

Contents

Preface *XVII*

Authors *XIX*

| | | |
|----------|--|----------|
| 1 | Introduction | 1 |
| 1.1 | Historical Aspects | 1 |
| 1.2 | Yeast as a Eukaryotic Model System | 1 |
| | Further Reading | 3 |
| 2 | Yeast Cell Architecture and Functions | 5 |
| 2.1 | General Morphology | 5 |
| 2.2 | Cell Envelope | 6 |
| | 2.2.1 Cell Wall | 7 |
| | 2.2.2 Plasma Membrane | 8 |
| 2.3 | Cytoplasm and Cytoskeleton | 8 |
| | 2.3.1 Yeast Cytoplasm | 8 |
| | 2.3.2 Yeast Cytoskeleton | 9 |
| | 2.3.2.1 Microtubules | 9 |
| | 2.3.2.2 Actin Structures | 9 |
| | 2.3.2.3 Motor Proteins | 11 |
| | 2.3.2.3.1 Myosins | 12 |
| | 2.3.2.3.2 Kinesins | 13 |
| | 2.3.2.3.3 Dynein | 12 |
| | 2.3.2.4 Other Cytoskeletal Factors | 13 |
| | 2.3.2.4.1 Proteins Interacting with the Cytoskeleton | 13 |
| | 2.3.2.4.2 Transport of Organellar Components | 13 |
| 2.4 | Yeast Nucleus | 14 |
| | 2.4.1 Overview | 14 |
| | 2.4.2 Nuclear Pore | 14 |
| | 2.4.2.1 Historical Developments | 14 |
| | 2.4.2.2 Current View of the Nuclear Pore | 15 |
| | 2.4.2.3 Yeast Nucleolus | 17 |
| | 2.4.3 Yeast Chromosomes | 17 |
| 2.5 | Organellar Compartments | 17 |
| | 2.5.1 ER and the Golgi Apparatus | 18 |
| | 2.5.2 Transport Vesicles | 18 |
| | 2.5.3 Vacuolar System | 20 |
| | 2.5.3.1 Yeast Vacuole | 20 |
| | 2.5.3.2 Vacuolar Degradation | 21 |
| | 2.5.4 Endocytosis and Exocytosis | 21 |
| | 2.5.5 Mitochondria | 21 |
| | 2.5.5.1 Mitochondrial Structure | 21 |
| | 2.5.6 Peroxisomes | 22 |
| | Further Reading | 23 |

- 3 Yeast Metabolism 25**
 - 3.1 Metabolic Pathways and Energy 25
 - 3.2 Catabolism of Hexose Carbon Sources 25
 - 3.2.1 Principal Pathways 25
 - 3.2.2 Respiration Versus Fermentation 26
 - 3.2.3 Catabolism of Other Sugars – Galactose 27
 - 3.2.4 Metabolism of Non-Hexose Carbon Sources 28
 - 3.3 Gluconeogenesis and Carbohydrate Biosynthesis 30
 - 3.3.1 Gluconeogenesis 30
 - 3.3.2 Storage Carbohydrates 30
 - 3.3.2.1 Glycogen 30
 - 3.3.2.2 Trehalose 31
 - 3.3.3 Unusual Carbohydrates 31
 - 3.3.3.1 Unusual Hexoses and Amino Sugars 31
 - 3.3.3.2 Inositol and its Derivatives 32
 - 3.3.3.3 N- and O-Linked Glycosylation 33
 - 3.3.4 Structural Carbohydrates 34
 - 3.4 Fatty Acid and Lipid Metabolism 35
 - 3.4.1 Fatty Acids 35
 - 3.4.2 Lipids 35
 - 3.4.3 Glycolipids 36
 - 3.4.3.1 Phosphatidylinositol and Derivatives 36
 - 3.4.3.2 Sphingolipids 38
 - 3.4.3.3 Glycosylphosphatidylinositol (GPI) 39
 - 3.4.4 Isoprenoid Biosynthesis 40
 - 3.5 Nitrogen Metabolism 42
 - 3.5.1 Catabolic Pathways 42
 - 3.5.2 Amino Acid Biosynthesis Pathways 44
 - 3.5.2.1 Glutamate Family 44
 - 3.5.2.2 Aspartate Family 44
 - 3.5.2.3 Branched Amino Acids 45
 - 3.5.2.4 Lysine 46
 - 3.5.2.5 Serine, Cysteine, and Glycine 46
 - 3.5.2.6 Alanine 46
 - 3.5.2.7 Aromatic Amino Acids 46
 - 3.5.2.8 Histidine 47
 - 3.5.2.9 Amino Acid Methylation 47
 - 3.6 Nucleotide Metabolism 48
 - 3.6.1 Pyrimidine Derivatives 48
 - 3.6.2 Purine Derivatives 48
 - 3.6.3 Deoxyribonucleotides 50
 - 3.6.4 Nucleotide Modification 50
 - 3.7 Phosphorus and Sulfur Metabolism 51
 - 3.7.1 Phosphate 51
 - 3.7.2 Sulfur 52
 - 3.7.2.1 Fixation and Reduction of Sulfate 52
 - 3.7.2.2 Cycle of Activated Methyl Groups 53
 - 3.8 Vitamins and Cofactors 53
 - 3.8.1 Biotin 53
 - 3.8.2 Thiamine 53
 - 3.8.3 Pyridoxine 54
 - 3.8.4 NAD 54
 - 3.8.5 Riboflavin Derivatives 54
 - 3.8.6 Pantothenic Acid and Coenzyme A 55
 - 3.8.7 Folate 55

