(from Columbia P+S)

19 September 1945

Dr. E.L.Tatum,
Dept. of Botany,
Yale University,
New Haven,Conn.

Dear Sir:

Your recent paper 'X-Ray Induced Mutant Strains of Escherichia Coli' has just come to my attention, and has proven very fascinating. I should be very much obliged to you for reprints of this paper and your preliminary one last summer. I shall take the liberty of writing to you at this length in support of a request that I hope you will entertain.

After doing some work on adaptation (part of which is nearly ready for publication) in Neurospora mutants, it occurred to me that no adequate investigation of a genetic nature had been made to demonstrate the existence or absence of sexual recombination in bacteria. Such things as the distribution of somatic and flagellar antigens in the Salmonella group very strongly suggest that such a process may occur, but no very successful attempt seems to have been made to determine the recombination of bacterial characters. The nutritional mutants described by yourself and Roepke et al. would seem to fill the bill. We did not have any of those organisms at this laboratory, but in a strain of E. coli (6522) I had been able to select out a methionineless strain by serial passage through basal medium plus sulfanilamide and methionine as Kohn and Harris described (J.Bact '41) and a prolineless strain was obtained quite fortuitously (so far as I know) on a plating of the parent wild type. (It was interesting that you also obtained a 'prolineless' as a spontaneous mutant.) No thorough investigation of the biochemical behaviour of either strain has been made, but it appears that the proline requirement of the latter is very much reduced or spared by small amounts of tryptophane, and possible other amino acids. Unfortunately I do not yet have a very satisfactory and convenient basal medium, so that I have not pursued this further. If you would like to have a culture of this strain for comparison with your other methionineless, I should be delighted to send it to you.

I have not yet gone very far in the genetic tests I mentioned (explicitly) on these strains: the methionineless is quite Rough and therefore possibly not so satisfactory. I had planned to do essentially what you have accomplished: prepare a double mutant by subjecting the prolineless to the same selective procedure used in obtaining methionineless, but that seems unnecessary now for

a demonstration that independent (X-ray mutable) genes exist. It has seemed to me, however, that despite the apparent stability of the types I now have, and what is I hope adequate technique to eliminate contamination that it would be highly desirable to have genetically marked strains before any attempt was made to perform the experiment. I should therefore be very much obliged to you for cultures of your biotin double mutant series for the purposes of this investigation. To diminish the possibility of contamination I would like to ask only for those double mutants in which the biotinless gene is associated with another very stable gene. In that case a simple biotinless will never have been in this laboratory (to the extent of our knowledge.) It should, furthermore, be advantageous to use stocks of heterogeneous origin in the event that there exist mating types, sterility factors, etc. I would propose to inoculate into the same tube (under varying conditions) two different mutants, and select for wild types (50 or 100% of which should be marked with biotin) by inoculating into minimal from that mixed culture. Experiments already performed show that there is in some cases little or no rapid symbiotic growth comparable to the Neurospora heterocaryons.

If an investigation of this sort has already occurred to you, please let me know, as I am sure that you can do a much better job and have better facilities for it than I; on the other hand, if your plans do not include work such as this I should appreciate very much the service I ask of you.

One further point: the fact that a variety of mutants can be obtained suggests very strongly that the bacteria are (at least during some phase) haploid. It is possible on the other hand however that diploid mutant heterozygotes could, if a sexual process exists, have a homozygous segregant in a later generation. Have you any information on this point? I note that (according to your paper) your cultures were incubated 4 hours after irradiation. Have you any suggestions as to the number of generations traversed in this time by your strain?

Very sincerely yours,

Joshua Lederberg, A.S. V-12 USNR.