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Dear Lederherg,

I am sorry for my delay in answering, but I sent you the strains about ten days ago and I know they take longer time than letters. I sent you 58-161 Hfr ,which is also labelled B-M-Ny$^R$ (though I have never tested whether it still is biotinless or not. My glucose contains of 58-161 biotin to give half growth/in presence of methionine ,and I never bothered to eliminate).

Before sending you Hfr I have retested it,and I got the following results: plating on surface with vitamin $B_1$ ,No. of prototrophs :

No. of cells of B-M-Ny$^R$

| No.of cells of W 583 | $2 \cdot 10^8$ | $2\ 10^7$ | $2\ 10^6$ | $2\ 10^5$ | $2\ 10^4$ | $2\ 10^3$ | $2\ 10^2$ |
|---|---|---|---|---|---|---|---|
| $2.5\ 10^8$ | | | | | $>10^3$ | 510 | 128 |
| $2.5\ 10^7$ | | | | $>10^3$ | $\sim 10^3$ | | |
| $2.5\ 10^6$ | | | $>10^3$ | $>10^3$ | 101 | | |
| $2.5\ 10^5$ | | 93 ≠ | 209 | 253 | 215 | | |
| $2.5\ 10^4$ | $>10^3$ | 670 | missing | 256 | | | |
| $2.5\ 10^3$ | $\sim 10^3$ | | | | | | |
| $2.5\ 10^2$ | 267 | | | | | | |

≠ slight contam.

same without vitamin $B_1$

| | | | | | |
|---|---|---|---|---|---|
| $2.5\ 10^8$ | | | $>10^3$ | $>10^3$ | 387 |
| $2.5\ 10^7$ | | | $>10^3$ | 422 | |
| $2.5\ 10^6$ | 76 | 78 | 112 | | |
| $2.5\ 10^5$ | 6 | 2 | | | |
| $2.5\ 10^4$ | 6 | | | | |

I use Difco agar which gave me so far good results without any treatment,but it is very likely that using a more purified medium might decrease yields.

As to other peculiarities of the strain,you will find them in the enclosed paper which I gave at the 100th meeting of the Genetical Society,in Cambridge, the 30th of June. Later I tried Hfr with W 826 and

W 836,with which it mates at a higher rate than 58-161,but the difference is less striking than with W 583 .

I am very anxious to know whether it will work properly in your conditions. I am sending you also B-M-Ny$^{R}$B$_{1a}$-, which is a biochemical mutant I obtained from it ; it needs also vitamin $B_1$ for growth, but such a gene is not allelic to $B_1$- of W 583 ; plating this strain with W 583 one gets recombinants in absence of vitamin $B_1$ at rate $10^{-6}$ - $10^{-7}$, and it is in these conditions that I obtained the possibile diploid I mentioned in the paper: it gave regularly mottled colonies on lactose and arabinose,unfortunately I lost it on the third subculture. It may prove useful in your studies on heterozygotes.

As to the reasons why Hfr behaves as it does, I have not been able to reach a definite conclusion, but I shall try to go on with this problem. I agree that differences in chemiotropic behaviour may be important . But the main use for me of this strain will be to try to make matings controlled under the microscope, and follow meiosis by isolation of early products of division. It may mean a full waste of time, but I think it is worth trying.

As a consequence of the work with Hfr,I started,with a Frenchman who has been working with me some time,a preliminary exploration of possible mating types. The research was negative under the point of view,but was successful in giving another coli strain showing recombination. The situation is still very obscure, and the fact that most of the characters are of one parental type only made me long doubt whether there was any recombination at all. Eventually I got some re-combination, ~~but [illegible]~~ I am enclosing a copy of a letter I just sent to Nature.

Linearity : I am a priori convinced of linearity,because I can hardly think of a non-linear system showing the regularities of recombination which your bacteria do show . But no doubt there are difficulties to reconcile this with the data. I am often fancying whether in the building of strain

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W 583,and possibly in its three first steps, thus affecting all derivatives, a chromosome mutation may have slipped in. I am also wondering whether it might not be worth while,though a very long job, to make again a W 583 starting from the original K 12 and see whether,after check of all allelisms, it gives the same map. I should not be surprised if the new strains gave $B_1$ and possibly xylose and something else on another chromosome. I am very interested to hear that your data on Lac and Mal in heterozygotes support the idea of a chromosome aberration.

I am leaving now for a holiday in my country . I should be grateful if you could send me, in september, the Lfr strains you mention in your letter; I should also be interested in having the original K 12,as,if I shall ever have the courage of starting the programme of rebuilding W 583,it is better to start with the original strain rather than with a back mutant.

If you write me to Cambridge your letters will reach me only with a delay of few days. Hoping your summer work will be successful,

Yours sincerely

Luigi Cavalli