PROGRESS IN

Nucleic Acid Research and Molecular Biology

Volume 29

Genetic Mechanisms in Carcinogenesis

edited by

WALDO E. COHN

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Biology Division
Oak Ridge National Laboratory
Oak Ridge, Tennessee

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Preface

In the Prefaces to previous volumes comprised (as is this one) of papers presented at a symposium, note was taken of the shift in emphasis from the original thrust of this serial publication—nucleic acid chemistry—to the present concern with the involvement of nucleic acids in a number of fields, including genetics, virology, and immunology, and in this volume carcinogenesis. One now seeks to explain the mechanisms of biological events in terms of the chemistry of the nucleic acids and specifically in terms of that icon of "molecular biology" the double helix, or, perhaps more fundamentally still, hydrogen-bonding and base-pairing. The symposium proceedings clearly fall into this area of interest.

The speakers were researchers whom we would have wished to invite to contribute to this publication even in the absence of such a unifying event as a symposium. Hence the decision was made to ask the participants (and contributors to the parallel "poster" sessions) to submit papers or extended summaries of their presentations for a work devoted to the symposium. This volume is the result.

I would like to announce a change in the editorship of this serial publication. Begun in 1963 with the late J. N. Davidson and me as editors (and as a continuing sequel to the classic three-volume work edited by Chargaff and Davidson, "The Nucleic Acids: Chemistry and Biology") I continued as sole editor after the untimely death of Davidson in 1972 (see the Obituary in Volume 13, pages xxi–xxiii). With Volume 30, this publication will again have two editors. Kivie Moldave will join me in the effort to maintain the standards set by the preceding volumes.

As stated often in earlier Prefaces, "we seek to provide a forum for discussion . . . and we welcome suggestions . . . as to how this end may best be served."

WALDO E. COHN

Abbreviations and Symbols

All contributors to this Series are asked to use the terminology (abbreviations and symbols) recommended by the IUPAC-IUB Commission on Biochemical Nomenclature (CBN) and approved by IUPAC and IUB, and the Editor endeavors to assure conformity. These Recommendations have been published in many journals (*1*, *2*) and compendia (*3*) in four languages and are available in reprint form from the Office of Biochemical Nomenclature (OBN), as stated in each publication, and are therefore considered to be generally known. Those used in nucleic acid work, originally set out in section 5 of the first Recommendations (*1*) and subsequently revised and expanded (*2*, *3*), are given in condensed form (I–V) below for the convenience of the reader. Authors may use them without definition, when necessary.

I. Bases, Nucleosides, Mononucleotides

1. *Bases* (in tables, figures, equations, or chromatograms) are symbolized by Ade, Gua, Hyp, Xan, Cyt, Thy, Oro, Ura; Pur = any purine, Pyr = any pyrimidine, Base = any base. The prefixes S–, H_2, F–, Br, Me, etc., may be used for modifications of these.

2. *Ribonucleosides* (in tables, figures, equations, or chromatograms) are symbolized, in the same order, by Ado, Guo, Ino, Xao, Cyd, Thd, Ord, Urd (Ψrd), Puo, Pyd, Nuc. Modifications may be expressed as indicated in (1) above. Sugar residues may be specified by the prefixes r (optional), d (=deoxyribo), a, x, l, etc., to these, or by two three-letter symbols, as in Ara-Cyt (for aCyd) or dRib-Ade (for dAdo).

3. *Mono-, di-, and triphosphates of nucleosides* (5′) are designated by NMP, NDP, NTP. The N (for "nucleoside") may be replaced by any one of the nucleoside symbols given in II-1 below. 2′-, 3′-, and 5′- are used as prefixes when necessary. The prefix d signifies "deoxy." [Alternativelv, nucleotides may be expressed by attaching P to the symbols in (2) above. Thus: P-Ado = AMP; Ado-P = 3′-AMP] cNMP = cyclic 3′:5′-NMP; Bt_2cAMP = dibutyryl cAMP, etc.

II. Oligonucleotides and Polynucleotides

1. Ribonucleoside Residues

(a) Common: A, G, I, X, C, T, O, U, Ψ, R, Y, N (in the order of I-2 above).

