

ICN — UCLA Symposia on Molecular and Cellular Biology

Vol. IX, 1978

DNA REPAIR MECHANISMS

edited by

PHILIP C. HANAWALT

ERROL C. FRIEDBERG

C. FRED FOX

ICN-UCLA Symposia on Molecular and Cellular Biology
Vol. IX, 1978

DNA REPAIR MECHANISMS

edited by

PHILIP C. HANAWALT

*Department of Biological Sciences
Stanford University
Stanford, California*

ERROL C. FRIEDBERG

*Department of Pathology
Stanford University Medical School
Stanford, California*

C. FRED FOX

*Department of Microbiology
and Molecular Biology Institute
University of California, Los Angeles
Los Angeles, California*



ACADEMIC PRESS New York San Francisco London 1978
A Subsidiary of Harcourt Brace Jovanovich, Publishers

COPYRIGHT © 1978, BY ACADEMIC PRESS, INC.

ALL RIGHTS RESERVED.

NO PART OF THIS PUBLICATION MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM OR BY ANY MEANS, ELECTRONIC OR MECHANICAL, INCLUDING PHOTOCOPY, RECORDING, OR ANY INFORMATION STORAGE AND RETRIEVAL SYSTEM, WITHOUT PERMISSION IN WRITING FROM THE PUBLISHER.

ACADEMIC PRESS, INC.

111 Fifth Avenue, New York, New York 10003

United Kingdom Edition published by
ACADEMIC PRESS, INC. (LONDON) LTD.
24/28 Oval Road, London NW1 7DX

Library of Congress Cataloging in Publication Data

Main entry under title:

DNA repair mechanisms.

(ICN-UCLA symposia on molecular and cellular biology ;
v. 9)

"One of the ICN-UCLA 1978 winter symposia on molecular and cellular biology, sponsored by ICU Pharmaceuticals, Inc. and organized through the Molecular Biology Institute of the University of California, Los Angeles."

1. Deoxyribonucleic acid repair—Congresses.

I. Hanawalt, Philip C., 1931- II. Friedberg, Errol C. III. Fox, C. Fred. IV. ICN Pharmaceuticals, Inc. V. California. University. University at Los Angeles. Molecular Biology Institute. VI. Series: ICN-UCLA symposia on molecular & cellular biology ; v. 9.

[DNLM: 1. DNA repair—Congresses. 2. Lyases—
Congresses. W3 I322 v. 9 1978 / QH467 D107 1978]

QH467.D17 574.8'732 78-15125

ISBN 0-12-322650-3

PRINTED IN THE UNITED STATES OF AMERICA

Preface

This volume documents the proceedings of a major international conference on DNA Repair Mechanisms, held at Keystone, Colorado in February 1978. The meeting was one of the 1978 ICN-UCLA Winter Symposia on Molecular and Cellular Biology, sponsored by ICN Pharmaceuticals, Inc., and organized through the Molecular Biology Institute of the University of California, Los Angeles.

The conference marked the fourth anniversary of the first comprehensive international meeting on the subject of DNA repair held at Squaw Valley, California in 1974. That meeting generated a great deal of enthusiasm and catalyzed many significant collaborative ventures among the nearly 200 participants. In the ensuing years the field has more than doubled in number of researchers and in the rate of proliferation of new information and publications on the subject. This surge of interest is due in part to the increased evidence that many types of repairable damage in DNA are also highly mutagenic and carcinogenic. Procedures for measuring the repair of damaged DNA have become refined and new ones have been developed in the past several years. In addition, new pathways for the repair of DNA damage by excision have been discovered and error-prone bypass modes have been elucidated. Enough new repair enzymes have been isolated and characterized that it has become imperative that a rational nomenclature be developed. Much more is known about the hereditary disease *Xeroderma pigmentosum* with respect to its deficiency in several DNA repair modes and evidence for repair defects in other human hereditary diseases is being established. DNA repair currently represents one of the most active fields of investigation in the overlapping spheres of molecular biology and clinical research on human genetic deficiency and aging.

