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NATIONAL RESEARCH COUNCIL
CANADA

ATOMIC ENERGY PROJECT

CHALK RIVER, ONT.

May 4, 1948.

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

Dear Lederberg:

Many thanks for your letter and your comments concerning the sectored colony technique.

My interest in this is due to the difficulty of interpreting some of the data on "delayed phenotypic expression" as due to recessiveness of the mutation and the presence of the two or four nuclei.

As you suggest, the data on induced mutation could be explained along these lines, but one usually irradiates resting nuclei, and the cytological evidence for the presence of more than one nuclei is from actively dividing cells. On the other hand the data on spontaneous mutation in growing cultures indicates a delay in phenotypic expression of two or three cell generations in addition to any arising from the presence of more than one nucleus. (That is, unless one assumes some such peculiar behavior of these nuclei as for example a nearly regular exchange of places of the inner two of a row of four).

From the Robinow pictures one would expect a mutation in a four-nucleate cell to give rise to one phenotypic mutant two generations later, and that thereafter the number of descended mutants would double with each successive generation. The spontaneous data fail to fit this expectation since the number more than doubles with each of the first three or four divisions, and three generations after the appearance of a single phenotypic mutant the number present is, not eight, but something like six times this number.

It is still possible that the average number of nuclei in resting bacteria is only slightly more than one and that the delayed effect of irradiation is due to some phenomenon which is active in producing the observed effect in spontaneous mutants. Thus, your sector technique may be useful in providing a missing piece of information, provided one can make quantitative allowance for the chance of induced inviability in the nuclei of treated cells.

Dr. Joshua Lederberg, 4.5.48

Again many thanks for your letter. I am interested in your remarks on the plateau and decline in the U.V. response curve. Kelner has some unpublished U.V. and X-ray dose effect curves from actinomycetes showing plateaux, and U.V. induced phage resistance bears a similar relationship to dose. I am doubtful however whether it is a matter of differential sensitivity of the mutant since one would occasionally expect an upward swing in the curve instead of the plateau, as for example in your material, if you irradiated the mutant and scored back mutants.

With all best wishes,

Sincerely,

H. B. Newcombe.

HBN/lml