Meetings

Mutagenic and Carcinogenic Agents

Molecular action of mutagenic and carcinogenic agents was the main theme of the annual symposium sponsored by the Biology Division of the Oak Ridge National Laboratory in Gatlinburg, Tennessee, 6–9 April 1964. The symposium provided an occasion for a thorough discussion of the status of our present understanding of these mechanisms. The results, as a whole, bore out our uncertainty about the nature of the mechanisms of these processes.

The action of acridine dyes and of alkylating agents in mutagenesis was examined. The role played in mutagenesis by the intercalation of dye molecules in between nucleotides of double-stranded DNA was discussed by L. S. Lerman (University of Colorado School of Medicine). While the evidence for intercalation appears convincing, its role in mutagenesis could not be demonstrated. The main difficulty lies in the existence of acridine derivatives which intercalate very effectively but are not mutagenic.

The most frequent alterations of DNA caused by alkylating agents are also well known. These alterations should lead either to CG → AT transitions or to the loss of a base, which then could be substituted randomly. However, the mutagenic role by the latter mechanism is dubious because there is little evidence that certain expected base substitutions, called transversions, actually occur. F. J. de Serres (Oak Ridge National Laboratory), testing a variety of mutagens on *Neurospora*, concludes that mutations in these organisms are produced predominantly by base pair substitutions.

The exciting recent discovery by R. B. Setlow (Oak Ridge National Laboratory) of an enzyme which excises thymine dimers from ultraviolet-irradiated DNA may have a profound impact on the study of mutagenesis and perhaps also of recombination. It reveals the existence of enzymatic mechanisms which remove altered nucleotide sequences and replace them with the correct ones. At the same time, however, this discovery pointed out the important difficulties in studying the molecular bases of mutagenesis. In fact, between the mutations which are formed at first in DNA and those finally detected, there exists a series of screens —error correction, degeneracy of the code, and variable influence of different amino acid substitutions on protein function. A case in point is again that of mutagenesis by acridines; it was reported by Setlow that these dyes interfere with the excision of thymine dimers. Thus they may cause mutagenesis by suppressing error correction.

An important question in mutagenesis is also its relation with recombination. Evidence presented by G. E. Magni (University of Parma, Italy) showed that in yeast mutation frequencies are increased in meiosis. The question whether recombination is involved in mutagenesis by acridines was also raised by J. W. Drake (University of Illinois) in his discussion of the *r*II cistrons of bacteriophage T4.

Sydney Brenner (Molecular Biology Laboratory, Cambridge, England) described a novel approach to the problem of polarity of fragments of the polypeptide chain produced in bacteriophage "amber" mutants.

Sensitization of bacteria to x-rays and ultraviolet rays was shown by H. S. Kaplan (Stanford University School of Medicine) to be greatly enhanced by incorporation into DNA of certain purine and pyrimidine analogues.

Great uncertainties exist about the molecular mechanisms of carcinogenesis. These mechanisms are most likely different from those of mutagenesis, because very few substances are able to cause both consequences. A really meaningful test of this point, however, must await a study of the two actions in the same cell type.

It was apparent from the discussion that it is not possible to conclude what the target of carcinogenic action is. On one hand, the study of the electronic configuration (Bernard Pullman, University of Paris, France) and of the reactivity (Charles Heidelberger, University of Wisconsin) of carcinogenic hydrocarbons suggests that they act by interacting with a protein. On the other hand, the study of carcinogenic alkylating agents tends to implicate an interaction with DNA (Peter Brookes and P. D. Lawley, Chester Beatty Research Institute, London, England). Unfortunately all carcinogens can interact with essentially all macromolecular components in the cells.

The striking relationship of carcinogenic hydrocarbons with a soluble protein of the skin was discussed by Heidelberger. This relationship has been known for some time; now its possible meaning for carcinogenesis has been reexamined. Models have been discussed which might explain carcinogenesis, at the level of regulation, as a stable shift in feedback systems. It has been suggested that the soluble protein may be a gene repressor which, upon interaction with the carcinogen, causes the discontinuation of its own production.

Hubert Chantrenne (University of Brussels, Belgium), in describing dramatic changes in RNA and protein synthesis of *Bacillus cereus* caused by incorporation of 8-azaguanine, discussed these effects with regard to regulatory mechanisms and the formation of abnormal enzymes.

The symposium ended with a brief discussion of viral carcinogenesis (Harry Rubin, University of California); this process can be considered as a genetic alteration of the cell caused by the persistence of viral genes.

This conference was sponsored by the Biology Division, Oak Ridge National Laboratory, and the U.S. Atomic Energy Commission. A publication of the symposium proceedings will appear as a supplement to the October 1964 issue of the *Journal of Cellular and Comparative Physiology*.

RENATO DULBECCO
Salk Institute for Biological Studies, San Diego, California

Anaerobic Microorganisms in the Soil

Significant advances have been made in the study of anaerobic bacteria in rumen and sludge digestion microbiology, but the study of anaerobic and microaerophilic bacteria in soil micro-