

July 25  
1950

Dear Luca:

Your letter of the 10th (and remains of the ms,) arrived just today. I wish it could have come a week ago, so that I could have given it long and thoughtful consideration. I am ~~greatly~~ greatly pressed to finish a mass of paper work by the end of the week so that we can leave for our vacation. I hope you will forgive the paucity of this reply. I tried to put your letter aside, but was so distracted by thinking about it that I could not proceed with my other work. As you will see, I wrote you just a few days ago to send some pictures.

Thank you for the cultures. W-583 arrived broken, but may be still recoverable. If you do not hear further, please assume it was OK. We will have time only to grow it out before leaving. I am pleased that the ms, also is in a good status. There is no objection at all ~~the~~ to the ms. for the Congress; ~~ITXYSXWOLIXXKATXKIX~~ it doesn't matter how you handle it. The furthest thing from my mind is the possibility of giving you any other paper.

Your conceptions of the self-elimination of the Hfr, and its possible relationship to centromeres are in (the usual!) astonishing agreement with our own. We have not been able to fit all the data together so nicely, however. Esther has been working more closely on the genetics of the Gal mutations: there is a cluster of at least four very closely linked loci, very close to the point of elimination. For, although they are very closely linked to each other, some are regularly hemizygous in the diploids, some are heterozygous. As you know, Lp agrees with the former. However, we do have some diploids heterozygous for the region, and we had already planned to try to cross Hfr into these, but there are technical difficulties that will take some time to iron out.

There is this difficulty that has hindered me from framing any unitary theory of elimination: Gal and Mal mark two distinct eliminated regions, usually corresponding to the F+ side. There are, however exceptions which appear to be independent of each other. But perhaps the Mal exceptions (i.e. cases where the F+ contribution persists) represent crossing over with the defective centromere, while the corresponding Gal exceptions are another process, perhaps failure of elimination. But if this is the case, one should find among the diploids both hemi- and heterozygotes for a given Gal locus, and this has not yet been found.

It is not crucial which Gal locus is represented in W-945, as all of the Gal loci seem to be very closely linked. (That is all of the full negatives, not such as represented in W-677, which is messy). W-945 may be Gal<sub>1</sub>, or possibly a new locus. W-583 carries what we call Gal<sub>2</sub>-. In usual diploids, Gal<sub>4</sub> is not eliminated; Gal<sub>1</sub> is eliminated, and from some of my older data so is Gal<sub>2</sub>. W-1294 is not supposed to be galactose-negative: it may carry some slow or suppressor mutations as well as Gal<sub>4</sub>-. Curiously, while Gal<sub>4</sub> is digenic in diploids from Het crosses, it is (in few cases available) only haplogenic in other non-disjunctional types.

The ~~///~~ easiest explanation of Mal and S is that they are terminal. This would require only a single break to account for their loss. I think the extent of elimination in this region must be quite regular; otherwise one might expect occasional discrepancies between these two loci, such as are never found.

The basic datum in Fried's work is that in crosses where M and Lac were unselected, and crosses were based on selection either of S x TL or P (linked to Lac) x TL, there was no significant correlation of M and Lac, although there were the now usual deviations from independent segregation of either: this does not prove that M and Lac are unlinked; it fails to prove that they are, and invalidates the previous evidence (Lac ratio in prototrophs) of the linkage. Certainly one could set up special schemes that would give the same result, where the linkage might be obscured by other forces.