The 1978 meeting was attended by nearly 400 participants. The format for the meeting included some novel aspects as well as the more traditional symposium style. An overall perspective on the field of DNA repair was provided in plenary sessions in which 17 speakers outlined current areas of active investigation and important problems in the field. Then, selected questions formed the focus of 13

workshop sessions coordinated by designated experts representing various views and approaches to the respective problems. Poster sessions were utilized to facilitate the presentation of new data from additional participants.

It is important that researchers in DNA repair periodically have the opportunity to gather at a conference of this sort. The field includes scientists in the diverse disciplines of biochemistry, genetics, photobiology, radiology, and environmental biology. Workers in these disciplines are affiliated with different national and international scientific societies and the field of DNA repair derives benefits from these multiple associations. However, it also requires multidisciplinary gatherings such as this conference to promote the free interchange of information essential to the advancement of the field.

This volume includes papers from the plenary session speakers and the workshop participants as well as short summaries by the workshop session conveners, describing the current state of agreement and dispute on specific topic areas. We have additionally included a number of manuscripts from a selected group of poster contributors. Difficult decisions had to be made because of the space limitations in the volume and we sincerely regret that we were unable to include papers from more of the excellent poster presentations. In choosing these we tried to include documentation of important new findings, theories, and approaches to complement the material covered in the other papers and have, wherever possible, stressed the availability of multiple biological systems of DNA repair and mutagenesis research. Finally, the volume includes contributions from the two keynote lecturers, Paul Howard-Flanders and Bruce Ames.

We have arranged the papers in the volume roughly according to their organization in the meeting, with an attempt to group plenary session contributions together with the relevant workshop and poster manuscripts. We hope that the result represents a logical and comprehensive treatment of the rapidly moving field of DNA repair as of early 1978.

We wish to acknowledge the financial sponsorship for this meeting provided predominantly by contracts with the U.S. Department of Energy and by the National Institutes of Health (in particular the National Cancer Institute, National Institute on Aging, National Institute on Child Health and Development, National Institute on Allergies and Infectious Diseases and the Fogarty International Center). We also solicited support from many major chemical and drug companies because of the obvious relationship of this conference topic to carcinogenic chemicals in the environment. We are pleased that the following companies were able to respond with support and we appreciate the commitment to scientific enquiry and concern expressed by these private organizations: E. I. du Pont de Nemours and Co., Merck and Co., Eli Lilly, and Hoffman-La Roche.

We appreciate the excellent suggestions and help we received from many of our colleagues in assembling the program for this meeting. Finally we are indebted to Fran Stusser and her staff and to the Keystone administration for their generally efficient handling of the arrangements for the meeting.

Philip C. Hanawalt
Errol C. Friedberg

Contents

Preface

xvii

1. REPAIRABLE DAMAGE: IDENTIFICATION AND QUANTIFICATION

- | | |
|---|----|
| 1. Repairable Damage in DNA
<i>Peter A. Cerutti</i> | 1 |
| 2. Distribution and Quantitation of DNA Damage: Workshop Summary
<i>Ann Ganesan</i> | 15 |
| 3. Lesions in Alkylated DNA Determined by Susceptibility to Alkali, Apurinic Endonuclease, or N-Glycosidase
<i>Thomas P. Brent, George W. Teebor, and Nahum J. Duker</i> | 19 |
| 4. Enzymatic Recognition of DNA Damages Induced by Ionizing Radiation
<i>Susan S. Wallace, Paul R. Armel, and Harold L. Katcher</i> | 23 |
| 5. <i>Micrococcus luteus</i> UV-Endonuclease-Sensitive Sites in Far- and Near-UV-Irradiated Chinese Hamster Ovary Cells
<i>Richard J. Reynolds and Paul H. M. Lohman</i> | 27 |
| 6. Repair of Alkylated DNA in Chinese Hamster Cells Measured by Loss of Enzyme-Sensitive Sites in Isolated DNA
<i>John J. Roberts and Jason Shackleton</i> | 31 |
| 7. Serologic Assay of DNA Base Damage
<i>Hazel L. Lewis and John F. Ward</i> | 35 |

