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Phage and transformation (1): Phages.—Bacteriophage T<sub>4</sub> is probably the best available system. Forward mutations to "r" phenotype are of low sensitivity; reverse mutations of "rII"—type mutants are of high sensitivity. Chemicals inducing point mutations, which alter DNA either chemically (treatment of free phages) or during its duplication inside the bacteria can be detected. The sensitive assay of reverse mutations induction responds only to those agents which induce the required specific base pair change, e.g., ¬CA agents which induce the required base pair changes, a set of about 6 rII mutant strains having the required base pair changes should be tested. Agents which induce only inactivating DNA alterations rarely induce point mutations. They do, however, inactivate phage, but only more detailed genetic tests can verify that the inactivation is not caused by an alteration of phage protein.

Transformation.—The ideal system is that of linked mutation induction, which at present, is limited to the induction of fluorescent mutants in the tryptophan operon. Forward mutations to fluorescence are of medium sensitivity. Reverse mutations to indole independence are of high sensitivity. In these systems, inactivating DNA alterations can be measured and quantitatively compared to mutagenic DNA alterations. It has been shown that radical producing agents, known to induce both chromosome breaks and large chromosome mutations, inactivate transforming DNA but do not induce point mutations. Thus, in most bacterial or phage systems, these agents would not induce mutations and might be erroneously labeled nonmutagenic. Only agents which directly act on resting DNA can be easily assayed. For agents, like base analogs, which induce mutations in duplicating DNA, such measurements are difficult.

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