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PASADENA

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KERCKHOFF LABORATORIES
OF BIOLOGY

June 15, 1948

Dr. Joshua Lederberg
The University of Wisconsin
College of Agriculture
Madison, 6, Wisconsin

Dear Lederberg:

Now that final exams are over and the students have gone home I can get down to answering your recent letter.

My first reaction is to question the assumption that lactose fermentation involves prior cleavage into the constituent hexoses. I gather that this assumption does underlie your interpretation and that most of your lactose - strains are glucose + and/or galactose +. Actually, there seems to be considerable doubt that hydrolysis precedes the fermentation in several yeasts and bacteria in spite of the presence of lactase in extracts. Unless you are quite certain of the pathway of this fermentation, I think it would be very unwise to draw genetic conclusions. Once you admit the possibility that lactose fermentation is not so simple as it looks, then your results are no longer necessarily at variance with the 1:1 idea.

In general, it seems to me that the evidence which is usually offered in opposition to the 1:1 notion is precisely from fields where the chemistry is either in doubt, as in this case, or else completely unknown.

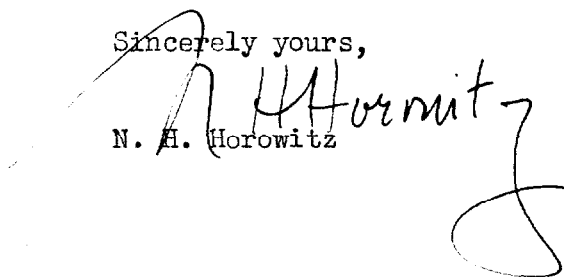
In answer to your question, I have no faith in the utter simplicity of any biological process, a priori. A process which can be written as one step may, in the cell, be controlled by specific coenzymes, *group donors,* in addition to the primary enzyme and substrates, and each of these *and inhibitors* elements will in turn be controlled by its own constellation of genes. Or, the cell may avoid the obvious reaction and carry out all sorts of odd maneuvers before it arrives, as, for example, in the conversion of anthranilic acid to OH-anthranilic acid by Neurospora.

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My estimate that something like 75% or more of mutations in Neurospora are of the "simple" kind is based on a calculation which attempts to take into account the selection against pleiotropic mutants. The theory is a little too complicated to go into here, and I want to chew on it a little more anyway.

Your method of sending reprints is O.K. Beadle just hadn't gotten around to distributing the last batch when I wrote you last.

Sincerely yours,


N. H. Horowitz

msf