(b) Base-modified: sI or M for thioinosine = 6-mercaptopurine ribonucleoside; sU or S for thiouridine; brU or B for 5-bromouridine; hU or D for 5,6-dihydrouridine; i for isopentenyl; f for formyl. Other modifications are similarly indicated by appropriate *lower-case* prefixes (in contrast to I-1 above) (*2*, *3*).

(c) Sugar-modified: prefixes are d, a, x, or l as in I-2 above; alternatively, by ***italics*** or boldface type (with definition) unless the entire chain is specified by an appropriate prefix. The 2′-*O*-methyl group is indicated by *suffix* m (e.g., -Am- for 2′-*O*-methyladenosine, but -mA- for 6-methyladenosine).

(d) Locants and multipliers, when necessary, are indicated by superscripts and subscripts, respectively, e.g., -m_2^6A- = 6-dimethyladenosine; -s^4U- or -^{4}S- = 4-thiouridine; -ac^{4}Cm- = 2′-*O*-methyl-4-acetylcytidine.

(e) When space is limited, as in two-dimensional arrays or in aligning homologous sequences, the prefixes may be placed *over the capital letter*, the suffixes *over the phosphodiester symbol*.

2. Phosphoric Residues [left side = 5′, right side = 3′ (or 2′)]

(a) Terminal: p; e.g., pppN . . . is a polynucleotide with a 5′-triphosphate at one end; Ap is adenosine 3′-phosphate; C > p is cytidine 2′:3′-cyclic phosphate (*1*, *2*, *3*); p < A is adenosine 3′:5′-cyclic phosphate.

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(b) Internal: hyphen (for known sequence), comma (for unknown sequence); unknown sequences are enclosed in parentheses. E.g., pA-G-A-C(C_2,A,U)A-U-G-C > p is a sequence with a (5′) phosphate at one end, a 2′:3′-cyclic phosphate at the other, and a tetranucleotide of unknown sequence in the middle. **(Only codon triplets should be written without some punctuation separating the residues.)**

3. Polarity, or Direction of Chain

The symbol for the phosphodiester group (whether hyphen or comma or parentheses, as in 2b) represents a 3′-5′ link (i.e., a 5′ . . . 3′ chain) unless otherwise indicated by appropriate numbers. "Reverse polarity" (a chain proceeding from a 3′ terminus at left to a 5′ terminus at right) may be shown by numerals or by right-to-left arrows. Polarity in any direction, as in a two-dimensional array, may be shown by appropriate rotation of the (capital) letters so that 5′ is at left, 3′ at right when the letter is viewed right-side-up.

4. Synthetic Polymers

The complete name or the appropriate group of symbols (see II-1 above) of the repeating unit, **enclosed in parentheses if complex or a symbol,** is either (a) preceded by "poly," or (b) followed by a subscript "n" or appropriate number. **No space follows "poly"** (2, 5).

The conventions of II-2b are used to specify known or unknown (random) sequence, e.g.,

polyadenylate = poly(A) or A_n, a simple homopolymer;

poly(3 adenylate, 2 cytidylate) = poly(A_3C_2) or $(A_3,C_2)_n$, an *irregular* copolymer of A and C in 3 : 2 proportions;

poly(deoxyadenylate-deoxythymidylate) = poly[d(A-T)] or poly(dA-dT) or $(dA\text{-}dT)_n$ or $d(A\text{-}T)_n$, an *alternating* copolymer of dA and dT;

poly(adenylate,guanylate,cytidylate,uridylate) = poly(A,G,C,U) or $(A,G,C,U)_n$, a random assortment of A, G, C, and U residues, proportions unspecified.

The prefix copoly or oligo may replace poly, if desired. The subscript "n" may be replaced by numerals indicating actual size, e.g., $A_n \cdot dT_{12\text{-}18}$.

III. Association of Polynucleotide Chains

1. *Associated* (e.g., H-bonded) chains, or bases within chains, are indicated by a *center dot* (not a hyphen or a plus sign) separating the *complete* names or symbols, e.g.:

poly(A) · poly(U) or $A_n \cdot U_m$
poly(A) · 2 poly(U) or $A_n \cdot 2U_m$
poly(dA-dC) · poly(dG-dT) or $(dA\text{-}dC)_n \cdot (dG\text{-}dT)_m$.