| | | |
|-----------|---|-----------|
| 3.8.8 | Tetrapyrroles | 55 |
| 3.8.9 | Ubiquinone (Coenzyme Q) | 56 |
| 3.9 | Transition Metals | 57 |
| | Further Reading | 58 |
| 4 | Yeast Molecular Techniques | 59 |
| 4.1 | Handling of Yeast Cells | 59 |
| 4.1.1 | Growth of Yeast Cells | 59 |
| 4.1.2 | Isolation of Particular Cell Types and Components | 59 |
| 4.2 | Genetic Engineering and Reverse Genetics | 59 |
| 4.2.1 | The Molecular Revolution | 59 |
| 4.2.2 | Transformation of Yeast Cells | 61 |
| 4.2.2.1 | Yeast Shuttle Vectors | 61 |
| 4.2.2.2 | Yeast Expression Vectors | 62 |
| 4.2.2.3 | Secretion of Heterologous Proteins from Yeast | 63 |
| 4.2.2.4 | Fluorescent Proteins Fused to Yeast Proteins | 63 |
| 4.2.3 | Yeast Cosmid Vectors | 64 |
| 4.2.4 | Yeast Artificial Chromosomes | 65 |
| 4.3 | More Genetic Tools from Yeast Cells | 65 |
| 4.3.1 | Yeast Two-Hybrid System | 65 |
| 4.3.2 | Yeast Three-Hybrid System | 66 |
| 4.3.3 | Yeast One-Hybrid (Matchmaker) System | 67 |
| 4.4 | Techniques in Yeast Genome Analyses | 67 |
| 4.4.1 | Microarrays | 67 |
| 4.4.1.1 | DNA-Based Approaches | 67 |
| 4.4.1.2 | Proteome Analyses | 68 |
| 4.4.2 | Affinity Purification | 70 |
| 4.4.3 | Mass Spectrometry | 70 |
| | Further Reading | 72 |
| 5 | Yeast Genetic Structures and Functions | 73 |
| 5.1 | Yeast Chromosome Structure and Function | 73 |
| 5.1.1 | Yeast Chromatin | 73 |
| 5.1.1.1 | Organization of Chromatin Structure | 73 |
| 5.1.1.2 | Modification of Chromatin Structure | 73 |
| 5.1.1.2.1 | Modification of Histones | 73 |
| 5.1.1.2.2 | Remodeling Chromatin Structure Overview | 81 |
| 5.1.2 | Centromeres | 85 |
| 5.1.3 | Replication Origins and Replication | 85 |
| 5.1.3.1 | Initiation of Replication | 85 |
| 5.1.3.2 | Replication Machinery | 88 |
| 5.1.3.2.1 | DNA Polymerases | 88 |
| 5.1.3.2.2 | Replication and Replication Factors | 89 |
| 5.1.3.2.3 | Postreplication Repair and DNA Damage Tolerance | 89 |
| 5.1.3.3 | Replication and Chromatin | 90 |
| 5.1.3.3.1 | Chromatin Reorganization | 90 |
| 5.1.3.3.2 | Silencing and Boundaries | 91 |
| 5.1.3.4 | DNA Damage Checkpoints | 93 |
| 5.1.3.4.1 | Checkpoints During Replication | 93 |
| 5.1.3.4.2 | DSB Repair | 94 |
| 5.1.4 | Telomeres | 96 |
| 5.1.5 | Transposons in Yeast | 98 |
| 5.1.5.1 | Classes of Transposable Elements | 98 |
| 5.1.5.2 | Retrotransposons in <i>S. cerevisiae</i> | 98 |
| 5.1.5.2.1 | Ty Elements and their Genomes | 98 |

