

Madison, Wis. March 10, 1952

Dear Cavalli:

From the date of your last airletter, my previous note will be waiting for your return from the London trip, along with the draft ms. I shall be looking for your version, and will be quite willing to assume any burden of composition. I hope your London visit with Hayes has been profitable.

A rather startling experimental result has come up during the past week. You will recall (and may possibly have confirmed) that filial TLB<sub>1</sub> stocks show an unusual perturbation of linkage when backcrossed to the BM parent. I have regarded this as the strongest objective evidence of structural heterozygosity. I now find that the modified behavior of filial TLB<sub>1</sub>-, as contrasted with parental, is due simply to the F+ character. W-1177 F+ stocks (securing by transduction from K-12 or other related stocks) show the same effect. Strangely enough, the modification ~~is~~ is confined to the TL line. BM F+ x TL F- gives the familiar results (e.g. 58-161 x W-677); BM F- x TL F+ and BM F+ x TL F+ appear to be alike. Cf. PP. 12-13 of the microfilm draft ms. of our Cold Spring Harbor paper. Unfortunately, the tabular data were not in the microfilm; the results can be summarized as follows (ratios in prototrophs):

58-161 X

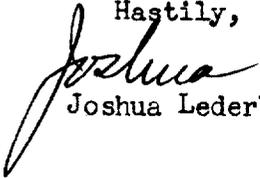
W-1177	Mal+	Lac+	S <sup>s</sup>	V <sub>1</sub> <sup>s</sup>
	20	21	15	67
W-1177F+	84	85	72	88

I do not have all the data, nor the space here to expand them, but it looks as if the essential relationships between unselected markers are preserved. I have been suspicious for a long time that M is not truly linked to Lac, and that something else determines the segregation of the linkage group Lac-V<sub>6</sub>-V<sub>1</sub>-L-T into prototrophs. Whatever that something else is appears to be regulated by the F-status. The possibility of unequal genetic contributions of the two parents is in question; also that in BMF+ populations, some of the cells are phenotypically F- (all of them after aeration), and that only F- x F+ occurs. However, I see no point in speculating about this at the present time. We have a long job of work ahead now in clearing this up. I hope we will not be unduly distracted in defending or opposing facile speculations before attempts have been made to test them.

My first approach is to study other parental combinations to "localize" the stocks in which the F+/- difference operates. Unfortunately, we have no way of producing or readily detecting F- "mutants" in other lines, and it will be some time before we have sufficient diauxotroph testers of independent origin.

I see no reason why this development should impede the publication of the sound results of our current work on F, although the scope of the problem has become enlarged. In a few places, more qualified language may be needed. As it is, the very fact that the problem is entering a new phase is itself good reason to summarize what we have already had. Several elements of our previous work appear to be accentuated-- particularly the environmental control of the F- phenotype of 58-161. Have you any ideas about this?

Hastily,

  
Joshua Lederberg