

February 9, 1955

Dr. David Skaar
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Dear Dave:

I have your letter of the 6th. I am sorry not to have let you know before that the Hfr (as well as Hfr) strains are now freely available. I am happy to enclose W-1895 (= W- Hfr)(Luca's original Hfr isolate).

As you know, my position on strains has been to hold on to them, until we had some clear understanding of them, as long as we were in the preliminary stages. When this stage has passed, as for Hfr, they are freely available, and there can be no strings attached. Therefore, I can hardly presume to tell you and Alan what experiments to do.

recent developments

I suspect, however, that you may not be au courant with ~~recent~~ here. For the last year (since just after the symposium at Oak Ridge) I have been busy with the micromanipulator, and have been able to work out a system for detecting the "conjugal" events. This is briefly described in the enclosed (unpublished) extract. As you see, the fertilization is certainly unilateral. I had hoped to try to work out a suitable method, with tracers or other isotopic labels, for detecting material transfer across the conjugants. The best way to do this, in my judgment, is by assaying individually isolated exconjugants, with the micromanipulator. If your contemplated experiments involve a different approach—presumably examining the colonies of selected recombinants—there would be no interference, and I would be delighted to help or advise in any way I can. It will surprise me very much if you intend to go into the manipulation business, but in due course that approach should reach the stage of being susceptible of this kind of experiment. What would interest me particularly would be the distribution of label among the several subclones of the F- exconjugant, comparing those that do and do not contain recombinants. One question: how would you propose to label bacteria specifically in their DNA? But it may fortunately turn out that little enough RNA is exchanged to interfere.

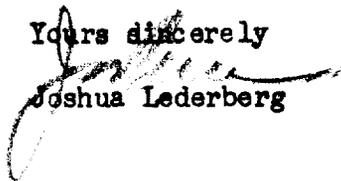
As to the linkage questions, I think you will have to refer to Cavalli for any real details on the Val and Az linkages. Rowley might have had a different locus with similar effects. I think we now do have to admit that, aside from crossing-over between E and the markers, that elimination is not uniformly ~~from~~ from the F+ (or Hfr) ~~side~~ side. Perhaps these exceptions represent cases where fertilization was reciprocal, or reversed in direction; there is no direct evidence for this, but the expected incidence is low. This is needed, e.g. to explain the close linkage of Lp - Gal₄, in view of the fact that Lp is regularly eliminated from Hfr-induced diploids, while Gal₄ is not.

In crosses, say, of Hfr Gal⁺ Lp⁺ x F⁻ Gal-Lp^S, most of the progeny are Gal⁺ Lp⁺, a few are Gal⁻ Lp^S; a very small fraction are crossovers. Since Lp is eliminated and Gal is not, we would have to place E precisely between them. If there were a consistent polarity of E breakage, then the recovery of Lp⁺ should depend on crossing over between E and Lp, and therefore between Gal and Lp. But the Gal-Lp crossovers remain quite rare. The same consideration would apply to the linkages between Gal's, some regularly eliminated, others ~~never~~ never, and, less dramatically to the Hyl-S story. If the locus of breakage is variable in B x K-12, which is not inconceivable if there are structural differences, it is certainly at a constant locus (or loci) in K-12.

I will send you W-1895, rather, under separate cover. Just as a matter of curiosity, I would like to know whoever else may be interested in it. I will also send you one of Hayes' Hfr's: W2323 (he gave no stock number on his label), stated to be M- S^r Az^r).

Bestwishes to Linda and the Skaarbirds.

Yours sincerely


Joshua Lederberg