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NATIONAL RESEARCH COUNCIL
CANADA

ATOMIC ENERGY PROJECT

Biology Branch

CHALK RIVER. ONT.

July 11th, 1949.

Dr. Joshua Lederberg,
Department of Genetics,
The University of Wisconsin,
Madison 6, Wisconsin.

Dear Joshua,

Many thanks for your letter. It would be difficult to justify doing a detailed study of duplex prototrophs here as my main concern at the moment is to establish the number of loci involved in mutations to sr and the various forms of sd (and from sd to sr, + , and the various intermediates), with a view to interpreting some of the irradiation experiments using these characters. However, I shall be only too glad to give you whatever relevant information I come across in my crosses.

My previous letter, I think, indicates all of the details of the various crossing techniques tried. The technique which I am now using is to spread washed mixtures of overnight cultures on the surface of minimal agar plus thiamin, incubate three days, pick into minimal medium plus thiamin, grow overnight, and streak a 1:10⁷ dilution on EMS-Lactose plus thiamin. Parent type contaminants are eliminated by the EMS and the reduced number of colonies in a streak makes it easier to spot mixtures.

The first evidence of mixed prototroph colonies was from the 58-161 x W-677 cross. Some of the streaks on EMB-Lac (plus phage T1) were Lac^+ in the absence of phage and Lac^- in its presence, suggestion a mixture of $Lac^+ V_1^S$ and $Lac^- V_1^R$. This is of course very easy to spot. In the cross Y-40 x Y-53 one would expect fewer $Lac^+ V_1^S$ and in fact mixtures containing it are rare. I shall enclose a table indicating the sort of mixture we do get from this cross. You will notice that the frequency of duplex prototroph colonies is somewhat in the vicinity of 5 percent in these experiments although it has been higher in others. Also, incidentally, SR seems to be to the left of MB.

I gather from Dr. Ford, who visited C.S.H. on his way to the Oak Ridge meetings, that the student you mention will be doing somewhat similar linkage studies on SR and SD while there. In view of this, I should be grateful if you could have a look at my own results when I get them and have them in presentable form. Also, I am taking the liberty of sending the manuscript of my Oak Ridge paper which outlines my own interests in this regard. Do not hesitate to let me know if there seems to be excessive duplication of effort as the linkage studies are of use to me primarily in the interpretation of old experiments and in the planning of new ones, rather than being an end in themselves. Also, I am anxious not to tread on anyone's toes.

With regard to the nuclear segregation hypothesis my main reservation is that we don't know whether there is consistently more than one nucleus in the resting bacterium, and Robinow suggests that when the nucleus first becomes stainable after renewed growth only one is visible. I agree that the B/1 zero-points are probably artifacts, and have found the number of them greatly reduced when large excesses of phage are used.

Incidentally zero-point mutations to B/sr are rare, (see table 2 of Oak Ridge paper), which suggests that the concentration of streptomycin which I have used inhibits almost all cell division. For this reason I think it unlikely that delayed action of the streptomycin could be responsible for the nearly equal estimates spontaneous rate obtained using the two Luria and Delbruck formulas. However, it would take much more work than I have done to be certain on this point.

Thank you again for the very detailed information in your letter.

Yours sincerely,

Howard B. Newcombe

HBN:ar