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21 August, 1951.

Dear Luca,

I would like to congratulate you on your paper, the subject matter of which, & the discussion, I thought excellent. You have obviously done much more work than I have. I don't know whether this is due to your greater innate energy or to your having technical assistance! Reading your paper made me realise the deficiencies in my own & led me to think that perhaps I have been rather unwise to attempt to theorise at this early stage. Actually I have now cut out all my phage analogies which Wollman tells me are unsound. As regards your paper, I thought most of the editorial & referee's criticisms fair & valid. I think that it would have been impossible for the general reader to read & understand without a great deal of effort. I have now finished revising it & think I have done it with some success. All I have actually done is to classify parts of it under headings where I thought it were helped, altered the construction of a considerable number of long sentences, added a few explanations where I thought the technological description was too difficult for the uninitiated reader & changed a few rather "unenglish" phrases. I hope you will not mind my taking these liberties with your paper but in fact I think you will find it in no way radically altered. I have typed it with triple spacing so that you can re-alter it as you wish. I will send it to the editor for approval & will bring it to Italy with me, together with the annotated original. It is hardly worth sending it by post at this stage. You need not thank me. I enjoyed doing

it because it made me read & absorb your views much more closely & deeply than I would otherwise have done. About Table 2. The trouble here is that the reader has to remember what A means & B means, in addition to 1, 2, 3, 4, 5, 6, (in terms of TLB, F & LGMXA) before he can start to appreciate the significance of the actual data. It would help a lot if the six columns could be headed with particulars of the actual mat, thus:

No. of prototrophs showing various arrangements of Lac, gal, Mal, Xyl, Ara markers from crosses:

Patterns of L,G,M,X,A marker characters	1. A.F− × B.F+ LGMXA− LGXMA+.	2. A.F+ × B.F− LGMXA− LGMXA+.	4. A.F− × B.F+ LGMXA+ LGMXA−	5. A.F+ × B.F− LGMXA+ LGMXA−
L G M X A			14	15·6
− − − − −		1		
− − − − +	290	25		
+ + − − +	208	276	1 / 19	2
− + + + −				

Key at bottom, thus —
L = Lactose.
G = Galactose.
X = Xylose & c.
+ = sugar fermented.
− = absence of fermentation.

And is there any need to have the LGMXA patterns arranged to read head-to-tail for columns 4, 5, 6? It seems to me much simpler to read right across all seven columns. This makes comparison easy without affecting any of the information presented. You may have some special point to make by the "head-to-tail" system, but I don't see it.

I feel that the major criticism which can be made against my own work — & a very valid one — is that it has been mainly concerned with only two strains. But unless one is in the fortunate position of being able to hand out various aspects of the problem to students, as I gather Lederberg can (not to speak of his wife!), it is a nice point whether to make as much progress as possible with one system or to consolidate your position in depth as you go along, which may prove tedious & slow. I have done only one significant

experiment recently but it may interest you to hear of it now as I propose to mention it at Pallanza. I reasoned that if the fertility of F+ x F+ crosses is due to the occurrence of F- cells (? F- phenocopies or simply due to temporary loss of F) in F+ clones, individual F+ x F+ contacts actually being sterile, then treatment of an F+ suspension with SM should render it pure F+, so that F+/smᵗ x F+ crosses should behave like F+ x F- crosses so far as segregation phenomena are concerned.

Here is the result of an experiment.

Cross	No. of prototrophs having phenotype:				Total no. tested
	Lac+ Mal+	Lac- Mal-	Lac+ Mal-	Lac- Mal+	
A/F+ x B/F-	0	14	1	0	15
A/F- x B/F+	14	0	1	0	15
A/F+ x B/F+	24	24	9	3	60
A/F+/smᵗ x B/F+	0	22	8	0	30
A/F+ x B/F+/smᵗ	18	0	1	1	20

A = 58-161 = Lac+ Mal+   NO SM selection or Sʳ tester strains used.
B = W-677 = Lac- Mal-   Crosses made on MA + B₁.
SM treatment reduced viable counts of both A & B to 5×10^{-5}.

I regard this as valid evidence which, when taken in conjunction with the somewhat similar but less dramatic effect of UV on either parent in F+ x F+ crosses (about which I wrote you via J.L.), becomes good evidence.

Oh! one other thing. I have been very interested in your F- phenocopy story but haven't tried to confirm it in aerated culture yet. However I did find that when I mated well washed 24 hr. agar cultures of 58/F+ & W/F- the prototroph count was about 100 times less than with young broth cultures. I thought this might be due to your F- phenocopy & it turns out to be

so. I crossed a washed 24 hr. agar suspension of 58/F+ with a washed young broth culture of W/F– & of W/F+. The ratios for both crosses were low but that with W/F+ was about twice as great as with W/F–. Testing the markers of prototrophs showed that with W/F+, 58 had behaved almost exclusively as F–, but the ~~crossed~~ prototrophs developing with W/F–, & other markers, showed that 58 still had a good deal of F+ activity. This F–phenocopy is a very peculiar business.

Hope you have been able to read my handwriting.

Au revoir—

Bill Hayes