June 25, 1958

Dr. Ed Adelberg
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Dear Ed:

I'd promised to keep in touch with you as regards our experiments on diploids from interrupted matings.

I'm sorry to say that our results with the Het stocks on hand have been rather disappointing, the yield in various cross es running about 1 diploid per 100 or so prototroph recombinants. This is altogether too tedious, so we are setting up some balanced marker systems which will pre-select heterozygotes. This has worked out rather well in the past, but we have to make up whole new constellations of stocks to fit the present problem, and in order to focus on Hfr_H (as the most thoroughly studied Hfr.) The preliminary results are encouraging in the sense that I think we can still attack the problem by this route, but we have no results as yet.

We have had a great deal of trouble with the instability of all our Hfr_H stocks, as they have an irrepressible tendency to revert to F^+. Have you run into this problem? We have some rather recent transfers from Hayes' own shipment, so I don't imagine we have especially troublesome cultures.

You indicated that you wanted to try your own hand independently at the diploid problem, with your own marker combinations. I am enclosing what is probably our best Het F^- at the present time: W-2723, which is Het F^- Lac_1^- V_1 TLB_1---. We tried heterozygosis for Lac as a means of diploid selection, but for various reasons this proved an inefficient system with Hfr_H. However, at least for qualitative examination of diploids, you will get some by crossing Hfr_H M^- x W-2723 on EMS Lac B_1 medium, and examining a sufficient sample of Lac^+ prototrophs.

I still am discouraged by what we will be able to learn that would answer the question why (e.g. in our 1954 PNAS paper) the Mal marker was hemizygous even when of paternal origin, but there is nothing better to do than see what happens with Hfr_H and timed interruption. The distinction between hemi- and homo-zygosity is a crucial question, and unfortunately rather tedious.

Luca Cavalli will be leaving next week; we've had a splendid time on these experiments and will of course be continuing them. We have not succeeded in completing any crucial tests of the mechanism of interruption. He and Esther have been very busy time-mapping the innumerable mutants in the various Gal cistrons, which are not more than seconds apart from one another. We are looking forwarding to seeing Francois at Royaumont next month-- will you be travelling this summer, or are you sensibly staying home?

Best regards

Joshua Lederberg