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STUDIES OF MUTATION RATES IN BACTERIA

AARON NOVICK and LEO SZILARD

(Institute of Radiobiology and Biophysics, University of Chicago, U. S. A.)

Mutation rates in bacteria can be conveniently measured with a Chemostat. In this instrument one can maintain a bacterial population of constant size growing, within certain limits, at an arbitrary rate, controlled by the low concentration of some required growth factor. As mutations occur, for example to phage resistance, the proportion of phage-resistant mutants in the population will increase along a straight line with time, in the absence of selection. The slope of such a line gives the mutation rate.

These studies were made in general with tryptophane as the controlling growth factor. Using B/lt, a tryptophaneless mutant of E. coli B, when the growth rate was varied it was found that the number of mutations which occur to phage T_5 resistance or to phage T6 resistance is proportional to elapsed time regardless of the number of generations that have occurred. In addition, the mutation rate depends on the growth factor used to control the growth rate as well as on other culture conditions. Anaerobic growth, for example, produces a lower mutation rate to T_5 resistance than aerobic growth. Furthermore, one bacterial strain was found to have a considerably higher mutation rate than the other strains studied.

The mutation rate is strikingly increased by the presence of certain purines in the medium. Theophylline (150 mg/l) gives almost a ten-fold increase in the rate to T_5 resistance. Pyrimidines are without effect. The T_5 rate is affected much more than the T6 rate by the purines.

The mutagenic effect of ultraviolet light and of γ-rays from a cobalt source have been studied by continuously exposing a population of bacteria in the Chemostat to a low intensity of ultraviolet or γ-radiation. Here, in contrast to induction by purines, the rate to T6 resistance is increased almost as much as the rate to T_5 resistance.

The mutation rate induced by purines can be counteracted completely by certain ribonucleosides (adenosine, guanosine, and inosine, but not xanthosine). At a concentration of 400 micrograms per liter adenosine reduces the effect of theophylline to one-half. The effect of only one purine, tetramethyluric acid, has been found to resist antagonism by the nucleosides. The desoxynucleosides have little anti-mutagenic effect, desoxyadenosine being only one-twentieth as effective as adenosine.

The spontaneous mutation rate is also depressed by the nucleosides but to a somewhat lesser extent. With T5 resistance, for example, the spontaneous rate is reduced by as much as seventy percent.

Ultraviolet and γ-ray induced rates are not affected by any of these compounds.

The depression of the spontaneous rate by the nucleosides suggests that a large part of the so-called spontaneous rate is due to purines or purine like substances that normally occur in the cell. Indeed the actual rate observed may be determined by the concentration of antimutagens as well as mutagens in the organism.