Contents

PART I CELL STRUCTURE AND GENETICS

1 Introduction: The Genetic Apparatus 3

The Eucaryotic Chromosome, 4
The Genetic Material, 7

2 The Cell Skeleton: Microtubule Assemblies 11

Occurrence of Microtubules, 12
Microtubule Ultrastructure, 13
Components of Tubulin, 18
Polymerization of Tubulin, 20
Initiation of Microtubule Assembly, 22
Microtubule Elongation, 28
Interactions of Microtubules with Mitotic Inhibitors, 30
Binding of Colchicine to Tubulin, 33
Formation of Paracrystals with Vinblastine, 35
Poisoning Action of Alkaloids, 36
Cytoplasmic Network of Microtubules, 38

3 The Cell Skeleton: The Contractile Network 43

Protein Components of Muscle, 44
Occurrence of Cytoplasmic Contractile Proteins, 48
Presence of Actin in Cytoplasmic Microfilaments, 51
Network of Contractile Proteins, 57
Stress Fibers and Cell Motility, 60
Microfilaments and Microtubules in the Cell Skeleton, 63
Disruption of Microfilaments by Cytochalasin B, 64
Intermediate Filaments, 67
Detergent Resistant Cytoskeleton, 69

4 Chromosome Segregation: Mitosis 71

The Mitotic Apparatus, 71
Development of the Centromere, 74

Distribution of Spindle Fibers, 78
Dynamic Equilibrium of Microtubules and Tubulin, 82
Microtubules and Actin Filaments in Chromosome Movement, 85
Structure of the Centriole, 90
Microtubule Organizing Centers, 95
Cytokinesis, 100

5 Chromosome Segregation: Meiosis **102**

Formation of the Synaptonemal Complex, 104
Reconstruction of the Set of Synaptonemal Complexes, 109
Crossing Over and Chiasmata, 116
Genetics of Meiosis, 124
Meiotic Mutants of Drosophila, 125
Relationship of Recombination and Nondisjunction, 133
Mitotic Recombination, 139

6 Somatic Cell Mutants **142**

Somatic Cell Lines, 143
Mutation and Epigenetic Variation, 146
Isolation of Auxotrophic Mutants, 147
Selection of Drug-Resistant Mutants, 150
Isolation of Temperature-Sensitive Mutants, 156
Measurement of Mutation Rates, 158
Mutation Rates in Somatic Cells, 162
Mutant and Gene Dosage in Cells of Different Ploidies, 166
Mutation Rates in Homozygous and Heterozygous Cells, 172
Identification of the Structural Gene for HGPRT, 174
Isolation of Mutants Deficient in HGPRT Activity, 176
Mutations in the Structural Gene for HGPRT, 179
Characterization of Structural and Regulator Gene Mutants, 182

7 The Cell Division Cycle **189**

Methods for Synchronizing Cell Division, 192
Protein Synthesis and Cell Growth During Interphase, 195
Control of Entry into S Phase, 198
Quiescent and Proliferating Cultures, 205
Synthesis of Proteins During S Phase, 210

8 Hybrid Cells: Nucleus and Cytoplasm **213**

Reciprocity of Nucleocytoplasmic Interactions, 214
Nucleocytoplasmic Interactions in Acetabularia, 215
Transplantation of Xenopus Nuclei, 216
Reactivation of Transplanted Nuclei, 220

Fusion of Somatic Cells, 225
Reactivation of Inert Nuclei, 227
Molecular Reconstruction of Reactivating Nuclei, 232
Formation of Cytoplasts and Karyoplasts, 236

9 Hybrid Cells: Chromosomes 242

Chromosome Loss in Heterospecific Hybrids, 243
Genetic Mapping in Cell Hybrids, 244
Mapping of the Human X Chromosome by Fragmentation, 252
X Chromosome Mapping by Translocation, 256
Expression of Differentiated Functions, 259
Division Cycles in Homokaryons, 266
Survival of Prematurely Condensed Chromosomes, 268
Gene Transfer with Isolated Chromosomes, 273
Transfection with Purified DNA, 278

PART 2 ORGANIZATION OF THE GENETIC APPARATUS

10 Introduction: Chromosomes and Chromatin 283

Continuity of DNA in the Chromosome, 285
Semiconservative Replication of the Chromosome, 289
Sister Chromatid Exchange, 292

11 Chromatin Components: Histones 299

Separation of Histones, 300
Sequences of the Arginine-Rich Histones, 303
Sequences of the Slightly Lysine-Rich Histones, 306
Microheterogeneity of Lysine-Rich Histones, 309
Sequence of Avian H5, 311
Evolution of Histone Sequences, 312
Modification of Histones, 317

12 Chromatin Components: Nonhistone Proteins 322

Diversity of Nonhistone Proteins, 323
Identification of Nonhistone Proteins, 325
HMG Proteins of Calf Thymus, 327
DNA Binding Proteins, 328
The A24 Semihistone, 329
Conclusions: Functions of Nonhistone Proteins, 330

13 The Nucleosome: Structure of the Particle 332

Repeating Length of DNA in Chromatin Subunits, 333
Visualization of Individual Particles, 339

Histone Octamer of the Nucleosome, 345
Variations in the Repeat Length of DNA, 349
Structure of the Core Particle, 353
Location of H1 between Cores, 356
Exposure of DNA on the Nucleosome Surface, 359
Periodicity of DNA Organization, 366
Phasing of Nucleosomes, 374
Interactions between Histones and with DNA, 381
Shape of the Histone Octamer and DNA Shell, 389

14 The Nucleosome: Organization in Chromatin **394**

Replication of Chromatin, 396
Assembly of the Nucleosome, 400
Chromatin under Transcription, 404
Active and Inactive Nucleosomes, 408
Constitution of Active Chromatin, 413
Coiling of the Nucleosome Thread, 416
Chromosome Integrity, 420