| | | | |
|----------|------------|--|------------|
| | 5.1.5.2.2 | Behavior of Ty Elements | 99 |
| | 5.1.5.2.3 | Expression of Ty Elements | 100 |
| | 5.1.5.3 | Ty Replication | 101 |
| | 5.1.5.4 | Interactions between Ty Elements and their Host | 102 |
| 5.2 | | Yeast tRNAs, Genes, and Processing | 103 |
| | 5.2.1 | Yeast tRNAs | 103 |
| | 5.2.1.1 | Yeast Led the Way to tRNA Structure | 103 |
| | 5.2.1.2 | Yeast tRNA Precursors and Processing | 105 |
| | 5.2.2 | Current Status of Yeast tRNA Research | 106 |
| | 5.2.2.1 | Yeast tRNAs and their Genes | 106 |
| | 5.2.2.2 | tRNA Processing and Maturation | 106 |
| | 5.2.2.3 | Participation of tRNAs in an Interaction Network | 109 |
| | 5.2.2.3.1 | Aminoacylation of tRNAs | 109 |
| | 5.2.2.3.2 | Rules, Codon Recognition, and Specific tRNA Modification | 111 |
| | 5.2.2.3.3 | Recognition of tRNAs in the Protein Biosynthetic Network | 111 |
| 5.3 | | Yeast Ribosomes: Components, Genes, and Maturation | 113 |
| | 5.3.1 | Historical Overview | 113 |
| | 5.3.2 | Ribosomal Components | 113 |
| | 5.3.2.1 | Ribosomal RNAs | 113 |
| | 5.3.2.2 | Ribosomal Proteins | 114 |
| | 5.3.3 | Components and Pathways of Yeast Ribosome Maturation | 114 |
| 5.4 | | Messenger RNAs | 116 |
| | 5.4.1 | First Approaches to the Structure of Yeast mRNAs | 116 |
| | 5.4.2 | Introns and Processing of pre-mRNA | 117 |
| | 5.4.3 | Provenance of Introns | 121 |
| 5.5 | | Extrachromosomal Elements | 121 |
| | 5.5.1 | Two Micron DNA | 121 |
| | 5.5.2 | Killer Plasmids | 121 |
| | 5.5.3 | Yeast Prions | 121 |
| 5.6 | | Yeast Mitochondrial Genome | 123 |
| | | Further Reading | 125 |
| 6 | | Gene Families Involved in Cellular Dynamics | 127 |
| | 6.1 | ATP- and GTP-Binding Proteins | 127 |
| | 6.1.1 | ATPases | 127 |
| | 6.1.1.1 | P-Type ATPases | 127 |
| | 6.1.1.2 | V-Type ATPases | 127 |
| | 6.1.1.3 | Chaperones, Cochaperones, and Heat-Shock Proteins | 128 |
| | 6.1.1.3.1 | HSP70 Family | 128 |
| | 6.1.1.3.2 | HSP40 Family | 129 |
| | 6.1.1.3.3 | HSP90 Family | 129 |
| | 6.1.1.3.4 | HSP60 Family | 132 |
| | 6.1.1.3.5 | HSP104 | 132 |
| | 6.1.1.3.6 | HSP26 and HSP42 | 132 |
| | 6.1.1.3.7 | HSP150 | 133 |
| | 6.1.1.3.8 | HSP31/32/33 | 133 |
| | 6.1.1.3.9 | HSP30 | 133 |
| | 6.1.1.3.10 | HSP10 | 133 |
| | 6.1.1.3.11 | Others | 133 |
| | 6.1.1.4 | Other ATP-Binding Factors | 133 |
| | 6.1.2 | Small GTPases and Their Associates | 133 |
| | 6.1.2.1 | RAS Family | 134 |
| | 6.1.2.2 | RAB Family | 134 |
| | 6.1.2.3 | RHO/RAC Family | 134 |
| | 6.1.2.4 | ARF Family | 134 |
| | 6.1.2.5 | Ran GTPase | 136 |
| | 6.1.3 | G-Proteins | 136 |