2. *Nonassociated* chains are separated by the plus sign, e.g.:

2[poly(A) · poly(U)] → poly(A) · 2 poly(U) + poly(A)
or $2[A_n \cdot U_m] \rightarrow A_n \cdot 2U_m + A_n$.

3. Unspecified or unknown association is expressed by a comma (again meaning "unknown") between the completely specified chains.

Note: In all cases, each chain is completely specified in one or the other of the two systems described in II-4 above.

IV. Natural Nucleic Acids

RNA	ribonucleic acid or ribonucleate
DNA	deoxyribonucleic acid or deoxyribonucleate
mRNA; rRNA; nRNA	messenger RNA; ribosomal RNA; nuclear RNA
hnRNA	heterogeneous nuclear RNA
D-RNA; cRNA	"DNA-like" RNA; complementary RNA

mtDNA	mitochondrial DNA
tRNA	transfer (or acceptor or amino-acid-accepting) RNA; replaces sRNA, which is not to be used for any purpose
aminoacyl-tRNA	"charged" tRNA (i.e., tRNA's carrying aminoacyl residues); may be abbreviated to AA-tRNA
alanine tRNA or $tRNA^{Ala}$, etc.	tRNA normally capable of accepting alanine, to form alanyl-tRNA, etc.
alanyl-tRNA or alanyl-$tRNA^{Ala}$	The same, with alanyl residue covalently attached. [*Note:* fMet = formylmethionyl; hence $tRNA^{fMet}$, identical with $tRNA_f^{Met}$]

Isoacceptors are indicated by appropriate subscripts, i.e., $tRNA_1^{Ala}$, $tRNA_2^{Ala}$, etc.

V. Miscellaneous Abbreviations

P_i, PP_i	inorganic orthophosphate, pyrophosphate
RNase, DNase	ribonuclease, deoxyribonuclease
t_m (not T_m)	melting temperature (°C)

Others listed in Table II of Reference 1 may also be used without definition. No others, with or without definition, are used unless, in the opinion of the editor, they increase the ease of reading.

Enzymes

In naming enzymes, the 1978 recommendations of the IUB Commission on Biochemical Nomenclature (*4*) are followed as far as possible. At first mention, each enzyme is described *either* by its systematic name *or* by the equation for the reaction catalyzed *or* by the recommended trivial name, followed by its EC number in parentheses. Thereafter, a trivial name may be used. Enzyme names are not to be abbreviated except when the substrate has an approved abbreviation (e.g., ATPase, but not LDH, is acceptable).

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2. *EJB* **15**, 203 (1970); *JBC* **245**, 5171 (1970); *JMB* **55**, 299 (1971); and elsewhere.†
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4. "Enzyme Nomenclature" [Recommendations (1978) of the Nomenclature Committee of the IUB]. Academic Press, New York, 1979.
5. "Nomenclature of Synthetic Polypeptides," *JBC* **247**, 323 (1972); *Biopolymers* **11**, 321 (1972); and elsewhere.†

Abbreviations of Journal Titles

Journals	*Abbreviations used*
Annu. Rev. Biochem.	ARB
Arch. Biochem. Biophys.	ABB
Biochem. Biophys. Res. Commun.	BBRC

*Contractions for names of journals follow.

†Reprints of all CBN Recommendations are available from the Office of Biochemical Nomenclature (W. E. Cohn, Director), Biology Division, Oak Ridge National Laboratory, Box Y, Oak Ridge, Tennessee 37830, USA.