8. Non-dimer UV Damage in DNA and Poly d(A-T) 39
Ross S. Feldberg
9. Photochemistry and Photobiology of DNA Containing 5-Iodouracil and 5-Iodocytosine 43
R. O. Rahn, R. S. Stafford, and C. T. Hadden

II. REPAIR PATHWAYS: MODELS, SYSTEMS, AND PERSPECTIVES

10. DNA Repair Pathways: Excision Repair in Permeabilized Cells 47
Philip C. Hanawalt and Charles Allen Smith
11. A New Classification of Pathways Repairing Pyrimidine Dimer Damage in DNA 57
Alvin J. Clark and Michael R. Volkert
12. Making and Correcting Errors in DNA Synthesis: *In Vitro* Studies of Mutagenesis 73
S. Boiteux, G. Villani, S. Spadari, F. Zambrano, and M. Radman
13. Cell Survival, Excision Repair, and DNA Replication in Eukaryotic Cells 85
J. E. Cleaver, J. I. Williams, L. Kapp, and S. D. Park
14. Electron Microscopy of UV-Induced Post Replication Repair Daughter Strand Gaps 95
Robert Carey Johnson and William F. McNeill
15. A General Method for Isolation of Repair-Deficient Mutants 101
Aziz Sancar and Claud S. Rupert
16. Historical Perspectives and Keynotes on DNA Repair 105
Paul Howard-Flanders
- 16+ . Ivar Johansen—A Tribute 112
Paul Howard-Flanders

III. MECHANISM AND DIVERSITY OF ENZYMATIC PHOTOREACTIVATION

17. Enzymatic Photoreactivation of DNA 113
Betsy M. Sutherland
18. Mechanism and Diversity of Photoreactivation: Workshop Summary 123
Claude Helene
19. Some Properties of a DNA Photoreactivating Enzyme from *Streptomyces griseus* 129
A. P. M. Eker
20. Low Molecular Weight Substances That Enhance DNA Photolyase Activity 133
Harold Werbin and John Madden

21. Mechanism of Action of the Photoreactivating Enzyme from <i>E. coli</i> : Recent Results <i>John Clark Sutherland</i>	137
22. Photosensitized Splitting of Thymine Dimers in DNA by Peptides and Proteins Containing Tryptophanyl Residues <i>Claude Helene, Michel Charlier, Jean-Jacques Toulme, and Francine Toulme</i>	141
23. Evidence for Photoenzymatically Repairable, Lethal "Nondimer" Photoproducts Formed in <i>E. coli</i> Cells by Near UV Light <i>Walter Harm</i>	147
24. Photoreactivation of <i>Escherichia coli</i> Irradiated with Ionizing Radiation <i>Tzu-chien V. Wang and Kendric C. Smith</i>	151
25. Ultraviolet-Light Triggered Disappearance of Photoreactivating Enzyme <i>Gary D. Small</i>	155
26. Cloning the <i>PHR</i> Gene of <i>Escherichia coli</i> <i>Claud S. Rupert and Aziz Sançar</i>	159

