

Madison. April 29, 1952.

Dear Cavalli:

Your letter of the 22d just received. I am sorry to hear of the impediments to your experimental work, and hope they will be temporary. I was pleased that the paper was acceptable to you. Please note any further changes that should be made. [Have I not recently sent you W-1177, by the way?] To take care of the history of Hfr, I have simply transposed the sentence to read: During selection for etc (Cavalli and Visconti 1948), a derivative of 58-161 was isolated which showed a remarkably high f. of r.... If you will agree, I would rather make as few references as possible to inaccessible "publications" such as the centennial mtg of the Genetical Society, if another reference (Cavalli 1950) exists.

I was a little surprised at your concern over the heading. Is not all of the work directly referred to (and not previously published in Cavalli 1950) from your experiments at Milan? Unfortunately, I am obliged to publish a fairly lengthy acknowledgment in the form of the footnote of the 1st page. For our JGM, I would appreciate your leaving room for the same, or else copying it in directly (except that Paper No... will be superfluous under your senior authorship). I would prefer not to make explicit comment about the origin of our collaboration, which is implied at various places: footnote p.1; top p.2. If you would like to publish this larger "experiment", why not do so in the JGM paper. But I think the results speak for themselves!

According to a recent letter, Hayes has rediscovered the segregational effects of F+, and has drawn just the conclusions we would predict. Still I think that much of the discussion ~~between~~ between Hayes and ourselves is semantically confused. We would rather stick to established terminology, and express the peculiarities as modifications of previously described processes. Hayes invents his terms and some of his ideas as he goes along but (except for genetic functions of lambda and "self-reproducing gametes", is describing the same things.) Have you had an opportunity to repeat his experiments directly? I concur with him as far as the success of crosses in the presence of streptomycin, but well-washed streptomycin treated cells are not so restricted in their ~~sex~~ compatibilities (if the experiments of one of my less advanced students can be trusted.)

I must admit that I am spending most of my time now on Hfr crosses. It is almost incredible, is it not? I am not sure exactly ~~what~~ what you had in mind to do with streptomycin, except as a selective agent. I have had no difficulty identifying the zygote-colonies on EMB lactose agar. There is nothing like normal or complementary segregation. Most of the zygote colonies from Hfr x W-1177 contain just two components: 1) identical with W-1177 2) Mal-Xyl-Mtl-S^r TLB₁-M⁺ [like W-1177] but Lac⁺ and V₁^R or ^S (about 2:1)! Prototrophs occur about 1/100 as frequently as these more frequent types. I am trying to construct some maps, comparing the unselected with prototroph data (by prototroph above I meant B₁+MTL⁺). I have not seen anything very interesting yet under the microscope. It has been a little help to vital-stain one parent with tetrazolium before mixing the cultures. I think there is pair-formation and clumping, which would suggest conjugation (as in the ciliate protozoa) rather than copulation, but it will be difficult to produce convincing evidence about the pairs except by direct micromanipulation studies, which are being planned. The segregation data may be understandable still in terms of elimination(s).

Hfr x Hfr ~~and~~ (by using further mutations in the original stock) and Hfr x F+ are also very fertile, but not so high as Hfr x F-. The segregation patterns appear to be different, but I have had difficulty collecting enough unselected zygote colonies.

May I ask you to consider a favor about the Hfr? It will be difficult for both of us to pursue the study calmly and unhurriedly if many other people insist on premature discussions of it. May I ask that the unselected crosses and immediate possibilities of cytological analysis not be discussed publicly until we have ourselves come to some definite conclusions about it? I have so far not discussed this with ~~any~~ anyone outside the laboratory besides yourself. Ordinarily, I would publicize such a thing immediately, but I ask time now for some thinking about it.

I don't know if you are interested in L-forms. Accidentally, I've found how to get them regularly from practically any Salmonella (fresh or old) and even E. coli K-12. Inoculate semi-solid gelatin-agar (as used to demonstrate and accentuate motility). Some L-forms can be seen with the phase microscope after a few hours by placing some of the spreading growth on a slide. If this is reinoculated into the same medium + penicillin 100-1000 u/ml, the bacillary forms are lysed, and interfere less with seeing the L-forms. I doubt if they

FOLD SIDES OVER AND THEN FOLD BOTTOM UP AND SEAL.
NO OTHER ENVELOPES SHOULD BE USED.

have any special genetic interest, but you might be interested to look at them. The published descriptions are very fussy, strain-specific and unpredictable.

Sincerely,

Joshua Lederberg
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