| | | |
|-----------|---|------------|
| 6.1.3.1 | Mating Pheromone G-Protein | 136 |
| 6.1.3.2 | Gpr1-Associated G-Protein | 137 |
| 6.1.3.3 | RGS Family | 137 |
| 6.1.3.4 | G-Like Proteins | 137 |
| 6.2 | Regulatory ATPases: AAA and AAA ⁺ Proteins | 138 |
| 6.2.1 | ATP-Dependent Proteases | 138 |
| 6.2.2 | Membrane Fusion Proteins | 139 |
| 6.2.3 | Cdc48 | 139 |
| 6.2.4 | Peroxisomal AAA Proteins | 139 |
| 6.2.5 | Katanin and Vps4p | 139 |
| 6.2.6 | Dynein | 139 |
| 6.2.7 | DNA Replication Proteins | 140 |
| 6.2.8 | RuvB-Like Proteins | 140 |
| 6.2.9 | Other AAA ⁺ Yeast Proteins | 140 |
| 6.3 | Protein Modification by Proteins and Programmed Protein Degradation | 141 |
| 6.3.1 | Ubiquitin-Proteasome System (UPS) | 141 |
| 6.3.1.1 | Initial Discoveries | 141 |
| 6.3.1.2 | Ubiquitin and Factors in the Ubiquitin-Mediated Pathway | 141 |
| 6.3.1.3 | E3 Ubiquitin Ligases | 142 |
| 6.3.1.3.1 | HECT-Type Ligases | 142 |
| 6.3.1.3.2 | RING Finger-Type Ligases | 143 |
| 6.3.1.3.3 | Functions of Selected E3 Ligases | 144 |
| 6.3.1.4 | Ubiquitin-Specific Proteases | 147 |
| 6.3.2 | Yeast Proteasomes | 147 |
| 6.3.2.1 | Initial Discoveries | 147 |
| 6.3.2.2 | Structure of the Proteasome | 148 |
| 6.3.2.3 | Regulation of Yeast Proteasome Activity | 148 |
| 6.3.3 | More Functions for Ubiquitin | 150 |
| 6.3.4 | Ubiquitin-Like Proteins (ULPs) and Cognate Factors | 151 |
| 6.3.4.1 | SUMO | 151 |
| 6.3.4.2 | Rub1 | 152 |
| 6.3.4.3 | Ubiquitin Domain Proteins | 152 |
| 6.3.4.4 | Substrate Delivery to the Proteasome | 153 |
| 6.4 | Yeast Protein Kinases and Phosphatases | 153 |
| 6.4.1 | Protein Kinases in Yeast | 153 |
| 6.4.1.1 | PKA as a Prototype Kinase | 153 |
| 6.4.1.2 | Yeast Possesses a Multitude of Kinases | 153 |
| 6.4.2 | Protein Phosphatases in Yeast | 158 |
| 6.5 | Yeast Helicase Families | 159 |
| 6.5.1 | RNA Helicases in Yeast | 166 |
| 6.5.1.1 | Structures and Motifs | 166 |
| 6.5.1.2 | Functions of RNA Helicases in Yeast | 167 |
| 6.5.2 | DNA Helicases in Yeast | 168 |
| 6.5.2.1 | Structures and Motifs | 168 |
| 6.5.2.2 | Functions of DNA Helicases | 168 |
| 6.5.2.2.1 | ASTRA Complex | 170 |
| 6.5.2.2.2 | RAD Epistasis Group | 170 |
| 6.5.2.2.3 | Monomeric DNA Helicases | 170 |
| | Further Reading | 173 |
| 7 | Yeast Growth and the Yeast Cell Cycle | 175 |
| 7.1 | Modes of Propagation | 175 |
| 7.1.1 | Vegetative Reproduction | 175 |
| 7.1.1.1 | Budding | 175 |
| 7.1.1.2 | Septins and Bud Neck Filaments | 178 |
| 7.1.1.3 | Spindle Pole Bodies and their Dynamics | 179 |