15 Euchromatin and Heterochromatin **428**

Chromosome Banding, 430
Structure of the Bands, 435
Mechanism of Banding, 437
Inactivity of Facultative Heterochromatin, 440
Time of X Inactivation, 444
Position Effect Variegation, 447
Formation of Facultative Heterochromatin, 450

16 Specialized Chromosomes: Chromomere Structure **455**

Lampbrush Chromosomes, 456
Polytene Chromosome Bands, 460
Replication of Polytene Chromosomes, 463
Puffing of Bands, 467
Puffs and Gene Products, 470
Transcription at Puffs, 473

PART 3 ORGANIZATION OF THE EUCARYOTIC GENOME

17 Introduction: Genes and Gene Number **479**

Genes and Complementation Groups, 480
The C Value Paradox, 488
Gene Number in Drosophila, 492
Essential and Nonessential Genes, 499

18 DNA Sequence Organization: Nonrepetitive and Repetitive DNA 503

Denaturation and Renaturation of DNA, 504
Complexity of Nonrepetitive DNA, 508
Kinetics of DNA Reassociation, 514
Families of Repetitive Sequences, 517
Interspersion of Repetitive and Nonrepetitive Sequences, 523

19 DNA Sequence Organization: Inverted and Tandem Repeats 531

Distribution of Inverted Repeats, 532
Fractionation of DNA by Buoyant Density, 538
Chromosomal Location of Satellite DNA, 541
Satellite DNAs of Arthropods, 545
Mammalian Satellite DNAs, 550
Evolution of Tandem Repeats, 559

20 DNA Replication 570

Organization of Replicons, 571
Regional Patterns of Replication, 576
The Replication Apparatus, 578

21 Organelle Genomes 583

Chloroplast and Mitochondrial DNA, 585
Inheritance of the Chlamydomonas Chloroplast, 591
Linkage Map of Chlamydomonas Chloroplast DNA, 595
The Petite Mutation of Yeast, 603
Recombination in Yeast Mitochondrial DNA, 608
Recombination Mapping with Petites, 611
Complementation Mapping of mit$^-$ Mutations, 615
Protein Synthesis in Organelles, 617
Organelle and Nuclear Genes and Products, 625
Replication of Organelle DNA, 631

PART 4 EXPRESSION OF GENETIC INFORMATION

22 Introduction: The Transcription Apparatus 641

Functions of RNA Polymerases, 644
RNA Synthesis in the Cell Cycle, 649

23 Structure of Messenger RNA 653

Recognition of mRNA and mRNP in Polysomes, 654
Poly(A) at the 3′ Terminus, 656

Poly(A)$^+$ and Poly(A)$^-$ mRNA, 660
Messenger Ribonucleoprotein Particles, 663
Methyl Capping at the 5′ Terminus, 668
Capping and the Initiation of Transcription, 675
Characterization of Individual Messengers, 683
Products of Messenger Translation, 687
Stability of Messenger RNA, 690

24 Complexity of mRNA Populations **694**

Reiteration Frequencies of Structural Genes, 697
Identification of Individual Genes, 705
Number of Expressed Structural Genes, 708
Abundance Classes of mRNA, 713
Overlaps between Messenger Populations, 719

25 Heterogeneous Nuclear RNA **728**

Fate of Rapidly Labeled hnRNA, 730
Size and Secondary Structure of hnRNA, 732
Nuclear Polyadenylation and hnRNA Turnover, 736
Capping and Internal Methylation, 744
Sequence Complexity of hnRNA, 746
Sequence Relationship of mRNA and hnRNA, 751
Control of RNA Processing, 756
Small Nuclear RNA, 758

26 Interrupted Genes and RNA Splicing **761**

Restriction Mapping of DNA, 762
Nucleic Acid Cloning, 763
Isolation of Eucaryotic Genes, 771
Bacterial Translation of Eucaryotic Genes, 777
DNA Sequence Determination, 785
Occurrence of Intervening Sequences: Globin Genes, 790
Duplicate Insulin Genes, 796
Ovalbumin and its Relatives, 797
Occurrence of Intervening Sequences: Higher and Lower Eucaryotes, 799
Genetics of Mosaic Genes, 807
Evolution of Interrupted Genes, 811
Sequences of Splicing Junctions, 815
Splicing of Nuclear Transcripts, 824
Alternative Splicing Pathways in Adenovirus, 832
Variable Splicing of SV40 Transcripts, 839
Diversity of Immunoglobulin Genes, 847

Rearrangement of V and C Genes, 853
Mobile Elements in the Genome, 861
Modification of DNA, 862

27 Ribosomal Gene Clusters 865

Synthesis of Ribosomal RNA, 866
Maturation of rRNA Sequences, 873
Repetition of Ribosomal Genes, 875
Organization of Transcription Units, 878
Structure of Nontranscribed Spacers, 885
Multiplication of Ribosomal Genes, 890
Structure of 5S Gene Clusters, 896
Evolution of Tandem Gene Clusters, 903

28 Gene Families 907

The Histone Gene Cluster: Organization, 908
The Histone Gene Cluster: Expression, 915
Globin Gene Relationships: Gene Numbers, 918
Globin Gene Relationships: Mutant Genes, 924
Drosophila Heat Shock Genes, 931
Chromatin in vitro: Transcription, 935
Chromatin in vitro: Fractionation, 944
Models for Gene Regulation, 949

Appendix 1 DNA Content of Haploid Genomes 958

Appendix 2 Determination of Genome Size by Reassociation of Nonrepetitive DNA 962

Appendix 3 Sequence Components of Eucaryotic Genomes 965

References 968

Index 1139