IV. BASE EXCISION REPAIR

27. Base Excision Repair of DNA <i>Errol C. Friedberg, Thomas Bonura, Richard Cone, Rhona Simmons, and Corrie Anderson</i>	163
28. Enzymology of Base Excision Repair: Workshop Summary <i>Stuart Linn</i>	175
29. DNA Glycosylases of <i>Escherichia coli</i> <i>T. Lindahl, P. Karran, and S. Riazuddin</i>	179
30. Uracil-DNA Glycosylase Mutants Are Mutators <i>Bruce K. Duncan and Bernard Weiss</i>	183
31. Endonucleases Specific for Apurinic Sites in DNA <i>Walter G. Verly</i>	187
32. The Endonuclease Activity of Exonuclease III and the Repair of Uracil-Containing DNA in <i>Escherichia coli</i> <i>B. Weiss, S. G. Rogers, and A. F. Taylor</i>	191
33. Base-Excision Repair in <i>Micrococcus luteus</i> <i>Jacques Laval and Josiane Pierre</i>	195
34. Enzymes from Human Fibroblasts for the Repair of AP DNA <i>Stuart Linn, Urs Kuhnlein, and Walter A. Deutsch</i>	199

V. NUCLEOTIDE EXCISION REPAIR IN BACTERIA

35. Enzymatic Pathways of Damaged Nucleotide Excision 205
Lawrence Grossman and Sheikh Riazuddin
36. Enzymology of Nucleotide Excision Repair 219
Evelyn Waldstein
37. A DNA-Binding Activity Associated with the *uvrA*⁺ Protein from *Escherichia coli* 225
Erling Seeberg
38. Cloning of *E. coli* DNA Repair Genes 229
W. Dean Rupp, Aziz Sancar, William J. Kennedy, Jon Ayers, and Jonathan Griswold
39. Endonuclease Activities in Extracts of *Micrococcus luteus* Against Gamma-Irradiated DNA 237
U. Hagen, G. Schafer, P. Haas, and T. Coquerelle
40. Excision Repair Pathways in Bacteria: Workshop Summary 241
Warren E. Masker
41. Excision Repair and Mutagenesis Are Complex Processes 247
Kendric C. Smith, David A. Youngs, Emmanuel Van der Schueren, Kenneth M. Carlson, and Neil J. Sargentini
42. *UVRD*, *UVRE*, and *RECL* Represent a Single Gene 251
Sidney R. Kushner, John Shepard, Gwynneth Edwards, and Valerie F. Maples
43. Alternative Pathways for Excision and Resynthesis in *Escherichia coli*: DNA Polymerase III Role? 255
Priscilla K. Cooper and Joyce G. Hunt
44. Pyrimidine Dimer Excision in Exonuclease Deficient Mutants of *Escherichia coli* 261
Warren E. Masker and John W. Chase
45. Conditions for Constitutive and Inducible Gap Filling of Excision and Postreplication Repair in Toluene Treated *E. coli* 267
R. Ben-Ishai, E. Pugravitsky, and R. Sharon
46. Effects of Phage Infection on *Escherichia coli* Excision Repair Measured *in Vitro* 271
Peter Strike
47. Repair of DNA Damage in Mycoplasmas 277
Jyotirmoy Das, Jack Maniloff, Utpal Chaudhuri, and Amit Ghosh

48. Role of the Gene *MTCA* in the Resistance of *Micrococcus radiodurans* to the Lethal Effects of Mitomycin C and Alkylation Mutagenesis 283
Philip R. Tempest and Bevan E. B. Moseley
49. On the Mechanism for Repair of Cross-Linked DNA in *E. coli* Treated with Psoralen and Light 287
Ronald S. Cole, Richard R. Sinden, George H. Yoakum, and Steven Broyles

