

September 26, 1955

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Dear Dave:

Thanks for your letter and the mass of accompanying material. Rather than wait for a complete digestion (which will take a while, in competition with other piles of papers on my desk) I thought I had better acknowledge right away and leave part for later. I ran into Alan in Chicago on Saturday, and we had a hasty conference. I am relieved to learn of the possibility that strain differences account for the discrepancies in seriation-- our experience with W-1895 agreed with yours, and not at all with Jacob's. Are you using the "Hayes Hfr" that I sent you, or another. If ours is ng.<sup>+</sup> and you have a different isolate that is better, would you let us have a copy so we can try to reconcile our other results generally.

Are you asking for a W-1895 Lp<sup>S</sup>? We will send you W-2252, which fits this prescription. You should also have a better multiple marker strain to tie in some of the other loci (at least Alan thought so), so we are also sending W-583 (= W-1 V<sub>1</sub><sup>R</sup> Mal<sub>1</sub><sup>-</sup> Ara<sup>-</sup> Xyl<sup>-</sup> Gal<sub>7</sub><sup>+</sup>), anticipating your interest in it. I still think the overall data are compatible with post-zygotic losses, and am not even certain that the blending results have to be explained differently, though this is not implausible (cf. enclosure). The following may be a reasonable compromise also: that the Hfr chromosome is always broken (proximally to Gal-Lp and to Mal-S) but that the distal fragments do not always penetrate. They do accompany the proximal sections frequently enough to account for the data of TCN & JL on post-zygotic losses; i.e., if there is crossing over with the distal fragment, and subsequent loss, one would save markers from the Hfr and eliminate from F- parent. We had conceded that our evidence showed that losses were often postzygotic, but could not exclude prezygotic losses as well. I had not wanted to invoke two distinct mechanisms, but this notion would not be too much of a strain. On this basis perhaps the effect of blending is not to cause breaks in the chromosome, but to reduce the frequency with which the Gal fragment is also brought in. From the diploid data, if these ~~are~~ are not to be arbitrarily disregarded, I would have to adhere to the idea that normally the breaks are always at the same site; we haven't done any comparable experiments with disrupted pairs.

Have you considered whether phage might be playing a special role in your disruption experiments? Rather than merely interrupt mating, it might be breaking up the Hfr chromosomes. You would then have a transduction of fragments, but via a conjugal bridge rather than the mature phage particle. Unless you have completed the comparisons, and find otherwise, this might account for differences between your results and Jacob's also.

I am happy to see this burst of tidying-up energy. I will talk to Bill Stone, and will be happy to send Wilmer wgl5 if he needs it to finish his end.

Your <sup>my</sup> version of comments on serotype is quite satisfactory (and rather smoothly stated), though I think it quotes my personal conversations rather than printed remarks. A better reference might be my paper at the Amherst Growth symposium, of which Tracy has a copy (and possibly still disagrees), but it hardly matters.

I am relieved to learn that you have the means to hang on. We dropped our Detrick connections several years ago, having been fed up with the formalities of military contracts. I will write to Buzzatti— but do you think I could honestly predict an awakening of your interest in marine biology? Do tell me what I can or should say in this connection, so I can quote by you indirectly.

As to F, I agree this should be published. The empiricism could go to MGB as effectively as anywhere, but I think you should have more credit for these observations than the mention in the PNAS paper (which was as emphatic as I could manage, and which had to be brought out for the purpose of the paper). But not having heard from you about it for some time, I thought you had lost interest. This summer, a new student came into the lab (Alan Richter) who seemed to be interested particularly in F, and just as a starter and for the experience, I suggested he review this particular problem. He has been running 58-161 through a chemostat, etc., so far has had no success at all in obtaining F— that way. I have not been able to find any notes at all on the experiment that Aaron did— have you any details on that. Nor can I find any record or trace of the cultures— any ideas there?

May I suggest the following arrangement: let Alan continue with his experiments: a) the chemostat, which probably won't work, and b) reinfection trials, on which I have had some discrepancies. I have also run into some apparently sterile cultures, and others with greatly ~~enhanced~~ enhanced fertility, which deserve some more looking at. Alan also has some odd results on effect of culture age on F status (of F+); these may have some bearing on "enhanced fertility" and sterility, as well as the odd ratios in some F+ x F+ crosses. This should not take terribly long, and in any event ought to be written up in time to support a collaborative paper with yourself as the senior author. Meantime, why not record the empirical procedure in MGB. Rather than my joining you as author on that, I would prefer that you merely indicated that the work had been done at Wisconsin and leave it at that. The purely empirical aspects are not likely to interest (or be understood) by anyone outside the MGB circle, and I would want to see at least some of the theoretical aspects tried out before wrapping it up for publication. If you have any notions, independent of what you started here, you can decide for yourself whether you can integrate them with the completion here, or reserve them for your own future programs.

What is the B transduction system you were considering— P1? I will be willing to bet you, say 2:1, that the auxotrophy, etc., found in S mutation cycles is not at all allelic with S, or don't you mean that?

Yours sincerely,

Joshua Lederberg