Genetics Department
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AIRMAIL

Dr. William Hayes
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Dear Bill:

Thank you for your letter of March 3. I was disappointed not to hear more right away on the success of attempts to separate the F agent from F+ bacteria, but hope you will have an opportunity to elaborate on this.

I wanted to get in touch with you again right away because I am planning a paper to be given in the latter part of April at a symposium on genetic recombination to be held at Oak Ridge. The report that you have received is more-or-less an outline of my own remarks. I wanted to ask you whether you would like to make any specific comment on this story that I would be entirely happy to quote verbatim and of course attribute directly to you. I would not, however, recommend that you include in such a citation your prediction that the Hfr parent is not going to be recovered from unselected crosses of the kind your letter mentions. I had studied some several hundreds of such unselected recombinant containing colonies and it was the presence of the Hfr parent in an appreciable fraction, about 1/5 to 1/3, of these && that led me to do the current single-cell experiments. I wanted to be absolutely sure that the recovery of the Hfr parent did in fact represent progeny from a single cell rather than from a pair of cells that might be temporarily stuck together in one way or another. As you see, the single cell experiment did bear out that presumption, which was however based on a very extensive series of previous experiments using plating methods.

However, I have been using only the original Hfr strain in all of these experiments. Tom Nelson has made a brief examination of your strain in comparison with ours,

and has found no substantial difference in behavior except for the following: In crosses of your Hfr strain with, for example W1177, there is in fact a very considerable augmentation in the yield of recombinants obtained by the addition of Vitamin B1 to the medium. However, this does not, as originally might have been concluded, mean that the proportion of B1- to B1+ recombinants is excessive in these crosses, since when the recombinants detected on B1- containing agar are themselves scored they are found to segregate about 9 B1- to 1B1+ as is typical for the other crosses. We have no explanation for this peculiar effect of thiamine in increasing the yield, but do not feel that it is based on any unusual segregation pattern of this parent. For this reason I will be surprised if your Hfr strains shows any different behavior in crosses analyzed in terms of the unselected zygote. However, do let me know what your results are on this point, and if they should prove to be substantially different on the other parent, it will of course be necessary to run a controlled comparison.

I am pleased to note that you are coming around again to a mating interpretation of E. coli recombination. I hope some of your many admirers will be as ready to admit the force of new facts.

I had been confused myself in the past on the formation of zygotes in saline suspension. Nelson informs me, however, that there is a considerable difference between the rate of recombination in saline and in the balanced salts mixture which is the base of the minimal medium. I find in fact that there is as well something like a 100-1000 fold increase in the rate of recombination in Hfr crosses conducted in a medium, such as penassay, that permits active growth, as compared with saline or mineral medium suspensions.

To return to your experiment number 1, I am a little confused by your reference to the absence of reciprocal segregants within individual prototroph containing colonies. Your previous statement that the Hfr marker S^s is missing from all the colonies would seem to contradict your statement that the reciprocal recombinant types had been found among other colonies. I assume you mean reciprocal with regard to some but not all of the markers. I am of course in complete agreement with you on

the experimental finding that the recombinants tend to be, as I put it in my report, have
orthotypic. This does not however/any bearing on the question as to the timing of the defect which results in this aberrant pattern. With regard to your second experiment and the use of phage, I would be interested to learn what the result would be of a cross reversed with respect to phage resistance. One might be able to find whether in a cross of F-V_1^r by F+V_1^s all of the zygotes did in fact receive a V_1^s factor from the F+ parent. Since resistance to phage is recessive to sensitivity to phage, such zygotes would be expected to be sensitive and wiped out by the action of the phage during whatever interval they were heterozygous, provided this interval were in fact long enough for the gametic contribution to become genetically effective.

Yours sincerely,

Joshua Lederberg

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