March 1, 1954

AIRMAIL

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Dear Bruce:

I have been postponing this letter for too long in hopes of getting something more explicit from you by way of an account of your microscopy and of your mapping experiments. But your remarks in that very amusing and delightful recording that you and Clive and Andy made have piqued me into writing now.

First, let me acknowledge that the reprints have just now arrived. I will, of course, also honor the requests on the postcards that you forwarded. It is rather amusing and astonishing how people will sometimes address these requests in cases of multiple authorship.

As I must have written to you at one time, I was doing some mapping work myself last spring. But at that time I was aware of the linkage only of the 543, 553 and SL13 stocks. As you say, the last of these is almost hopeless as far as any serious quantitative work is concerned. However, I did get slightly higher yields by using a stock derived from a trail which I believe I sent you as SW1048. In a sense this stock had been automatically selected for its potential transinducability.

I am not sure that I can follow the rationale of your mapping procedure. In regard to the 543 and 553 results I had of course gotten the same relations that you report, at least on a quantitative basis. However, whereas the transductions to SW543 will give rise to roughly equal proportions of the two types, depending on the precise stock used as the donor, all transductions to 553 have been almost exclusively of the gm type and it is only with some difficulty that one has been able to demonstrate any linked transductions except with the use of serum. This has implied to me that the Fla factor involved in this stock is so far removed from H_1 that there is simply a very high probability that the H_1 will not be carried in along with the Fla. I was not able to detect any quantitative difference in the yield of types with donors that might carry the 543 Fla^- or not. For this reason, I more-or-less abandoned attempts to map this region and these were the only workable factors at the time. It was from your letters that I later learned that there was additional useful material and godspeed to you in it. However, I hope that you will be able to clarify for me the logical basis of your mapping argument. It seems to me that even in the preliminary stages it would be of the utmost importance to establish the ratios of the types obtained and not merely a qualitative determination of whether they occur at all. One of your letters mentioned that SW543--x 28 gave no motile transductions. [illegible] Or do you mean that you get only single and no double transductions? This could be the most decisive argument, especially the comparison of SW543 as a donor with the Fla^+ mutant from it. How did that work out?

28 x SW1092

Do you have any more definite information on the inhibition of trails with specific sera in linked transductions? My results on this have been

rather ambiguous, but I am not absolutely certain that one would expect to get complete inhibition of motility of individual cells.

In connection with some experiments attempting to discover complementary crossover types, I had occasion to apply the technique of micromanipulation that I have been learning for the coli work to a couple of transduction experiments. I would appreciate it very much if you could give me some sort of summary of your own experiments in this line as you have been promising. I will endeavor to exchange accordingly. I am planning to say just a little about this at a meeting at Oak Ridge in April and I would, of course, like to be able to refer to your prior findings if you wish. My own results make sense in the following way: first, there is an interval of 2-4 generations of simple segregation of non-motile from motile cells that I would ascribe to nuclear separation. After this, one may get several kinds of sequence. The most frequent is an interval of up to 5 generations of biclonal reproduction, that is with both progeny of each division coming out motile. This process may then continue indefinitely in a few cases, giving a swarm, or may then terminate abruptly with each motile cell now initiating a "semi-clone" the equivalent in lineage of a trail. I have seen no further branching of these semi-clones even though I have followed several of them for intervals of 25 to 40 generations in all. (This does not mean, of course, that I have separated cells at each fission. The generations are calculated from the cumulative sum of the logs of the clone sizes at each separation of the single motile cell. The termination of a semi-clone was usually due to some accident but in a few cases it appeared to be spontaneous. I also made some direct transfers of semi-clonal motile cells to soft agar and none of them have yet given rise to a crack. I suspect that this is an indication that only a small fraction of the semi-clonal cells give rise to cracks under macro conditions, and this may well explain why we do not see such evidence of the early branching. In one case I have had some of the cells corresponding to the 5th to 8th division mentioned before, giving rise to swarms, while others initiated semi-clones.

What should we make of this? These data are still rather fragmentary, but I think that they may not reflect in fact, irregular replication. Instead they might possibly be explained by the polytenic condition of the chromosome fragment originally transduced. That is to say the degree of replication indicated by these experiments might be already inherent in the chromosome fragment. This would account for the confinement of the apparent replication to these early divisions. I must admit that my estimate of the number of divisions is based on the number of motile cells seen in rather large clones as I have not yet had an opportunity to study very many in detail during that intermediate stage. It is possible that the actual distribution of the polytenic material is made over a somewhat longer interval of time and this will also accentuate the appearance of irregular replications. Do let me know if these results are consistent with your own, and if I can quote any of your prior findings. I want to emphasize, that my main interest in this is searching for the crossover complements. However, I have had so little trouble with the experiment and it has been so much fun so far that I have not been able to resist the temptation that they offer.

I will not say very much more about the work going on at the moment as much of it is summarized in the report that I have sent to you under separate cover. Any comments that you might care to make on its content would be of interest.

I hope we will have an opportunity to renew our tape-recording type of interchange, though the technique is still somewhat awkward in our hands. Part of the trouble is, I suppose, that there is only one tape recorder and several addressees.

Do you suppose there is in fact any way that we could get hold of your BBC broadcast--I'd love to hear it.

With best wishes and regards from all,

Yours sincerely,

Joshua Lederberg

/mg