

YALE UNIVERSITY

DEPARTMENT OF MICROBIOLOGY

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Dear Josh:

I hasten to reply to your good letter of October 10, so that at least some of your questions can be answered while they are still "hot". As Ben said, I was in California most of the summer, and your letter arrived too late to be forwarded (we were travelling all of the month of August). When I arrived I found a pile of departmental problems, new staff people, and theses. Before I got all of this squared away I had to begin teaching, since I started off the main departmental course. Fortunately this ends for me at the end of this week, and except that I must again go off to California at the end of the week for a two week stay there I have nothing to do (except get off to the printer a complete revision of my chapter in Dubos). I think I have answered all of my mail which could be answered directly but things which require some "looking up" tend to get delayed.

For the problem in hand:

1. You are perfectly at liberty to make any mention of the high mutation rate you wish.
2. I was very much interested in Dr. Skaar's results. Although I have not yet gone over all of our data, particularly some of the stuff done this summer, I would say that your results differed from ours in that we have not yet found any evidence of segregation of Ms^+ from 58-278 S^r . We have crossed the latter with organisms resistant to chloromycetin, and also with some resistant to a substituted streptomycin which appears to have a different site of action and resistance pattern, and all of the prototrophs tested appear to be S^r . On the other hand we have found that in all crosses involving Ms^+ , with anything else, ~~we find that~~ practically 100% of the prototrophs have Ms^+ . Our last experiments were designed to throw some light on the high frequency of transfer of the latter, which is still not clear.

I must confess that we have not carried the question of mechanism very far; most of our work during the past year has been on the substituted streptomycins. However, in the course of this we have used materials which incidently do carry on the problem. My present thoughts on the matter are these: I have had the first paper on the properties of the high mutating strain in MS form for almost a year but have not sent it in because I was not entirely satisfied with some of the data and wanted to have more of the second paper in form before I sent in the first. I did report, however, to the U.S.P.H.S. what we did have and our plans on it for this year. I therefore feel some obligation to go ahead with part of it, anyway. ~~Will you~~ (One of the problems, for example, was the specificity of the high-rate of mutation. It does not appear to affect penicillin or chloromycetin resistance but the phage rates we have gotten appear to be higher than for some of the comparison strains). Will you let me work over what we have gotten when I come back from San Francisco at the beginning of next month and send you a summary. It may be that some of what we have in the second paper will fit in with what you have, so as to make a joint publication worthwhile; I will let you use your judgment on that and am certain you will give me a frank appraisal. Beyond that, I feel that your laboratory can carry the problem further than we could here, particularly since we have certain commitments to carry on the substituted streptomycin work as rapidly as we can. In other words, after the limits suggested above, I feel you can do better with this than I can and should go on with it as you like.

If you have any further thoughts on this, please let me know.