Environmental Carcinogens

Polycyclic Hydrocarbons and Carcinogenesis. RONALD G. HARVEY, Ed. American Chemical Society, Washington, D.C., 1985. x, 406 pp., illus. $74.95. ACS Symposium Series, 283. From a symposium, Philadelphia, Aug. 1984.

Polycyclic aromatic hydrocarbons (PAH's) have been known as environmental carcinogens since Pott noted the high incidence of scrotal cancer among chimney sweeps in London more than 200 years ago. Yet studies of just the last few decades have revealed a puzzling disparity in tumorigenic potency among PAH's that are structurally related. More recently it has been established that a number of steps, including metabolic activation, reaction with DNA, and mutation at replication, usually follow the entry of such a carcinogenic chemical into a cell before cell transformation occurs. Subtle structural differences among the PAH's govern the course of each step and hence the biological outcome. Our current understanding of molecular events occurring at each step is comprehensively reviewed in this collection of papers developed from an American Chemical Society symposium.

Dipple provides an introduction that summarizes key discoveries, notably the pioneering work by E. Miller and J. Miller showing the importance of metabolic activation, the studies of Brookes and Lawley pointing to the interaction of carcinogens with DNA, and the role, demonstrated by Sims and generalized by Jerina and Daly, of bay-region diol epoxides in PAH reactivity with DNA. Benzo(*a*)pyrene, the prototype PAH, is activated to the 7,8-diol-9,10-epoxide (BPDE) in four isomeric forms, (+)syn, (−)syn, (+)anti, and (−)anti. In newborn mice the (+)anti isomer is the most tumorigenic. Harvey summarizes the syntheses devised in his laboratory for the preparation of biologically active dihydrodiol and diol expoxide metabolites, upon which the work of so many others depends. Quantum chemical calculations that provide a basis for the bay-region theory of PAH carcinogenesis are reviewed by Lehr *et al.*, who summarize the remarkably good correlations between reactivity or mutagenicity and quantum chemical parameters that estimate pi electron stabilization upon conversion of the epoxide to a benzylic carbocation.

Yang and coworkers contrast the different stereoselective metabolic activation pathways undergone by the weak carcinogen benz(*a*)anthracene and the two potent carcinogens benzo(*a*)pyrene and 7,12-dimethylbenz(*a*)anthracene by the cytochrome P-450 liver enzymes. Cavalieri and Rogan and also Marnett discuss an alternative activation pathway to monooxygenation by the cytochrome P-450 system, namely one-electron oxidation by cellular peroxidases such as prostaglandin H synthetase. These may produce totally different activation products and adducts with DNA, or a different distribution of activation products. A higher proportion of syn BPDE is produced in peroxide-dependent oxidation than in cytochrome P-450–dependent epoxidation, for example. Another example, given by Kadlubar and Beland in a comprehensive chapter on metabolic activation of arylamines and arylamides, is 2-naphthylamine, which is activated to the unique 2-imino-1-naphthoquinone by prostaglandin H synthetase, whereas the most important products in the cytochrome P-450 system result from N-conjugation with sulfuric, acetic, or glucuronic acids. The one-electron oxidation pathway may be important, since metabolic activation by this route may occur in tissues with low mixed-function oxygenase activity. Beland *et al.* also describe nitro-PAH activation, which involves both oxidative and reductive pathways at the nitro group.

Hecht *et al.* discuss, inter alia, the puzzling tumor-enhancing effect of a bay-region methyl group in PAH's, and Glusker reveals the buckling produced by steric hindrance between the methyl and adjacent bay-region hydrogens, which may play a role in provoking this high tumorigenicity. Crystal structures of PAH-modified nucleosides and computer models of DNA adducts based on these structures are also presented by Glusker. Computer models are also offered by K. Miller *et al.*, who describe a comprehensive computer modeling effort with energy calculations to reconcile data on stereoselective binding of benzo(*a*)pyrene metabolites and adduct conformations. Geacintov summarizes his careful spectroscopic studies and kinetic analyses that indicate a unique conformation of the important (+)anti BPDE-DNA adduct in which the long axis of the pyrene moiety is nearly perpendicular to the base planes and the other isomers are largely "quasi-intercalated." Spectroscopic studies of physical intercalation into DNA by PAH metabolites are also described by Le Breton. Methods for the detection and identification of adducts, including recent post-labeling and immunological techniques, are reviewed by Jeffrey.

Finally, forefront work on mutational consequences of DNA damage by PAH's is taken up by Eisenstadt. Base substitutions, primarily at G-C pairs, are the primary outcome of benzo(*a*)pyrene modification in the *lacI* system of *Escherichia coli*, but other categories of mutations have also been noted in this and other genetic systems.

In all, this comprehensive, up-to-date book in which a wealth of information is reviewed by generally distinguished contributors will certainly be a valuable reference to researchers in the field.

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Bacterial Phylogeny

Evolution of Prokaryotes. KARL H. SCHLEIFER and ERKO STACKEBRANDT, Eds. Academic Press, Orlando, Fla., 1985. x, 367 pp., illus. $30. From a symposium, Munich, Sept. 1984.

The refinement of nucleic acid technology in recent years has had a major impact on studies of bacterial taxonomy. Earlier technologies for measuring overall DNA homologies were useful only for characterizing very closely related organisms. Now, however, molecular cloning, Southern hybridization, and DNA/RNA sequencing methods have made it possible to zero in on specific genomic determinants and assay their similarities and differences across large taxonomic distances. In some cases, the results have been spectacular, as in the recent identification of distinctive forms of ribosomal RNA in the groups now known as the Eubacteria and the Archaebacteria. The significance of this discovery became apparent almost immediately because the nucleic acid–based classification corresponded so well to a number of other recently elucidated characteristics of basic cellular organization that differed sharply between the two classes of prokaryotes (for example cell wall and membrane lipid composition).

The important insights gained from RNA studies were major factors in the organization of the symposium of which *Evolution of Prokaryotes* is the proceedings. Several papers in the volume describe the RNA sequencing and oligonucleotide cataloging methodology, sometimes with considerable speculation on the significance of the results obtained to date. The last paper describes the history of bacterial taxonomy and proclaims the present to be "a time in which the out-