

February 25, 1958

Dr. Sol H. Goodgal
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Dear Sol:

I should have acknowledged your letter and shipment of cultures before this but I had hoped to be able to avoid bothering you again. I am really very sorry to be such a nuisance to you.

For the last few weeks I have been able to put some time into hemophilus work but unfortunately my transformation experiments have been rather unrewarding.

This may well be because we have gotten such good growth on ordinary penassay medium that most of my experiments have been done with that. A few runs were done with the addition of defibrinated blood and that has not seemed to help.

It seems to me there are at least two things that might be at fault:

1. The potency of our DNA which we had received from you. This had, I am afraid, just been left in the refrigerator for several months and I have no independent test of its activity. I could of course simply go ahead and make our own preparations, but I hate to do that until we have a system of which we know the other parts are satisfactory.

2. A much more likely difficulty is a misunderstanding on my part of the conditions for competence. From your letter and from Shaeffer's papers, I conclude that there is a peak of competence near the end of exponential growth or perhaps early in the stationary phase. If I interpret correctly your letter of July 11, 1957, the purpose of adding glycerol and freezing is simply to stabilize the competent state of the cells. We have therefore not used this procedure but worked directly with the cell crop. One point that puzzles me is that you say you grow from a relatively small inoculum to a population density of 10^9 per ml with aeration. That part is all right. "Then transfer the cells to a smaller flask and grow without aeration or shaking an additional 90 minutes." Do you mean that you do this without adding any fresh medium?

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If that is the case you really are not permitting any appreciable further growth since a culture of that density is not likely to grow without aeration. Is it the purpose of transferring the cells to a smaller flask to further restrict the degree of aeration of the culture? In that case I might understand that competence is being induced by transferring a nearly grown culture to non aerobic conditions where over-all growth will now be strictly limited. If I could understand that conception as being correct, I could hope to duplicate the conditions more intelligently. What I have to ask of you is some discussion of this question and to try to beg from you another small quantity of a workable DNA preparation.

Does it matter if the DNA is added before the cells become competent? Or can the DNA be added to the culture at an earlier time so long as the cells are permitted to go through the stage of competence?

We are going to have a symposium on Genetics in Medical Research to be held here in April. I am enclosing a program. We have a very limited number of open spaces for dormitory facilities, but if you would be interested to attend I will try to reserve one for you! Please let me know.

Yours sincerely,

Joshua Lederberg
Professor of Medical Genetics

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encl.