

STANFORD UNIVERSITY MEDICAL CENTER

DEPARTMENT OF GENETICS

June 14, 1977

Dr. Donald Fredrickson
Director
National Institutes of Health
Washington, D.C. 20014

Dear Don:

I learned recently -- I have to say from a newspaper reporter -- that questions have been raised about the biohazard implications of transfection experiments recently published from my laboratory involving *Staphylococcus* and *Bacillus subtilis*. I understand further that one of your committees in the NIH is pursuing the question whether the regulation of recombinant DNA research should be extended to embrace other forms of genetic exchange.

You are, of course, cognizant that, at my encouragement, Dr. Ehrlich promptly reported these findings -- even before they were submitted for publication -- to Dr. Gartland in the belief that these aspects of the natural history of bacteria would be pertinent to the current discussions about the development of regulatory procedures.

During several months of further scientific discussions of this subject, and the submission of this material for (re-) review by an NIH Study Section, I had no intimation that this was viewed as a hazardous experiment. To the contrary it seems to show that some concerns about "artificial hybrids" may be based on a faulty premise about what goes on in nature. I have to speculate that just this rationale is the source of what may be a counter attack.

In the same vein, I believe that it is appropriate for me to communicate some additional findings of our continued work with this system, being pursued by one of my graduate students, Mr. Jerald Feitelson and myself, even though we are just in mid stream and have some hesitation about the "publication" of results before they have been repeated and controlled many more times.

What I have to say is not really surprising from a theoretical prediction, but needed to be established empirically. The exchange of a plasmid from *Staphylococcus* to *Bacillus* occurs quite readily in mixed cultures of these bacteria if the lysis of *Staphylococcus* cells is promoted by the addition of penicillin. It is not even necessary to go through the steps of a purification of the *Staphylococcus* DNA to accomplish the genetic transfer. We are continuing to look at the question of even simpler circumstances that might still facilitate this type of genetic exchange. I am quite confident, however, that there is no barrier to its occurrence in nature; and that if there is an urgent public need to prevent the uncontained genetic interaction of *Staphylococcus* with *Bacillus*, we will have to legislate against people sneezing in the open

June 14, 1977

country. (For as you surely are very well aware, a great many healthy individuals are carriers of plasmid-carrying Staphylococcus strains in their respiratory tract).

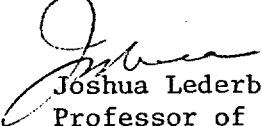
You will have heard many arguments already about public policy motivations for regulating laboratory research. I will not persevere in that direction. I do feel it necessary to caution against attempts to legislate against natural phenomena, however, we might wish they did not occur. Else we would be in a posture like that of attempting to declare that $E \neq MC^2$ as a way of coping with the problem of nuclear proliferation, or of declaring that microbial evolution does not occur in nature, as a way of coping with infectious disease. If cell-biological interaction between bacteria is subject to interdiction, there will be grave problems of defining what is a prohibited act. It will be impossible to contrive mixed cultures of micro-organisms and guarantee that genetic exchange is not occurring. No microbiology whatsoever can guarantee that the cultures are not mixed. In the end we will be putting restraints on laboratory work per se, when similar processes -- and here I evoke sneezing quite literally -- of an everyday kind are beyond any possible scope of regulation.

Granted any premises whatever about the conceivable biohazard of 'in vitro' constructions of DNA segments, one then can conceive of an applicable framework to govern those constructive acts. Efforts to apply the same principles to natural phenomena are doomed unless the intention is to impose the most serious inhibitions and stigmata on all microbiological and eventually all biological research.

If there is a real desire to reduce the biohazards that afflict us everyday, it should be directed to facilitating rather than hindering research on the evolution of pathogenic micro-organisms and on their transmission from person to person. Cleaning up the infectious load in public places, and detecting and containing early virus infections transmitted by people who circulate with their disease throughout the community, would be far more realistic measures than what is being attempted in these days under the banner of an anti-Frankensteinian crusade.

A similar parable would be to require that every patient suffering from undiagnosed or infectious disease be subject at least to 'P-2' containment within a hospital: after all, until the infection has been diagnosed who can guarantee that it will not be harbinger of the universal pandemic? (And, of course, this must still be done within the cost containment criteria demanded by other public policy considerations.)

Yours sincerely,



Joshua Lederberg
Professor of Genetics

Dr. Donald Fredrickson

-3-

June 14, 1977

P.S.

Yes, it is difficult for me not to be bitter about the current situation. For some time I tried very hard to see it as a legitimate controversy connected with actual concerns about biohazard. It is becoming increasingly apparent that this is really a screen for much more deeply rooted ideological campaign for "the social control of science" and, in turn, indeed for the doctrinal containment of inquiry.

Forgive me, in my previous correspondence, for having tried to detain you with questions about how to improve the efficiency of technology transfer to health applications, and how to prevent the stultification of research in the course of misapplications of the peer-review-project system. We are evidently all in a life-or-death struggle to keep research possible at all!

A handwritten signature in cursive script, appearing to read "John", followed by a period.