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Progress Report for 1949-50

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The genetic changes in bacterial cultures grown in radioactive phosphorus have been shown to arise in part from radioactivity and more importantly from the reaction of the decaying atom. Both the geometry and the metabolic versatility of bacteria have been utilized to create a condition in which these effects were clearly separable. The total ionization received by the cells in different media can be shown to be almost identical experimentally, as well as by calculation, while the mutation rate varies with the disintegrations of P-32 located in the nucleoproteins. A mechanism is thus presented both for explaining the magnitude effect of internally absorbed unstable isotopes and also to indicate a chemical mechanism by which certain mutations are made manifest. The pattern of genetic changes - qualitative as well as quantitative is distinguishly different from that produced by external radiation.

The design of these experiments requires the growth of bacteria in a field of constant radiation. It was shown that this growth could be quite normal while causing a great increase in mutation frequency. More recently bacteria have also been cultured in a field of an x-ray machine where they grew well receiving 5000 r per hr. for 10 hrs.

From these and similar experiments it appears that while resting bacteria are relatively sensitive to radiation, growing ones not only are more resistant but reproduce in a manner indistinguishable from unirradiated controls.

In the external (x-ray) - radiation experiment it was shown also that total P does not influence the induction of mutation by radiation. In the internal, (P-32 radiation experiments) it was only the change of total P which produced different mutation rates. The experimental method of incorporating P-32 in different amounts was thus found valid.

The genetic change measured, was the appearance of streptomycin resistance in E. coli. Although there is evidence that this change always occurs at the same locus, many physiologically different streptomycin resistance types were found. The differences among the mutant types were related to growth and survival rate; and requirement for, and sensitivity to, various levels of streptomycin. Under the influence of different mutagenic conditions the proportion of types change in a manner suggesting either the selective production of certain mutants or the interaction of types within a culture. By being able to sort out the mutant types, it has been possible to accurately describe the mutation rate (under background conditions) in the face of the multiplicative origin of a large proportion of the mutants. On the basis of the knowledge of this rate it has been possible to devise rapid and accurate methods for determining mutation rates and types.

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In studying the interaction of mutant types, interest was focused on the phenomenon of streptomycin dependence. A certain proportion of mutants which are to some extent resistent to streptomycin, also require it for growth and survival. Since it is the appearance of these types which greatly varies with different radiation effects, it was important to understand the metabolic nature of streptomycin dependence. It was soon shown that even when a large conc. of the drug was required, no detectable amt. was actually utilized. In fact none of the mutants destroyed or removed any of the streptomycin from solution - whether they required it or not. The streptomycin could then be recovered (after the growth of the mutants) and measured - and finally reintroduced to stimulate the growth of new streptomycin requiring cultures. No trace substance organic or inorganic, was found capable of replacing the streptomycin in the requirement phenomenon. It was possible, however, to completely destroy the antibiotic quality of the drug while still completely maintaining its growth stimulating effect.

We have thus been able to contribute to an understanding of the genetic effect of radioactive isotopes and hope to continue to explore the genetic effects of atomic recoil by means of slow neutron (pile) irradiations. The period between a genetic change and its actual manifestation can be carefully studied by these methods because of the rapid succession of bacterial generations and the immense populations which may be tested. The variations in mutant types provides a tool for the qualitative analysis of different mutagenic effects associated with radioactivity. It will however, be necessary to explore further the nature of bacterial genetics to provide a basis for the underttanding of these variations and interactions. Previously obscure phenomena of bacterial genetics can now help to elucidate basic genetic mechanisms.

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