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 outlines of a monophyletic tree of all organisms are becoming increasingly clear" thanks to the new methods. This optimistic expression reflects the tacit assumption of virtually all the authors that dendrograms of ribosomal RNA sequence similarities directly reflect phylogenetic relationships and that all branches must be connected in a single point at the base. From a logical perspective, of course, it is curious to consider that the diagrams invariably get sharper (and focus on fewer groups) as the data get fuzzier (by showing less relatedness), and I wonder if the insistence on monophyletic hypotheses is not cheating us of some useful new ways to interpret taxonomic data.

Happily, the papers presented in *Evolution of Prokaryotes* are not limited to discussions of sequencing and construction of oligonucleotide catalogs. The organizers wisely chose to include comparative discussions of many aspects of bacterial physiology, including transcription, translation, photosynthesis, respiration, chemolithoautotrophy (the ability to grow without an organic carbon source by using energy derived from the metabolism of inorganic compounds), CO_2 fixation, the citric acid cycle, and arginine metabolism. In addition, two papers deal with transposable elements. The standard of presentation is quite good, especially for a symposium volume published within a year of the actual meeting. Although much of the material is rather specialized, I found the book full of useful information and very instructive about certain topics that are normally accessible only to specialists, such as particular adaptations of the citric acid cycle in various bacterial groups and the taxonomic distribution of different photosynthetic electron transport systems.

Though my reaction to the book is favorable because it has such a broad physiological approach to the topic of bacterial evolution, I do note two particular deficiencies in subject matter. The first is the absence of the environmental microbiologist's insight into the unique ecological role bacteria play by virtue of their incredibly diverse biochemical activities and ability to live in many different environments. Basic microbiology textbooks explain how bacteria control the levels of various chemicals over the entire earth, but topics such as sulfur oxidation or nitrification and denitrification are considered in this book only from the perspective of cellular energetics. Surely the way bacteria respond to and regulate changes in the chemical composition of the biosphere is highly relevant to any discussion of how they acquired the particular constellations of biochemical properties they now display.

The second deficiency is that the treatment of mechanisms for genomic change in bacteria is very cursory. The discussion of transposable elements is limited, and other aspects of bacterial genetics are neglected. Conjugal spread of plasmids, which frequently encode taxonomically important biochemical systems, is discussed only in the paper on chemolithoautotrophy. Other topics relevant to evolution (such as transfer and uptake of heterologous DNA, inducible mutator systems, and the effects of stress regimens on genomic stability) are hardly mentioned, and there is no overall review of one of the most significant examples of bacterial evolution to occur in our time—the emergence of genetically mobile resistance mechanisms in response to human use of antibiotics.

There are two levels where the lack of emphasis on genetics is significant. At the detailed level of specific cases, many intriguing but poorly understood observations are reported that could readily be clarified by genetic approaches that are now routine. For example, the chapter on the citric acid cycle tells us that *Escherichia coli* can mutate to produce novel citrate synthase enzymes that have properties similar to the enzymes typical either of *Acetobacter* or of *Bacillus*, organisms that fall into distinctive taxonomic groups on the basis of ribosome and cell envelope structures. We would learn a great deal about possible evolutionary mechanisms by finding out how the *E. coli* genome changed to produce these novel activities and how the resulting DNA segments compare to their analogs in the *Acetobacter* and *Bacillus* genomes. At a more theoretical level, it is helpful to remember that we now possess a large corpus of information about various aspects of mutation, rearrangement, and exchange in the genomes of laboratory and natural populations of bacteria. This is important because established evolutionary theory is still founded on outmoded assumptions about the mechanisms of genetic variation, basically accepting the doctrine that change arises from the relatively constant appearance of random, independent localized alterations of sequence organization. Such a view of the nature of hereditary change is far out of touch with current knowledge (both for bacteria and for eukaryotes). Thus, it is possible that studies of prokaryotic evolution may make their most important contribution to evolutionary biology in general by introducing an element of genetic sophistication to the subject.

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Books Received

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Alternative Energy Sources VI. T. Nejat Veziroğlu, Ed. Hemisphere, Washington, D. C., 1985. Four volumes.Vol. 1, Solar Energy and Applications. xviii, 553 pp., illus. $87. Vol. 2, Solar Applications/Waste Energy. xviii, 618 pp., illus. $87. Vol. 3, Wind/Ocean/Nuclear/Hydrogen. xviii, 613 pp., illus. $87. Vol. 4, Conservation/Management/Policy. xviii, 601 pp., illus. $87. From a conference, Miami Beach, Dec. 1983.

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The Anatomy of a Business Strategy. Bell, Western Electric, and the Origins of the American Telephone Industry. George David Smith. Johns Hopkins University Press, Baltimore, 1985. xxiv, 238 pp., illus. $20. The JohnsHopkins/AT&T Series in Telephone History.

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The Bicentennial Census. New Directions for Methodology in 1990. Constance F. Citro and Michael L. Cohen, Eds. National Academy Press, Washington, D.C., 1985. xvi, 404 pp. Paper, $23.95.

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