CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA, CALIFORNIA

DIVISION OF BIOLOGY

March 4, 1958

Dr. Joshua Lederberg
Genetics Department
University of Wisconsin
Madison

Dear Josh:

I have been reading the Ciba Symposium on Drug Resistance in Microorganisms and feel impelled to comment on your discussion (p. 97) regarding the problem of distiguishing between qualitative and quantitative gene mutations.

Fling and I anticipated the difficulty you refer to in our first paper on the two tyrosinases of Neurospora (Genetics 38, p. 373). The model we had in mind was one in which one protein serves as precursor of the other, but the same argument would hold for your fetal hemoglobin model. We pointed out that the difficulty disappears when more than two allelic forms of the protein are known, since it is not possible, by any plausible mechanism, to explain an allelic series of structurally different proteins on the basis of merely quantitative changes at the locus. As we pointed out, the problem then becomes the more familiar one of determining allelism. This does not entirely solve the difficulty, of course, but it shows that the uncertainty in this case is fundamentally the same as in every other genetic analysis--i.e., proof of allelism can only be approached asymptotically.

With regard to the tyrosinases, we now have at least two, and probably three, forms in addition to the original T^S and T^L types. The genetic data so far are consistent with allelism for all four, or five, forms.

I see that my friend Kossikov was at the meeting and gave his yeast results. I met him in Moscow last summer. He was formerly a Drosophilist and worked with Muller. His paper is what I would call a typical neo-Lysenkoist production. Was there really no discussion, or was it deleted for the sake of politeness?

Regards to you and to Esther.

Yours,

Norman

N. H. Horowitz