October 7, 1948

Dr. Luigi Cavalli
Department of Genetics
Whittingehame Lodge
44 Storey's Way
Cambridge, England

Dear Dr. Cavalli:

I was most pleased to receive your letter and to hear of your plans for setting up a laboratory for genetic research on bacteria. I will of course assist you in any way that I can, and correspond with you on any detail. Under separate cover, I am sending reprints of some of our publications.

I was especially pleased to note your interest in problems of crossing-over and would be inclined to agree that E. coli would provide very suitable material. However, there are certain obvious limitations, especially that among the recombinants, only those which are "prototrophic" are detectable, so that one is restricted to the segregation of "indifferent" characters (sugar fermentations; phage resistance, etc) within the particular class of prototrophs. This limitation is not too serious, however, and an extension along the lines, and beyond, of my paper in Genetics, November 1947, would be quite fruitful. If Dr. Fisher has not already shown this to you, you might be interested to see an elaboration of the procedure for estimating "absolute" distances which is incorporated in a letter to him dated May 18, 1948, which accompanied a reprint of my paper in Genetics.

Fortunately, additional stocks are now available which provide an abundance of linked fermentation markers. I am sending you 58-161, a foundation biotin; methionine-less stock, and W-583. The latter was derived by a series of steps from Y-53 (mentioned in the paper) and in addition to the threonine, leucine, thiamin-less and Lactose- of Y53, carries 4 additional fermentation markers (Maltose-; galactose-; arabinose-; xylose-) as well as $V_1^r$. I have not yet mapped these factors, except that $Mal_1$- is closely linked to BM, and the others somewhat more loosely, but I think that because of the ease of scoring prototrophs for sugar fermentations and phage resistance they will be very suitable for crossover studies. One innovation may be suggested: using a synthetic EMB-sugar medium for scoring for fermentation. This disposes of any confusion that might arise from contamination of the prototrophs with adjacent parental cells. It is also very feasible to conduct the platings for obtaining prototrophs by spreading on a synthetic EMB, and thus secure an immediate classification of the prototrophs with respect to the sugar used. This will be especially useful in testing the rarer classes.

I might add that a new development has arisen that may simplify the problem immensely. Whereas the prototrophs, typically, may be reasoned to be haploid and fully reduced, stocks have been found yielding prototrophs upon crossing that are not fully reduced, and appear to be diploid heterozygotes, since they later segregate out to give all recombination classes. However, (a) the segregation is not random, but strongly biased for various factors, and (b) I have good evidence that some loci are represented once, not twice, suggesting that this alteration of the life cycle in these stocks is associated with heteroploidy, or a deficiency on one of the chromatids of the heterozygotes for a region near the Mal locus. The problem is not yet worked out, but the situation has already been useful since recombinants can be secured from the heterozygotes without nutritional selection, and even the elusive multiple-requirement types can be recovered.

The cultures are readily maintained by monthly or quarterly transfer on nutrient agar slopes. The phage should of course be refrigerated, and may be cultivated on 58-161.

With my best wishes, and regards to Dr. Mather and Dr. Fisher,

Yours sincerely,

Joshua Lederberg
Asst. Prof. of Genetics

/b