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Madison, Wisconsin
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Dr. Joseph Lein
Bristol Laboratories Inc.
Syracuse, New York

Dear Joe:

Welcome home!

I can see that you were as much seduced by Japan as has been every other one of my friends here who has been over there. We can't wait for the experience ourselves.

I am really delighted to hear that you are moving ahead on the substitutional chemotherapy program. I fully understand your position with regard to the virus application and will use my discretion. However, as I am sure you understand, you can hardly hope to keep a monopoly on a general idea for very long. Such notions usually crop up in many places at about the same time.

On the whole, I think it is a wise thing to start the exploration of this possibility with the system that you can most conveniently handle, namely, the antibacterials. If it should prove to be outstandingly successful, which would be rather much to hope for, then of course you would use your own judgment about the range of systems to apply it to.

A propos applications in tumor chemotherapy, I can see at least as much rationale in using the substituted products of E. coli against tumors as I can see the use of antibiotic broths. The time may come, however, when you may wish to consider as the sources of the substituted products, the tumor cells themselves.

Would you not expect that most antitumor agents would be likely to be quite toxic to early developmental stages? If so, then I would think that a measure for use in the extraction of some agents might be, for example, toxicity to growing chick eggs. Perhaps this is already much more cumbersome a technique than you would prefer to have.

The idea of using concentrated groups of metabolites as sources of substituted products is entirely sound. After all, from the broadest point of view what you are trying to do both in the actinomycet broth program and in this one is to get reasonable amounts of the largest possible variety of hitherto untested organic molecules. So it should hardly matter very much what your starting materials are.

The account of your progress in the delineation of antibiotics particularly active on synthetic medium sounds most exciting. Even if some of the compounds prove not to be of tremendous chemotherapeutic value, if nothing else, you may latch on to a series of very useful

anti-metabolites of specific activity. This question of the unique sensitivity of strain K12 does puzzle me. The only thing related to it that I can think of at the moment is that it and strain C and to a lesser extent strain B are among the most generally sensitive of E. coli strains to various colicins. It is hard to imagine what relationship they would have to the product you are now testing. K12 and C are, furthermore, both rather degraded from a serological point of view having long since lost most of the typical somatic antigens of E. coli group. If you will let me know how the results of your current tests of strain specificity work out, it might give me something a bit more definite to go on on what the unique sensitivity of K12 might be correlated with.

I am a little surprised that you are having much trouble growing many strains on the Davis medium. If you are aerating the cultures by bubbling, I would suggest that you supplement the through-put air with a little carbon dioxide, for example, by passing the air over some sodium bicarbonate before it enters the tubes. We have had some trouble from this source in the past.

À propos vitamin C, it looks as if someone has beaten you to the punch on this. While you were away in Japan, I sent Amel a sample of a product called "Daily C" which is precisely what I was speaking for. Whether this has any affect whatsoever on colds, who knows? Before Bristol or any of its affiliates got into this particular game, I would hope that there would be some laboratory experimentation, at least to substantiate possible antibacterial activity of such a preparation.

Esther and I are leaving Tuesday to attend a meeting sponsored by the Oak Ridge National Laboratory on Genetics of Somatic cells. Then after coming back Saturday, beginning the following week, we have our symposium here on Genetics in Medical Research. I am afraid this is going to be rather a chore, and that is one reason I hasten to answer your record now.

For these reasons, I have not anticipated coming down to Chicago, but if you will be there, I will reconsider the possibility of coming down for a day. If I do come down, I will look for you, but if you want to tell me what hotel you're staying at, this might be helpful. I will let you know if anything especially exciting turns up at the meetings.

À propos substitutional chemistry for tumor activity, I am sure that one of the reasons you mentioned using groups of materials was the prospect of getting analogues of nucleic acid components. Certainly one would want to push that aspect of it at least as hard as any of the others.

Dr. Cavallia-Sborga, with whom I had the luck to collaborate before, is going to be in the lab for just a couple of months this spring, and I am hoping to do some concentrated research for a change.

Signing off for now, with all best regards.

Yours,

Joshua

JL:ac

P. S. As your secretary is going to tell you, there is some dis-synchrony between our two machines. If you have too much trouble reading this disk, do you want me to go to the service agency here and adjust ours to your records, or vice versa? I was assured at the last occasion that this machine had been adjusted to the universal standard of speed, whatever that happens to be.

End.

Josh.