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Department of Medical Genetics

May 8, 1957

Mr. Dennis Flanagan
Scientific American
415 Madison Avenue
New York 17, N.Y.

Dear Mr. Flanagan:

Thank you for your letter of May 6.

You have an interesting proposal, and one I would like to think more about. If I were not rather busy with other writing commitments, with some administrative duties, and with a trip to Australia coming (August 1-November 15) I would be less cautious. However, if it were possible to proceed without a fixed deadline, we might go ahead.

However, I must say that the Hotchkiss-Weiss article did not seem to me among the best of its genre in your magazine, or the best that could be done with that kind of subject. Perhaps you have a lower but more realistic estimate of your public's ability to assimilate genetic concepts in more abstract terms. I am quite prepared to admit that my own ms. on a related topic (Genetic Transduction) erred in the opposite direction, and I would hope there is a happy mean. But I suppose that genetics is almost certain to be one of the more difficult areas to popularise, since our conclusions rest on such an extended chain of inferences. It turned out that my writing that article at least towards, if not successfully for, the Scientific American was a happy mistake, by helping it find a most suitable home in the American Scientist which is presumably a more sophisticated vehicle. A copy is enclosed for your interest.

For some of these reasons, and also because the subject has been rather thoroughly anticipated, I do not think it would be wise to go ahead with another article on bacterial-genetic recombination. In its place, I would mention that I have been spending some time lately on another (distantly related) topic, the role of bacterial cell-walls in their behavior and life-cycles. For a long time the "L-forms" of bacteria have been an obscure but provocative problem that many bacteriologists have wanted not even to think about, for lack of any rational approach to them. Many workers have ascribed an almost mystical significance to L-forms as part of the life-cycle of bacteria, even as representing the possible inter-transformability of bacteria into rickettsia and viruses. Our own work, based on that of many others, now helps to rationalize the subject, insofar as the "L-forms" appear to be the kind of growth form which bacteria can assume if they are deprived of their rigid walls. They can be so deprived either by external inhibition, or by an internal metabolic block of genetic origin. Indeed, the mechanism of

action of penicillin has been elucidated by this group of studies as precisely the inhibition of bacterial wall synthesis, the unique therapeutic specificity of this antibioticthus resting on the unique chemical makeup of the bacterial cell walls, which has no counterpart in the mammalian cell.

We have published only a couple of preliminary notes on this subject, which I am sending. Some time before we leave for Australia, I hope to have done a more comprehensive ms. In connection with that, I hope to be able to send you a draft of a paper for S.A. But if that doesn't work out, then I'll send the technical paper for Miss Weiss to redo. In any case, I would not want the S.A. article to appear in print before our technical contribution.

It seems to me this topic should lend itself far better than more abstract genetics for S.A. It has a definite but not too prolonged a history, the problem can be stated in rather concrete terms, and above all both the problem and evidence to its situation can be given photographically, e.g., in a sequence of photomicrographs that shows the evolution of a protoplast from a growing cell treated with penicillin.

Meanwhile, Miss Weiss might look over the enclosures, and some indicated references, and advise you and me on the suitability of the topic. The references are underlined in red pencil on the reprints.

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Yours sincerely,

Joshua Lederberg
Professor of Medical Genetics