August 1, 1952

Mr. Philip E. Hartman
Biological Laboratory
Long Island Biological Association
Cold Spring Harbor, L.I., N.Y.

Dear Mr. Hartman:

Thank you for your letter of July 29.

Concerning the biochemistry of divers resistant mutants, I have been in correspondence with Dr. Colwell for some time. She is having some difficulty in reproducing her published experiments, but this seems to be a matter of the purity of the reagent, a point not previously emphasized. I am looking forward to a satisfactory confirmation of her experiments (which, prima facie, might still very well represent a selection of mutants. Quinones seem to behave very much like penicillin in the selection of auxotrophs in minimal medium).

Our experiments with streptomycin-resistance included an examination of the Merck strain of E. coli. They had lost their described non-aerobic S^r mutant, and neither they nor I have been able to repeat the experiment, even starting with their culture. I do not doubt that there may be biochemical differences among S^r mutants, and it would certainly be worthwhile to study such mutants before they are exposed to streptomycin. Whether an S^r mutant is resistant to streptomycin in a non-streptomycin environment is a nearly metaphysical question. The mutant character can only be defined operationally, namely that 100% of the mutant cells survive when they are exposed to SM, whereas almost all non-mutant cells fail to develop. I do not doubt there may be physiological adjustments to the presence of SM when an S^r cell is exposed to it, but there is no evidence that such exposure induces specific genetic changes.

I would be very much interested to receive further details of the Cu/induced small colony variants, and Dr. DeLamater's new techniques. E. coli certainly is very near the limit of useful microscopical techniques.

Sincerely,

Joshua Lederberg