SUMMARY REPORT:

Bacterial Genetic Research
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by Joshua Lederberg

For the past several years, we have been concerned with clarifying the genetic life cycle of <u>Escherichia coli</u>. Until recently, most bacteriologists believed that bacteria reproduce only by fission, and are devoid of any sexual reproductive process. This viewpoint is, in fact, embodied in the name "Fission Fungi," which is applied to the Class of bacteria, and in a once-popular definition of bacteria that distinguished them from other living things by their supposed absence of a) "true" nuclei, and b) sexual reproduction. Since we can hope to achieve effective control of activities of the microorganisms, whether in medicine, industry, or agriculture, only if we have a correct and clear understanding of their biology, it is of more than academic importance that recent evidence points to the occurrence of more or less typical nuclei in most bacterial cells, and that a sexual method of reproduction occurs in at least one bacterial species, <u>Escherichia coli</u>, the common "colon bacillus."

So far, sexuality in E. coli has been studied almost entirely by purely genetic methods: in particular, it has been possible to show that, very occasionally, genetically distinguishable variants are capable of exchanging and reshuffling their genetic differences, a process technically described as gene recombination. The detailed features of the recombination process are such as almost certainly to require the occasional fusion of cells, so as to allow their different genetic determinants to intermingle, prior to their segregation in new or "re-" combinations.

Since recombination occurs only between one pair of cells per million under the most favorable conditions yet discovered, it is not difficult to understand why no convincing picture of the morphological basis of this process has yet been obtained.

Some progress has been made, however, toward the desired unification of genetic and cytological interpretations. Under certain conditions, bacterial cells can be propagated from a stage in their life cycle just following fusion, but without immediately undergoing segregation. Thus, these cultures consist of cells which individually carry genetic determinants from the two parents, as can be shown by direct single-cell isolation (in collaboration with Dr. M. R. Zelle of Cornell University). The genetic behavior of these heterozygous cultures shows signs of aberrancy not yet fully understood, but leaves no question as to their origin from the union of two parents (i.e., by a sexual process). When examined cytologically the nuclei of heterozygous cultures are clearly different from the nuclei of their parents, but this difficult microscopical analysis has not yet progressed to the point where definitive interpretations are possible.

Incomplete as it is, our new understanding of the genetic life/of this bacterium makes possible experimental analyses which could not hitherto be carried out. One line of research, for example, involves the patterns of genetic determination of enzyme production. Results to date have shown that these patterns are rather more complex than would have been anticipated, and create the opportunity of a long-term study of the ways in which different genetic changes may affect different aspects of the biosynthesis of bacterial enzymes. In another line of research, the effects of antiseptic agents on heterozygous bacteria are being studied. This technique permits the conclusion that some

antiseptics—such as physical radiations; nitrogen mustard; formaldehyde; hydrogen peroxide; acetic anhydride, and other chemicals, —kill bacteria either by virtue of, or in close coincidence to gross genetic damage, whereas other bactericides, such as high temperatures, iodine, basis dyes, streptomycin, and others kill without associated genetic effects.