| | | |
|-----------|---|------------|
| 7.1.2 | Sexual Reproduction | 181 |
| 7.1.3 | Filamentous Growth | 181 |
| 7.1.4 | Yeast Aging and Cell Death | 183 |
| 7.1.4.1 | Yeast Lifespan | 183 |
| 7.1.4.2 | Yeast Apoptosis | 184 |
| 7.1.4.2.1 | External Triggers of Yeast Apoptosis | 184 |
| 7.1.4.2.2 | Endogenous Triggers of Yeast Apoptosis | 185 |
| 7.1.4.2.3 | Regulation of Yeast Apoptosis | 185 |
| 7.2 | Cell Cycle | 186 |
| 7.2.1 | Dynamics and Regulation of the Cell Cycle | 186 |
| 7.2.1.1 | Some Historical Notes | 186 |
| 7.2.1.2 | Periodic Events in the First Phases of the Cell Cycle | 188 |
| 7.2.1.2.1 | CDK and Cyclins | 189 |
| 7.2.1.2.2 | Regulation of the CDK/Cyclin System | 190 |
| 7.2.2 | Dynamics and Regulation of Mitosis | 193 |
| 7.2.2.1 | Sister Chromatids: Cohesion | 193 |
| 7.2.2.2 | Spindle Assembly Checkpoint | 196 |
| 7.2.2.3 | Chromosome Segregation | 198 |
| 7.2.2.4 | Regulation of Mitotic Exit | 199 |
| 7.3 | Meiosis | 200 |
| 7.3.1 | Chromosome Treatment During Meiosis | 200 |
| 7.3.2 | Regulation of Meiosis | 201 |
| 7.3.2.1 | Early, Middle, and Late Meiotic Events | 201 |
| 7.3.2.2 | Sporulation | 202 |
| 7.3.3 | Checkpoints in Meiosis | 202 |
| | Further Reading | 204 |
| 8 | Yeast Transport | 207 |
| 8.1 | Intracellular Protein Sorting and Transport | 207 |
| 8.1.1 | “Signal Hypothesis” | 207 |
| 8.1.2 | Central Role of the ER | 207 |
| 8.1.3 | Intracellular Protein Trafficking and Sorting | 208 |
| 8.1.3.1 | Some History | 208 |
| 8.1.3.2 | Membrane Fusions | 210 |
| 8.1.3.2.1 | SNAREs and All That | 210 |
| 8.1.3.2.2 | Small GTPases and Transport Protein Particles | 211 |
| 8.1.3.3 | ER-Associated Protein Degradation | 214 |
| 8.1.3.4 | Golgi Network | 215 |
| 8.1.3.5 | Vacuolar Network | 216 |
| 8.1.3.5.1 | Autophagy | 216 |
| 8.1.3.5.2 | Cytoplasm-to-Vacuole Targeting (CVT) Pathway | 217 |
| 8.1.3.5.3 | Nomenclature in Autophagy and Cvt | 218 |
| 8.1.3.6 | Endocytosis and the Multivesicular Body (MVB) Sorting Pathway | 218 |
| 8.1.3.6.1 | Endocytosis by Vesicles Budding from the Membrane | 218 |
| 8.1.3.6.2 | Endosomal Sorting Complexes Required for Transport (ESCRTs) | 219 |
| 8.1.3.7 | Exocytosis | 221 |
| 8.2 | Nuclear Traffic | 221 |
| 8.2.1 | Nuclear Transport | 221 |
| 8.2.2 | Nuclear mRNA Quality Control | 223 |
| 8.2.3 | Nuclear Export of mRNA | 224 |
| 8.2.4 | Nuclear Dynamics of tRNA | 225 |
| 8.3 | Membrane Transporters in Yeast | 226 |
| 8.3.1 | Transport of Cations | 226 |
| 8.3.2 | Channels and ATPases | 226 |
| 8.3.2.1 | Channels | 226 |
| 8.3.2.2 | ATP-Dependent Permeases | 226 |

- 8.3.3 Ca²⁺-Signaling and Transport Pathways in Yeast 227
 - 8.3.3.1 Ca²⁺ Transport 227
 - 8.3.3.2 Ca²⁺-Mediated Control 228
 - 8.3.3.3 Ca²⁺ and Cell Death 228
- 8.3.4 Transition Metal Transport 228
 - 8.3.4.1 Iron 229
 - 8.3.4.2 Copper 230
 - 8.3.4.3 Zinc 231
 - 8.3.4.4 Manganese 232
- 8.3.5 Anion Transport 232
 - 8.3.5.1 Phosphate Transport 232
 - 8.3.5.2 Transport of Other Anions 233
- 8.3.6 Nutrient and Ammonium Transport 233
 - 8.3.6.1 Transport of Carbohydrates 233
 - 8.3.6.2 Amino Acid Transport 234
 - 8.3.6.3 Transport of Nucleotide Constituents/Nucleotide Sugars 234
 - 8.3.6.4 Transport of Cofactors and Vitamins 234
 - 8.3.6.5 Ammonium Transport 234
- 8.3.7 Mitochondrial Transport 235
 - 8.3.7.1 Transport of Substrates 235
 - 8.3.7.2 Electron Transport Chain 236
 - 8.3.7.3 Proton Motive Force – ATP Synthase 239
- Further Reading 240

9 Yeast Gene Expression 241

- 9.1 Transcription and Transcription Factors 241
- 9.2 RNA Polymerases and Cofactors 241
 - 9.2.1 RNA Polymerase I 242
 - 9.2.2 RNA Polymerase III 243
 - 9.2.3 RNA Polymerase II 245
 - 9.2.4 General Transcription Factors (GTFs) 246
 - 9.2.4.1 TBP 246
 - 9.2.4.2 TFIIA 247
 - 9.2.4.3 TFIIB 247
 - 9.2.4.4 TFIIE and TFIIF 247
 - 9.2.4.5 TFIIH 247
 - 9.2.4.6 TFIIIS 247
 - 9.2.4.7 TFIIID 247
 - 9.2.4.8 First Simplified Pictures of Transcription 247
 - 9.2.5 Transcriptional Activators 248
 - 9.2.5.1 TAFs 249
 - 9.2.5.2 SRB/Mediator 249
 - 9.2.5.3 Depicting Transcriptional Events 249
- 9.3 Transcription and its Regulation 251
 - 9.3.1 Regulatory Complexes 251
 - 9.3.1.1 SAGA 251
 - 9.3.1.2 PAF Complex 252
 - 9.3.1.3 CCR4–NOT Complex 252
 - 9.3.1.4 Other Factors and Complexes 253
 - 9.3.2 Modification of Chromatin During Polymerase II Transcription 254
 - 9.3.2.1 Early Endeavors 254
 - 9.3.2.2 Chromatin-Modifying Activities and Transcriptional Elongation 254
 - 9.3.2.3 Models for Specific Chromatin Remodeling During Transcription 255
 - 9.3.2.3.1 GAL4 System 256

