

ISTITUTO SIEROTERAPICO MILANESE

'SERAFFINO BELFANTI'

ENTE MORALE AGGREGATO ALLA UNIVERSITÀ DI MILANO

Direttore Scientifico: Prof. Augusto De Barbieri

Direzione Scientifica

Via Darwin, 20 - MILANO

TELEFONO n. 35.74.41 (5 linee)

Jan. 24, 1956

Dear Joshua, I am sorry for answering late your letter of Jan. 2. I have been busy with various time-wasting occupations; I should now be relatively free from them.

Book. I think the agreement was that you would write chapters 3, 4 and 8 so that your present plan is quite satisfactory. I agree also about writing each chapter in full. The two chapters I sent you were prepared in a different way. The first one was in an almost final form, except for data from papers I could not find, and which I hope you may be in a better position to read, in case they contain interesting information on the early stages of sulphur drug resistance. The second one was a draft. As I adopted a somewhat new classification of drug actions etc, I was interested to have your opinion about the plan followed before setting down to write it in full. As you ~~are~~ ^{seem to be} now in a relatively free period, it would be ideal if you could write chapters 3 and 4. This would give me a more reasonable basis for writing chapter 5, for which I have prepared now much material, but ~~xxxxx~~ does to a larger extent than any other chapter depend on what has been said before regarding adaptation of individual cells and of higher organisms. Chapter 8 is to some extent independent of the rest. Once I have your chapters 3 and 4 in hand I can go deep into writing the rest, and leave to you the final revision. The convention about referring to lines was the distance in cm. from the first line in each page.

Hfr. It will take me some time to trace all the early history of the strain. However, it was isolated some five or six times before it was lost in 1955, and still now I find it useful to isolate it at intervals. However, I have never tested recent reversions for F+ behaviour. Looking back at old protocols, I find that mutants established from the first Hfr, which were isolated obviously ~~xxxx~~ once or more after the first initial isolation by which the strain was established (after selection for nitrogen mustard resistance) and were tested for Hfr behaviour after isolation, were later found to be F+. There is more than one occurrence of this phenomenon, though it is difficult to establish frequencies of reversions.

I lost the strain about a year ago because liophils died out, and in view of its instability it was not kept on slants. Since I had it back from you I have practised two or three isolations, but as I say I did not take interest in possible reversions. I would accept the idea that it is now more stable, but cannot say anything definite about it.

I have recently had some ~~suspect~~ ^{suspect} that the closeness of the linkage between Hfr and Gal has decreased. Other facts let me think that Hfr is likely to be some ambulatory factor, as you say. You

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F+ → Hfr

will also have heard of Jacob and Wollman's recent findings, claiming that F+ x F- crosses are all due to ~~F+~~ Hfr mutations. There is one major difficulty there: why ~~are~~ is the progeny of F+ x F- crosses F+? This was the datum that led Hayes to his vector theory, but I do not see how it could agree with the present theory of the Passorians. Their evidence comes from fluctuation tests, and replica plating, which permitted them to isolate several independent hfr's, which showed different behaviours. Incidentally, this is a case where the technique developed in our paper for streptomycin resistance and chloramphenicol resistance might be useful to say how much of their theory is correct. Unfortunately, the disadvantage of Hfr in respect of F* must be fairly high in mixed cultures, thus making the experiment a difficult one.

The only interesting result, on which I am planning to send shortly a note to some journal, is that there is a sort of "mating reaction" in K-12; i.e. Hfr x F- show fairly strong agglutination in suitable mechanical conditions, while F+ x F- ~~show~~ or hfr x F+ show a less strong one, and this would be, if any, the simplest screening test for new fertile strains. It may, in some more or less distant future, become a diagnostic tool in bacteria! I believe this is a magnification of the reaction that brings the cells of opposite sex together; some complementarity of the surfaces of cells of different sex must be the cause of it, as well as mating itself. The observation was a byproduct, of statistical origin, of an entirely different experiment. Mixing Hfr and F- cells together I noticed a decrease in the number of viable F- cells (incidentally, I understand Hayes has made a similar observation: he thinks it due to ~~the~~ a phenomenon similar to lambda induction, due to some other phage or Hfr itself). Trying to make ~~some~~ counts for a kinetical study, I found plate counts ~~were~~ showed an abnormal scatter, which made the counts themselves unreliable. I therefore tested the hypothesis, that the unreliability of counts were due to clumping. The lesson is: use the microscope more often. Unfortunately, clumping makes the counts less reliable, and I find it difficult to study the killing phenomenon properly; but it is by itself sufficiently interesting, perhaps, to deserve publication of its own.

I will answer Larry soon. I should certainly like to have gone to Denver; it seems a very attractive place. I feel I shall stick to this country, however, for a few more years, waiting for a better job. If none comes, ^{in the} meanwhile, I hope chances ~~will~~ of finding good jobs in the States will not fade out.

Yours

Luca