

August 24, 1959.

Dr. L. Cavalli,
Dept. Genetics,
U. Cambridge, England.

Dear Cavalli:

I am sending this note in company with some cultures derived mostly from your 58-161Hfr (my W-1033) which I hope will reach you in time to be of use directly on your return to Cambridge.

The cultures include:

W-1059 Lac₁- [a UV mutant from W-1033]
W-1073 Mal₁-(Lac₁-) [a UV mutant from W1059]
W-814 Lac+ Mal₁- etc..... [a Lac+ reversion from W-677]
W-909 Gal-, Las, etc. + [a Gal- mutant from Y-10, TLB₁-]

These cultures are especially useful in demonstrating recombination in complete medium. For example, after 3-4 days of growth together in complete liquid medium, W-1059 + W-814 was plated out on EMB-[Maltose + Lactose = Malac] As many as 20% or more of the colonies may be Malac-, and show various new combinations of the other markers! I cannot say to what extent selection may distort the true amount of recombination, but it must be very high indeed! Comparable experiments using Y-87 (also B-M-Lac₁-) instead of W-1059 gave no Malac- at all, so that there is little question now of the uniqueness of your Hfr stock.

It is also possible to plate out somewhat younger mixtures of marked stocks, e.g. W-1073 + W-909, on a single sugar medium, like EMB Lac, and to find mosaic colonies which might represent segregating zygotes. These may constitute 1 - 2% of the mixed cultures, although some of the mosaic colonies may, of course, represent accidental conjunctions of independent colonies. The mosaics are, as one might expect, much simpler in structure than those from complex heterozygotes, and usually consist of large, nearly semicircular sectors of + and - with a common radius in a single colony. Sometimes, one of the components is but a small wedge, or even a central piece which do extend to the periphery. It is very likely that the segregating diploid be picked out with some precision after a little practice, because most of them contain a recognizable recombinant.

The segregation data are very peculiar, but support my previous s that the Mal locus in particular is not segregated at random, but m partly eliminated.

For example, 30 Lac V colonies were taken from W-1073 x W-909. 28 of these consisted of one parental combination, L+M+G-, and the one recombination, L-M+G- ! One colony contained only the two parentals, and may have been fortuitous. One contained both parentals as well as the same recombinant, L-M+G-. Here again, the second parent might have been fortuitous.

I have gotten quite ~~comppzable~~ results with other crosses between L033 derivatives and marked stocks from Y-10. In all cases, the pattern points to the elimination of a chromosome or segment from the BM (Hfr) parent, which is in agreement with the patterns of the persistent heterozygote. It seems unlikely that an entire chromosome is eliminated because of the evidence of linkage to a lethal deficiency in the Het stocks. Conceivably, however, this is unrelated, and we are dealing with something comparable to Auerbach's unstable centromere in Drosophila (Genetics, Jan. '47)

My experience is a little ambiguous in regard to the oppositional character of Hfr. I have been developing the mutants from L033 in order to use as closely related stocks as possible in experiments on the source of the biased elimination. So far, I have not found recombinants in W-1033 x W-1073, but believe to have gotten a few in W-1084 (a Lac+ reversion from W-1073) x W-1059. But these experiments are still incomplete.

The success of these experiments bodes well, I think, for your forthcoming cytological studies. If, in suitable crosses, the zygote frequency reaches 1% it may even be feasible to look in ~~synthetic complete~~ liquid complete medium for the fusion process. However, the 1% figure may represent a delay in "germination" of the zygotes which accumulates them somewhat. As I may have mentioned, I have a student coming next month to work on the cytology of the persistent heterozygotes, and the work that we are doing should fit together very well. I have hopes that we may learn how to recognize the zygotes cytologically from our studies, which in turn may help to verify your descriptions.

Sincerely,

Joshua Lederberg

P.S. If you