections and are thus unlikely in a transgenic situation is open to question on several counts. First, most of these interactions, except for that of heteroencapsidation between related viruses (*4*), have not been sought experimentally, and molecular studies that could reveal such interactions have not been widely applied to field situations. Second, heteroencapsidation or recombination will only take place when a viral genome is exposed, that is, when it is being expressed or replicated. There is strong evidence that this occurs in different cellular compartments for different viruses, but there is no information as to whether the products of transgenes are similarly compartmentalized. Third, the use of transgenic plants will involve their wide-scale deployment, thus increasing the potential for risk (risk = hazard × frequency). This leads to a dilemma as to whether to undertake wide-scale field releases of such transgenic plants—this is the only situation in which current issues can be resolved, but if a problem were to arise, it would then be too late to correct it.

Is there any way that these problems can be bypassed? There is evidence, at least with some viruses, that the region of the coat protein that determines vector specificity is not important for protection against viral infection (*5*). Thus, one can effect biological containment by rendering a protein incapable of vector interactions while maintaining its capacity to afford viral protection. This approach to biological containment could have application to all virus-related transgenes. What is needed is an understanding of interactions that might lead to undesirable properties of a transgene product so that a gene could be refined or tailored to remove "bad" features while