VI. EXCISION REPAIR IN MAMMALIAN CELLS

50. Endonuclease from Calf Thymus That Acts on DNA Irradiated with Low UV Doses 291
Evelyn Waldstein, Shoshana Peller, Aja Robel, and R. B. Setlow
51. On the Nature of the Human Endonuclease Activity Directed Against Ultraviolet-Irradiated DNA 295
George Teebor, Mindy Goldstein, Krystyna Frenkel, Nahum Duker, and Thomas Brent
52. Partial Purification and Characterization of Three Thymine Dimer Excising Activities from Human KB Cells 301
Kem H. Cook, and Errol C. Friedberg
53. Introduction of T4 Endonuclease V into Frozen and Thawed Mammalian Cells for the Determination of Removal of UV-Induced Photoproducts 307
A. A. van Zeeland
54. Removal of T4 Endonuclease V Sensitive Sites and Repair Replication in Confluent Human Diploid Fibroblasts 311
Charles Allen Smith
55. Studies on the Molecular Mechanisms of Nucleotide Excision Repair in UV-Irradiated Human Cells in Culture 315
Ursula K. Ehmann, Kem H. Cook, and Errol C. Friedberg
56. Kinetics of UV-Induced Excision Repair in Human Fibroblasts. Simultaneous Studies of Incision-Produced Single-Strand Breaks and the Removal of Endonuclease-Sensitive Sites Using the DNA Unwinding Technique 319
Klaus Erixon and Gunnar Ahnstrom
57. The Removal of UV-Induced Pyrimidine Dimers from the Replicated and Unreplicated DNA of Human Fibroblasts 323
Raymond Waters
58. Distribution of UV-Induced DNA Repair Synthesis in Human Chromatin 327
Michael J. Smerdon and Michael W. Lieberman
59. Excision Repair in Mammalian Cells 333
Farid E. Ahmed and R. B. Setlow

60. A Possible Role for Poly ADP-Ribose in DNA Repair 337
Robert C. Benjamin and D. Michael Gill

VII. INDUCIBLE/ERROR-PRONE REPAIR IN PROCARYOTES

61. Conditioned Repair Responses: Workshop Summary 341
B. A. Bridges
62. The Involvement of *E. coli* DNA Polymerase III in Constitutive and Inducible Mutagenic Repair 345
B. A. Bridges
63. Studies of the *recA* and *lexA* Genes of *Escherichia coli* K-12 349
Kevin McEntee
64. An *Escherichia coli* Mutant with an Altered Inducible *rec+*/*lex+* Dependent DNA Repair Pathway 361
Lorraine J. Gudas and David W. Mount
65. Induction and Repression of the *recA* Gene of *Escherichia coli* 367
Peter T. Emmerson and Stephen C. West
66. Complexity in the Regulation of SOS Functions in Bacteria 371
Evelyn M. Witkin and Paul Kirschmeier
67. *tif-1* Mediated Recovery from UV Blockage of DNA Synthesis in *Escherichia coli*: A Mechanism of Induced Mutagenesis? 375
Steven G. Sedgwick
68. The Role of Proteases in SOS Regulation 379
M. S. Meyn, T. Rossman, P. Gottlieb, and W. Troll
69. Transcriptional Regulation of the *recA* Region of *E. coli* 383
Ann McPartland, Linda Green, and Harrison Echols
70. Dose Response Relations for UV-Induced Repair Phenomena 387
D. J. Fluke and Ernest C. Pollard
71. Pathways Involved in Repair of Alkylation Damage in *E. coli* 391
P. F. Schendel, M. Defais, P. Jeggo, L. Samson, and J. Cairns
72. The UV Inducibility of P32 Synthesis 395
H. M. Krisch and G. Van Houwe
73. The Dependence of UV Mutagenesis in Phage T4 on DNA Ligase, Polymerase, and Nuclease Functions 401
Daniel B. Yarosh

