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FILE No.....

NATIONAL RESEARCH COUNCIL
CANADA

ATOMIC ENERGY PROJECT

CHALK RIVER. ONT.

October 31st, 1949.

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

Dear Joshua,

I was extremely glad to hear from you on the subject of "delayed mutations". With regard to "segregation delay", I had not realised that as many as half of your fermentation mutants appeared as sectors (the proportion is not stated in your note on the tetrazolium method of detecting mutants), and in the absence of anything critical from my own data I had hesitated to do more than indicate that a segregation delay had not been ruled out as a contributory factor.

In this connection, have you any information relating dose, killing, and ratio of "sector" to "non-sector" mutations, since with increasing dose the proportion of survivors with two viable nuclei should decline and together with it the proportion of mutations which appear as sectors? I had thought of doing experiments to see if this could be demonstrated, but gave them up as they looked extremely time consuming. It it turned out that the proportion of sector mutations did not decline with increasing dose one might be forced to consider the possibility that the gene is effectively double in some of the cells, although at the present time a nuclear interpretation of sectoring certainly looks more likely,

I am grateful to you for having pointed out the necessity of correcting for increase in C when obtaining average rates. When this is done my own data give approximately a five fold difference between the two estimates of mutation rate to phage resistance.

The model which you have used is easier to visualise than one in which mutations may occur between fissions; I had not realised however that this would give estimates from p_o and from r which differ more widely than in the case of the Luria and Delbruck model. It is difficult at the moment to see how the two models can be distinguished. If you eventually succeed in getting heterozygotes which segregate for SR and SD, and thus solve the dominance problem for this mutation it would eliminate one of the unknowns, and perhaps enable dominant and recessive mutations to be compared. Assuming dominance of SR, an estimate of pure phenotypic lag could perhaps be got for this mutation from irradiation experiments.

I am very much looking forward to discussing with you the anomalous segregation phenomena in E. coli this Christmas. I shall be going back to problems associated with induced mutation, but my assistant will continue working on segregation effects using the SR and SD mutants.

Thank you very much for letting me have yours and Doudoroff's results. Is there any chance that SR introduced into the other parent would yield a heterozygote which segregates? In some of my experiments SD was introduced reciprocally into the two parents, and the minority class was recovered in one out of the two crosses.

Sincerely,

Howard

HBN:bc

Howard B. Newcombe