| | | |
|-----------|---|------------|
| 9.3.2.3.2 | PHO System | 256 |
| 9.3.2.3.3 | Other Studies | 257 |
| 9.3.2.3.4 | Global Nucleosome Occupancy | 258 |
| 9.3.3 | Nucleosome Positioning | 259 |
| 9.4 | DNA Repair Connected to Transcription | 259 |
| 9.4.1 | Nucleotide Excision Repair (NER) | 259 |
| 9.4.2 | Mismatch Repair | 261 |
| 9.4.3 | Base Excision Repair | 261 |
| 9.5 | Coupling Transcription to Pre-mRNA Processing | 261 |
| 9.5.1 | Polyadenylation | 261 |
| 9.5.2 | Generation of Functional mRNA | 263 |
| 9.5.2.1 | General Principles | 263 |
| 9.5.2.2 | Control and Pathways of mRNA Decay | 265 |
| 9.5.2.2.1 | Exosome-Mediated Pathways in Yeast | 265 |
| 9.5.2.2.2 | Nonsense-Mediated mRNA Decay (NMD) | 267 |
| 9.6 | Yeast Translation Apparatus | 268 |
| 9.6.1 | Initiation | 269 |
| 9.6.2 | Elongation and Termination | 270 |
| 9.7 | Protein Splicing – Yeast Inteins | 271 |
| | Further Reading | 271 |
| 10 | Molecular Signaling Cascades and Gene Regulation | 273 |
| 10.1 | Ras–cAMP Signaling Pathway | 273 |
| 10.2 | MAP Kinase Pathways | 275 |
| 10.2.1 | Mating-Type Pathway | 275 |
| 10.2.2 | Filamentation/Invasion Pathway | 278 |
| 10.2.3 | Control of Cell Integrity | 279 |
| 10.2.4 | High Osmolarity Growth Pathway | 280 |
| 10.2.5 | Spore Wall Assembly Pathway | 280 |
| 10.2.6 | Influence of MAP Kinase Pathways in Cell Cycle Regulation | 281 |
| 10.3 | General Control by Gene Repression | 281 |
| 10.3.1 | Ssn6–Tup1 Repression | 281 |
| 10.3.2 | Activation and Repression by Rap1 | 283 |
| 10.4 | Gene Regulation by Nutrients | 283 |
| 10.4.1 | TOR System | 283 |
| 10.4.1.1 | Structures of the TOR Complexes | 283 |
| 10.4.1.2 | Signaling Downstream of TORC1 | 284 |
| 10.4.1.3 | Signaling Branches Parallel to TORC1 | 286 |
| 10.4.1.4 | Internal Signaling of TORC1 | 286 |
| 10.4.1.5 | TOR and Aging | 286 |
| 10.4.2 | Regulation of Glucose Metabolism | 287 |
| 10.4.2.1 | Major Pathway of Glucose Regulation | 287 |
| 10.4.2.2 | Alternative Pathway of Glucose Regulation | 289 |
| 10.4.3 | Regulation of Galactose Metabolism | 289 |
| 10.4.4 | General Amino Acid Control | 290 |
| 10.4.5 | Regulation of Arginine Metabolism | 293 |
| 10.5 | Stress Responses in Yeast | 294 |
| 10.5.1 | Temperature Stress and Heat-Shock Proteins | 294 |
| 10.5.2 | Oxidative and Chemical Stresses | 295 |
| 10.5.2.1 | AP-1 Transcription Factors in Yeast | 295 |
| 10.5.2.2 | STRE-Dependent System | 296 |
| 10.5.2.3 | PDR: ABC Transporters | 296 |
| 10.5.3 | Unfolded Protein Response | 298 |
| | Further Reading | 299 |