VIII. REPAIR IN LOWER EUCARYOTES

74. DNA Repair in Lower Eucaryotes: Workshop Summary 405
R. H. Haynes, L. Prakash, M. A. Resnick, B. S. Cox, E. Moustacchi, and J. B. Boyd
75. Pathways of DNA Repair in Yeast 413
Louise Prakash and Satya Prakash
76. The Importance of DNA Double-Strand Break Repair in Yeast 417
Michael A. Resnick
77. On the Inducibility of Error-Prone Repair in Yeast 421
F. Eckardt, E. Moustacchi, and R. H. Haynes
78. The Fate of Mitochondrial DNA and of Mitochondrial Genetic Markers after UV Irradiation of *Saccharomyces cerevisiae* 425
E. Moustacchi, M. Heude, and S. Hixon
79. Recombination and Repair in Simple Eukaryotes 429
B. S. Cox
80. Ultraviolet Light Induced Mutagenesis in *Saccharomyces cerevisiae* 437
Chris Lawrence and Roshan B. Christensen
81. Regulation by Proteinases of a Putative *Rec*-Nuclease of *Neurospora* 441
M. J. Fraser, S. Kwong, D. M. Galer, and T. Y. -K. Chow
82. Genetics of DNA Repair in the Cellular Slime Mold, *Dicryostelium discoideum* 445
D. L. Welker and R. A. Deering
83. DNA Repair in *Drosophila* 449
James B. Boyd
84. Mutagen Sensitivity of *Drosophila melanogaster* IV. Interactions of X Chromosome Mutants 453
P. Dennis Smith

IX. STRAND BREAK REPAIR IN MAMMALIAN CELLS

85. DNA Strand Break Repair in Eukaryotes: Workshop Summary 457
Franklin Hutchinson
86. Estimation of DNA Strand Breaks in Single Mammalian Cells 465
Bjorn Rydberg and Karl J. Johanson
87. Repair of DNA Breaks Induced by Gamma Rays and Fast Neutrons in Chinese Hamster Cells 469
Gunnar Ahnström and Karl-Anders Edvardsson

88. A Relationship between DNA Single-Strand Breaks and DNA-Protein Crosslinks
in Intercalator-Treated Mouse L1210 Cells 473
Kurt W. Kohn, Warren E. Ross, and Regina A. G. Ewig
89. DNA Damage and Mammalian Cell Killing 477
M. M. Elkind
90. Rejoining of DNA Strand Breaks in Nondividing Cells Irradiated *in Situ* 481
J. T. Lett, P. C. Keng, and C. Sun

X. REPLICATIVE BYPASS MECHANISMS IN MAMMALIAN CELLS

91. Replicative Bypass Mechanisms in Mammalian Cells: Workshop Summary 485
Alan R. Lehmann
92. DNA Replication in Ultraviolet-Irradiated Mammalian Cells 489
Howard J. Edenberg
93. Pyrimidine Dimers in DNA Strands of Mammalian Cells Synthesized after
UV-Irradiation 493
Rogério Meneghini and Carlos F. M. Menck
94. On the Presence of UV-Endonuclease Sensitive Sites in Daughter DNA of
UV-Irradiated Mammalian Cells 499
Steven M. D'Ambrosio and R. B. Setlow
95. The Mechanism of Postreplication Repair in Mammalian Cells 505
Jay Doniger
96. A Model for Postreplication Repair of UV Damage in Mammalian Cells 509
Martin F. Lavin
97. The Kinetics of Postreplication Repair in Mammalian Cells as Studied by the
Alkaline Elution Technique 513
Raymond E. Meyn and Susan E. Fletcher
98. DNA Replication in Normal and Defective Human Cells after UV Irradiation 517
A. R. Lehmann
99. Replicative Repair in *Xeroderma pigmentosum* (XP) Variants 519
Yoshisada Fujiwara
100. DNA Bifilarly Substituted with Bromodeoxyuridine in the First Round of Synthesis 523
Kouichi Tatsumi and Bernard Strauss

101. DNA Template Breakage and Decreased Excision of Hydro-Carbon Derived Adducts from Chinese Hamster Cell DNA Following Caffeine-Induced Inhibition of Postreplication Repair 527
John J. Roberts, Frank Friedlos, and Edgar S. Belka

