

September 20, 1950.

Dr. R. R. Mellon,
Western Pennsylvania Hospital,
Institute of Pathology,
Pittsburgh, Pa.

Dear Dr. Mellon:

I am sorry not to have answered your letter of August 7 sooner, but I was spending the summer out of town and could not give it the attention it deserved.

Lindgren is quite right in pointing out the existence of genetic variations which can be shown not to be gene mutations, and his "red yeast" case certainly provides such an example, although I do not quite agree with his interpretations of it. Without crossing tests, it is of course impossible to verify the genetic basis of a variation. However, from my own experience with *E. coli*, I doubt that such pseudo-mutations are very common, although your own case of mucoid - to- smooth in streptococci may very well be such. In general, I think it safest to regard variations as gene mutations, unless it can be shown otherwise. The role of acetate in your system is the sort of thing that makes it very doubtful that the M-S change is an ordinary mutation, and it may very well be based upon the loss of some cytoplasmic constituent, like kappa in *Paramecium*.

A propos acetate, I would appreciate having a (another ??) copy of your paper on the acetate effect which appeared a couple of years ago in *J. Bact.* Do you have any further data on this system, in particular on the population dynamics of the shift? I would be delighted to hear about it.

Yours sincerely,

Joshua Lederberg,
Associate Professor of Genetics