January 9, 1951.

Dr. Maria Umberto Dianzini,
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Italy.

Dear Dr. Dianzini:

Thank you very much for your kindness in sending your E. coli strains and your two reprints.

I am especially glad that you sent the paper "Mutazioni indotte...", for it brings out certain details which are obscure in your note in Experientia. May I take the liberty of discussing them with you?

The most important of these concerns the technique and interpretation of your manometric tests. I interpret the phrase: "I germi prelevati dalle colture su agar con soluzione fisiologica..." to mean that the bacteria were grown on plain nutrient agar, without sugar or perhaps with just glucose. This is extremely important because of the phenomenon of enzymatic adaptation, i.e., that bacteria frequently are unable to assimilate certain carbohydrates unless they have been grown in their presence. This has to be distinguished from the parallel phenomenon of mutation and selection for the ability to use substrates previously non-utilizable (v., e.g., Monod & Audureau, Ann. Institut Pasteur, 72:868, 1946, or Monod, Growth, 11:223-289 1947). Your data therefore refer not to the potential ability of the organism to attack the sugars, but to the rather low and variable activities which they may have in the absence of adaptation.

I was particularly interested in your work because I had the impression that you were dealing with characteristics like those in my work on recombination., and that you had, for example, been able to transform a nonsucrose-fermenter into a sucrose fermenter. A simple streaking on Eosin-methylene blue sucrose medium shows, however, that while your UQ strain is a powerful sucrose-fermenter, the other three strains (I, SG, and I (SG-16)) are essentially non-fermenters. At least in terms of the cultural characteristics which I have been studying, there is no difference between I and I(SG-16). I venture to predict that you will find, if the cells are grown on nutrient sucrose agar, that UQ will give a much higher rate of sucrose-oxidation than any of the other three strains.

I do not mean to imply that you have not achieved an interesting transformation, the proof of which will require further careful and thoughtful investigation, but it does appear that your report is likely to be misunderst in its present form, for I am sure that most readers will have thought that your

determinations were carried out on adapted cells. May I presume to suggest that a further research in this dissection on your part might be most fruitful?

A second question has also arisen in my mind, but largely obscured by the first. You have seen yourself that the metabolic characteristics of your straihs, as measured by your own technique, have not been entirely constant and reliable even in the absence of any treatment (e.g., on p. 164; 2) "il germe, dopo 22 passagi su afar saccarosio al 2%, hasattacato il substrato." This raises the question whether the variations you find with nucleoprotein treatment may not be induced by the NP, but rather that the NP provides the most favorable conditions for the overgrowth of the variant cells.

One final point: you refer in your papers to Boivin's transformation of E. coli. Unfortunately, his strains have been lost, so that it is impossible to reproduce his experiments on serological transformations. However, it should be pointed out that he has retracted the claim to have induced a change in enzymatic properties of E. coli, for much the same reasons as raised in the previous paragraph. (Cold Spring Harbor Symp., volume 12, p.9, 1947.)

I shall look forward to hearing from you again, and with my sincere appreciations for your cordiality,

Yours truly,

Joshua Lederberg,
Associate Professor of Genetics.

P.S. I shall be happy to send you all reprints which are still available.