- 11 Yeast Organellar Biogenesis and Function 301**
- 11.1 Mitochondria 301
 - 11.1.1 Genetic Biochemistry of Yeast Mitochondria 301
 - 11.1.2 Mitochondrial Functions Critical to Cell Viability 303
 - 11.1.2.1 Superoxide Dismutase 303
 - 11.1.2.2 Iron Homeostasis 304
 - 11.1.3 Biogenesis of Mitochondria: Protein Transport 305
 - 11.1.3.1 Presequence Pathway and the MIA Pathway 307
 - 11.1.3.2 Membrane Sorting Pathway: Switch Between TIM22 and TIM23 307
 - 11.1.3.3 β -Barrel Pathway 308
 - 11.1.3.4 Endogenous Membrane Insertion Machinery 308
 - 11.1.4 Mitochondrial Quality Control and Remodeling 308
 - 11.2 Peroxisomes 310
 - 11.2.1 What They Are – What They Do 310
 - 11.2.2 Protein Import and Cargo 311
 - Further Reading 312
- 12 Yeast Genome and Postgenomic Projects 313**
- 12.1 Yeast Genome Sequencing Project 313
 - 12.1.1 Characteristics of the Yeast Genome 314
 - 12.1.2 Comparison of Genetic and Physical Maps 315
 - 12.1.3 Gene Organization 315
 - 12.1.3.1 Protein-Encoding Genes 315
 - 12.1.3.2 Overlapping ORFs, Pseudogenes, and Introns 316
 - 12.1.4 Genetic Redundancy: Gene Duplications 317
 - 12.1.4.1 Duplicated Genes in Subtelomeric Regions 317
 - 12.1.4.2 Duplicated Genes Internal to Chromosomes 318
 - 12.1.4.3 Duplicated Genes in Clusters 318
 - 12.1.5 Gene Typification and Gene Families 318
 - 12.1.5.1 Gene Functions 318
 - 12.1.5.2 tRNA Multiplicity and Codon Capacity in Yeast 319
 - 12.1.5.2.1 tRNA Gene Families 319
 - 12.1.5.2.2 Correlation of tRNA Abundance to Gene Copy Number 320
 - 12.1.5.2.3 tRNA Gene Redundancy and Codon Selection in Yeast 320
 - 12.2 Yeast Functional Genomics 322
 - 12.2.1 Early Functional Analysis of Yeast Genes 322
 - 12.2.2 Yeast Transcriptome 322
 - 12.2.2.1 Genomic Profiling 322
 - 12.2.2.2 Protein–DNA Interactions 323
 - 12.2.3 Yeast Proteome 324
 - 12.2.3.1 Protein Analysis 324
 - 12.2.3.2 Proteome Chips 325
 - 12.2.3.3 Protein–Protein Interactions and Protein Complexes: The Yeast Interactome 325
 - 12.2.4 Yeast Metabolic Networks 327
 - 12.2.4.1 Metabolic Flux 327
 - 12.2.4.2 Yeast Metabolic Cycle 328
 - 12.2.5 Genetic Landscape of a Cell 329
 - 12.2.6 Data Analysis Platforms 329
 - 12.3 Yeast Systems Biology 330
 - 12.4 Yeast Synthetic Biology 332
 - Further Reading 334

- 13 Disease Genes in Yeast 335**
 - 13.1 General Aspects 335
 - 13.1.1 First Approaches 335
 - 13.1.2 Recent Advances 335
 - 13.2 Trinucleotide Repeats and Neurodegenerative Diseases 341
 - 13.2.1 Neurodegenerative Disorders 342
 - 13.2.2 Huntington's Disease 342
 - 13.2.3 Parkinson's Disease 343
 - 13.2.4 Alzheimer's Disease and Tau Biology 343
 - 13.2.5 Other Proteinopathies 344
 - 13.3 Aging and Age-Related Disorders 344
 - 13.4 Mitochondrial Diseases 344
 - Further Reading 346

- 14 Yeasts in Biotechnology 347**

Paola Branduardi and Danilo Porro

 - 14.1 Introduction 347
 - 14.1.1 Biotechnology Disciplines 347
 - 14.1.2 Microorganisms in Biotechnology 348
 - 14.2 Yeasts: Natural and Engineered Abilities 348
 - 14.2.1 Yeast as a Factory 348
 - 14.2.2 Natural Production 349
 - 14.2.2.1 Commercial Yeasts 349
 - 14.2.2.2 Food Yeast 349
 - 14.2.2.3 Feed Yeasts 351
 - 14.2.2.4 Yeast Extract 351
 - 14.2.2.5 Autolysed Yeast 352
 - 14.2.3 Engineered Abilities: Recombinant Production of the First Generation 352
 - 14.2.3.1 Metabolic Engineering 352
 - 14.2.3.2 Engineered Products 353
 - 14.2.3.2.1 Isoprene Derivatives 353
 - 14.2.3.2.2 Pigments 354
 - 14.2.3.2.3 Other Valuable Biocompounds 354
 - 14.2.3.2.4 Small Organic Compounds 356
 - 14.2.3.2.5 Biofuels 357
 - 14.2.3.2.6 Further Developments 358
 - 14.2.4 Engineered Abilities: Recombinant Production of the Second Generation 358
 - 14.3 Biopharmaceuticals from Healthcare Industries 359
 - 14.3.1 Human Insulin 359
 - 14.3.2 Other Biopharmaceuticals 361
 - 14.4 Biomedical Research 362
 - 14.4.1 Humanized Yeast Systems for Neurodegenerative Diseases 363
 - 14.4.1.1 Parkinson's Disease 363
 - 14.4.1.2 Huntington's Disease 363
 - 14.4.1.3 Alzheimer's Disease 363
 - 14.4.2 Yeast Models of Human Mitochondrial Diseases 363
 - 14.4.3 Yeast Models for Lipid-Related Diseases 364
 - 14.4.4 Yeasts and Complex Genomes 364
 - 14.5 Environmental Technologies: Cell Surface Display 364
 - 14.6 Physiological Basis for Process Design 366
 - 14.6.1 Process Development 367
 - 14.6.2 Production Process 368
 - Further Reading 370