XI. VIRAL PROBES FOR DNA REPAIR

102. Viral Probes for Mammalian Cell DNA Repair: Results and Prospects: Workshop Summary 531
Rufus S. Day, III
103. Studies on UV-Induced Viral Reversion, Cockayne's Syndrome, and MNNG Damage Using Adenovirus 5 535
Rufus S. Day, III, and Chuck Ziolkowski
104. Production of Viral Structural Antigens by Irradiated Adenovirus as an Assay for DNA Repair in Human Fibroblasts 541
Andrew J. Rainbow
105. Simian Virus 40 as a Probe for Studying DNA Repair Pathways in Mammalian Cells 547
Alain R. Sarasin and Philip C. Hanawalt
106. Repair of UV Irradiation Damage in Simian Virus 40 551
Jon I. Williams and James E. Cleaver
107. Defective Host-Cell Reactivation of UV-Irradiated Herpes Simplex Virus by Bloom's Syndrome Skin Fibroblasts 555
Clifford Selsky, Ralph Weichselbaum, and John B. Little
108. Protease Inhibitors Prevent UV-Enhanced Virus Reactivation in *E. coli* but Not in Monkey Kidney Cells 559
C. D. Lytle, J. G. Goddard, and F. L. Buchta
109. UV-Reactivation of Herpes Simplex Virus is Mutagenic and Inducible in Mammalian Cells 563
William C. Summers and Uma Bandyopadhyay Dasgupta
110. The Effect of DNA Damage on the Induction of Simian Virus 40 (SV40) in Transformed Hamster Cells 567
Glen B. Zamansky, John B. Little, Paul H. Black, and Joan C. Kaplan
111. Recent Developments in the Biochemistry of Genetic Recombination 573
Era Cassuto
112. In Initiation of Genetic Recombination in *E. coli*: Studies on Cutting in *trans* as a Function of Time 579
Peter Ross

113. Repair and Recombination of UV-Irradiated Phage Lambda 585
John B. Hays and Sieghild Bohma

XII. HEREDITARY REPAIR DEFECTS IN MAN: XERODERMA PIGMENTOSUM

114. *Xeroderma pigmentosum* 589
Dirk Bootsma
115. *Xeroderma pigmentosum*: Workshop Summary 603
Jay H. Robbins
116. DNA Repair Nucleotide Sequences Which Prevent Premature Death of Neurons in Humans: Evidence from Studies on *Xeroderma pigmentosum* 609
Jay H. Robbins, Alan D. Andrews, and A. N. Moshell
117. The Relationship between Neurologic Disease, Acute Sun Sensitivity, and Post-Ultraviolet Colony-Forming Ability in *Xeroderma pigmentosum* 613
Alan D. Andrews, Susanna F. Barrett, and Jay H. Robbins
118. DNA Repair and Clinical Characteristics of 96 *Xeroderma pigmentosum* Patients in Japan 617
Hiraku Takebe, Yoshisada Fujiwara, Masao S. Sasaki, Yoshiaki Sato, Takehito Kozuka, Osamu Nikaido, Kanji Ishizaki, Seiji Arase, and Mituo Ikenaga
119. Response of Mammalian Cells to Chemical Damage 621
B. Strauss, K. Bose, M. Altamirano, R. Sklar, and K. Tatsumi

XIII. REPAIR DEFICIENCY AND HUMAN DISEASE: OTHER HEREDITARY DEFECTS

120. DNA Repair Defects and Human Disease 625
James German
121. Cell Killing and Mutagenesis in Repair-Defective Human Cells 633
C. F. Arlett and S. A. Harcourt
122. *Ataxia telangiectasia*: A Model Inherited Disease Linking Deficient DNA Repair with Radiosensitivity and Cancer Proneness 637
M. C. Paterson
123. *Ataxia telangiectasia*: Characterization of Heterozygotes 651
Martin F. Lavin, Philip C. Chen, and Chev Kidson
124. Repair Deficiency in *N*-Methyl-*N'*-Nitro-*N*-Nitrosoguanidine Treated *Ataxia telangiectasia* Fibroblasts 655
Dominic A. Scudiero