Biochemistry	Bchem
Biochem. J.	BJ
Biochim. Biophys. Acta	BBA
Cold Spring Harbor Symp. Quant. Biol.	CSHSQB
Eur. J. Biochem.	EJB
Fed. Proc.	FP
Hoppe-Seyler's Z. physiol. Chem.	ZpChem
J. Amer. Chem. Soc.	JACS
J. Bacteriol.	J. Bact.
J. Biol. Chem.	JBC
J. Chem. Soc.	JCS
J. Mol. Biol.	JMB
Nature, New Biology	Nature NB
Nucleic Acid Research	NARes
Proc. Nat. Acad. Sci. U.S.	PNAS
Proc. Soc. Exp. Biol. Med.	PSEBM
Progr. Nucl. Acid Res. Mol. Biol.	This Series

Some Articles Planned for Future Volumes

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D. APIRION

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P. N. BORER

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L. BOSCH

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H. BUSCH

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JAMES A. LAKE

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JAMES L. MANLEY

Participation of Aminoacyl-tRNA Synthetases and tRNAs in Regulatory Processes
G. NASS

Synthesis, Processing, and Gene Structure of Vasopressin and Oxytocin
D. RICHTER

Contents

CONTRIBUTORS xiii

PREFACE xix

ABBREVIATIONS AND SYMBOLS xxi

SOME ARTICLES PLANNED FOR FUTURE VOLUMES

Introduction 1

W. K. Yang

I. Genetic Factors in Cancer

Evolution of RNA Tumor Viruses: Analogy for Nonviral Carcinogenesis 7

Howard M. Temin

Model Hereditary Cancers of Man 17

Alfred G. Knudson, Jr.

Bacterial "Inserted Sequence" Elements and Their Influence on Genetic Stability and Evolution 27

Werner Arber

Significance of Specific Chromosomal Translocations and Trisomies for the Genesis of Murine and Human Tumors of the Lymphocyte–Plasmacyte Lineage 35

George Klein (Summary prepared by W. W. Au)

Short Communications

Quantitation of One Aspect of Karyotype Instability Associated with Neoplastic Transformation in Chinese Hamster Cells 39

L. S. Cram, M. F. Bartholdi, F. A. Ray, G. L. Travis, J. H. Jett, and P. M. Kraemer

Mechanism of Mutation at the Adenine Phosphoribosyltransferase Locus in CHO cells 42

A. Simon and M. W. Taylor

Development of a Transplantable Mouse Myeloid Leukemia Model System: A Preliminary Report 47

W. W. Au, H. E. Luippold, and J. A. Otten

II. Genetic Elements in Radiation and Chemical Carcinogenesis

Molecular Studies of the Radiation Leukemia Virus (RadLV) and Related Retroviruses of C57BL/Ka Mice 53

R. A. Grymes, M. L. Scott, J. P. Kim, K. E. Fry, and Henry S. Kaplan

Endogenous Retrovirus and Radiation-Induced Leukemia in the RFM Mouse 75

Raymond W. Tennant, L. R. Boone, P. A. Lalley, and W. K. Yang

Genetic and Probability Aspects of Cell Transformation by Chemical Carcinogens 87

Charles Heidelberger, J. R. Landolph, R. E. K. Fournier, A. Fernandez, and A. R. Peterson

Short Communications

Replication and Demethylation of O^6-Methylguanine in DNA 99

E. T. Snow, R. S. Foote, and S. Mitra

Quantitative Assay of Low Level of Benzo[*a*]pyrenediol Epoxide Bound to DNA by Acid-Induced Liberation of Tetraols followed by Chromatography and Fluorometric Detection 103

R. O. Rahn, J. M. Holland, and L. R. Shugart

Transfer of Phorbol Ester Promotability by Transfection of DNA from Promotable into Nonpromotable Cells 107

N. H. Colburn, C. B. Talmadge, and T. D. Gindhart

Specificity of Interaction between Carcinogenic Polynuclear Aromatic Hydrocarbons and Nuclear Proteins: Widespread Occurrence of a Restricted Pattern of Histone Binding in Intact Cells 111

M. C. MacLeod, J. C. Pelling, T. J. Slaga, P. A. Noghrei-Nikbakht, B. K. Mansfield, and J. K. Selkirk

III. Mechanism of Viral Carcinogenesis

Role of Polyoma T Antigens in Malignant Cell Transformation 119

Walter Eckhart

Avian Leukosis Viruses and Cancer: Genetics of Insertional Mutagenesis 127

Harriet L. Robinson

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