

Joshua Lederberg
Madison, Wisconsin
June 4, 1956

Dr. Joseph Lein
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Dear Joe:

I was very pleased to hear your extended account of parent work and to see how smoothly everything is going both routine and exploratory. So I don't have very much to add right now except for a few casual comments.

Penicillin - I would imagine this agent would be most useful not alone, in view of its low therapeutic activity, but in combination with penicillin. Was it ever tried on that basis? I also believe that Cephalosporin B has a similar activity and might be worth looking at. Finally, do you know anything of Synnematin, which I believe is another penicillin derivative? Is this last material commercially available at the present time? I would be interested in getting a sample of it for trials in comparison with penicillin for the induction of protoplasts and would appreciate any information you may have about it.

I was interested too in the progress of your trials with lipase. Here is another substance I am trying to get a handy source of in connection with the same project and have the same request to make of you. What have you been using?

I didn't quite understand what you meant about the viscosity effects of various substances on the semi-solid agar. Do you mean that the medium failed to gel when these particular broths were used? What is your precise recipe in making up the medium with these broths? From what you said I wondered if you have been using a medium of the same consistency that we have, namely, one which is quite solid by casual inspection. I would be willing to bet that the major effect of Actinomycete broths would be primarily a matter of pH as it is a little hard for me to see what else can be influencing the rigidity of the agar-gelatin combination. Your comment on the fantastic toxicity of some broths to fish was interesting in the light of a previous suggestion that you look into your material as a possible replacement for Rotenone in the poisoning of lakes. There may be more of a market in this area than you had anticipated.

Your reaction to my suggestions about a virus splitter were rather amusing, but I hope you don't give up the idea completely. I am not sure that it would take an enzyme to accomplish the desired result, and my feelings about this particular approach are that it would be best followed up on a purely empirical basis once given the initial idea. Since we do have newly available, highly purified preparations of different viruses, why not?

I would be interested in some more details on the effect of Eserin on motility of E. coli. Did the very high levels of the drug that you had to use inhibit motility without inhibiting the growth of the bacteria? If you are interested in DFF, you can get samples from the Edgeworth Arsenal Station where the Army has been investigating this type of effect. I would suggest you simply write to the Commanding Officer there.

To: J. Lein

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In our last visit we discussed possible military applications of some of your atropine drugs. Have you taken this up at all with the Defense Department? I would urge that you not neglect this particular approach purely from patriotic motives. I don't know what interest your company would have in the matter, but I would also suspect that the Defense Department would be interested in sponsoring further development work in that type of area under contract and this is something also worth looking into.

We may be making two trips this summer that might interest you, Joe. The first is a possible excursion eastward that might make it possible for us to visit you at Syracuse around the end of July or middle of August. If that should turn out, how would that strike you? What the precise relevance of the second has for you, I don't know, Joe, but there is also a possibility that I will be traveling to Tokyo, Japan the first week in September as a U.S. supported delegate to the International Genetics Symposium there. If you or Amel have any comments to make on a trip of this kind, I'd be glad to hear them.

Thanks for your comments on the yeast activity. Bob Wright has been in touch with Lindegren lately and got what must have been a very similar recipe and this has been rather useful.

In regard to your anti-glucoses, it occurs to me that if you are going to handle your tests on a diffusion plate assay basis, you might do just as well to use a straight-forward indicator like bromocresol purple rather than Eosin methylene blue agar for the test. The reason for this is that EMB agar is rather tricky in trying to interpret results of uniformly spread plates although it is the ideal medium when you are trying to detect sectors of non-fermenting among fermenting colonies.

That's all for now.

So long.

Josh

JL:jlg