125. An Investigation of DNA Repair Potential in Bloom's Syndrome 659
Raymond R. Tice, Jack M. Rary, and Michael A. Bender
126. Single-Strand DNA Breakage and Repair in Bloom's Syndrome Cells 663
R. A. Vincent, Jr., M. D. Hays, and R. C. Johnson
127. Effects of DNA Damaging Agents on Cultured Fibroblasts Derived from Patients with Cockayne Syndrome 667
M. H. Wade and E. H. Y. Chu
128. Sister Chromatid Exchanges in *Dyskeratosis congenita* after Exposure to Trimethyl Psoralen and UV Light 671
D. Martin Carter, Alan Gaynor, and Joseph McGuire
129. Fanconi's Anemia a Condition Possibly Associated with a Defective DNA Repair 675
Masao S. Sasaki
130. X-Ray Sensitivity of Fibroblasts from Patients with Retinoblastoma and with Abnormalities of Chromosome 13 685
John B. Little, Ralph R. Weichselbaum, John Nove, and Daniel M. Albert

XIV. MUTAGENESIS AND CARCINOGENESIS

131. Environmental Chemicals Causing Cancer and Genetic Birth Defects 691
Bruce N. Ames
132. Chemical Damage and Mutagenesis in Mammalian Systems: Workshop Summary 699
C. F. Arlett
133. Biological Consequences of X-Ray-Induced DNA Damage and Repair Processes in Relation to Cell Killing and Carcinogenesis 701
John B. Little
134. Chemical Modification of Radiation-Induced Mutagenesis and Its Role in Carcinogenesis 713
James E. Trosko and Chia-cheng Chang
135. Biological and Biochemical Evidence That DNA Repair Processes in Normal Human Cells Act to Reduce the Lethal and Mutagenic Effects of Exposure to Carcinogens 717
Veronica M. Maher, Delia J. Dorney, Robert H. Heflich, J. William Levinson, Alan L. Mendrala, and J. Justin McCormick
136. Evidence for the Involvement of Different Repair Mechanisms in Mutagenesis and Cell Killing in V79 Cells 723
M. Fox and S. McMillan
137. Effects of Liquid Holding on Cell Killing and Mutation Induction in Normal and Repair-Deficient Human Cell Strains 729
J. W. I. M. Simons

138. Fixation and Expression of Recessive Mutations in Mammalian Cells as a Model
for the Study of Carcinogenesis 733
Anne Kinsella, Suzanne Mousset, Claude Szpirer, and Miroslav Radman

139. Mammalian Cell Mutagenesis as a Biological Consequence of DNA Damage 739
J. Justin McCormick and Veronica M. Maher

XV. CONSEQUENCES OF DNA DAMAGE AND REPAIR

140. Relation between DNA Repair, Chromosome Aberrations, and Sister Chromatid
Exchanges 751
Sheldon Wolff

141. DNA Repair in Differentiation 761
Chev Kidson

142. The Relationship between Cellular Aging and Genetic Defects 769
Robin Holliday

143. The Acute and Chronic Effects of Ultraviolet Energy on Mammalian Skin 779
John H. Epstein

144. Death of *Escherichia coli* Cells as a Consequence of Damage to DNA by
Far-Ultraviolet Radiation 783
P. A. Swenson

145. Action of Three Mutagens on HeLa DNA Replication 789
Robert B. Painter

146. UV Irradiation and the Mammalian Cell Cycle 793
Andrew Collins, Bob Johnson, Stephen Downes, Foch Yew, and Kornel Burg

147. Cloning of a Gene That Controls Radiation Sensitivity, Cell Division, and Capsular
Polysaccharide Synthesis, the *lon(capR)* Gene 797
Barbara Zehnbaauer and Alvin Markovitz

- Author Index 801
Subject Index 805