15 Hemiascomycetous Yeasts 371*Claude Gaillardin*

- 15.1 Selection of Model Genomes for the Génolevures and Other Sequencing Projects 371
- 15.2 Ecology, Metabolic Specificities, and Scientific Interest of Selected Species 373
 - 15.2.1 *Candida glabrata* – A Pathogenic Cousin of *S. cerevisiae* 373
 - 15.2.2 *Lachancea (Saccharomyces) kluyveri* – An Opportunistic Anaerobe 375
 - 15.2.3 *Kluyveromyces lactis* – A Respiro-Fermentative Yeast 376
 - 15.2.4 *Eremothecium (Ashbya) gossypii* – A Filamentous Plant Pathogen 377
 - 15.2.5 *Debaryomyces hansenii* – An Osmotolerant Yeast 378
 - 15.2.6 *Scheffersomyces (Pichia) stipitis* – A Xylose-Utilizing Yeast 379
 - 15.2.7 *Komagataella (Pichia) pastoris* – A Methanol-Utilizing Yeast 380
 - 15.2.8 *Blastobotrys (Arxula) adenivorans* – A Thermotolerant Yeast 381
 - 15.2.9 *Yarrowia lipolytica* – An Oily Yeast 382
- 15.3 Differences in Architectural Features and Genetic Outfit 383
 - 15.3.1 Genome Sizes and Global Architecture 383
 - 15.3.2 Chromosome Architecture and Synteny 383
 - 15.3.3 Arrangements of Genetic Elements 385
 - 15.3.3.1 Replication Origins, Centromeres, and Telomeres 385
 - 15.3.3.2 Gene Arrays 386
 - 15.3.3.2.1 Megasatellites 386
 - 15.3.3.2.2 Tandem Gene Arrays 387
 - 15.3.3.2.3 Yeast Pseudogenes 387
 - 15.3.4 Gene Families and Diversification of the Protein Repertoires 388
 - 15.3.4.1 Biological Divergence 388
 - 15.3.4.2 Diversification of the Gene Repertoire 389
 - 15.3.5 tRNAs and rRNAs 391
 - 15.3.6 Other Noncoding RNAs 392
 - 15.3.7 Introns 393
 - 15.3.8 Transposons 395
 - 15.3.9 Mitochondrial DNA 395
 - 15.3.10 DNA Plasmids 397
- 15.4 Molecular Evolution of Functions 397
 - 15.4.1 Proteome Diversification and Loss or Gain of Functions 398
 - 15.4.1.1 Loss and Relocalization of Pathways 398
 - 15.4.1.2 Diversification of Paralogs 398
 - 15.4.1.3 Horizontal Transfers 398
 - 15.4.1.4 Evolution of Cell Identity 399
 - 15.4.1.5 Heterochromatin, Gene Silencing, and RNA Interference 399
 - 15.4.2 Changes in Transcriptional Regulation 400
 - 15.4.2.1 Evolution of the GAL Regulon 400
 - 15.4.2.2 Glucose Effects and Adaptation to Anoxic Conditions 401
 - 15.4.2.3 Stress Responses 401
 - 15.4.2.4 Recruitment of New Transcription Factors and DNA-Binding Sites 402
 - 15.4.2.5 New Combinatorial Controls 403
 - 15.4.2.6 Nucleosome Positioning in Evolution 403
 - 15.4.3 Changes in Post-Transcriptional Regulations 404
 - Further Reading 405

16 Yeast Evolutionary Genomics 407*Bernard Dujon*

- 16.1 Specificities of Yeast Populations and Species, and their Evolutionary Consequences 407
 - 16.1.1 Species, Complexes, and Natural Hybrids 407
 - 16.1.2 Reproductive Trade-Offs 408

| | | |
|--------|---|-----|
| 16.1.3 | Preference for Inbreeding | 409 |
| 16.1.4 | Population Structures Examined at the Genomic Level | 410 |
| 16.1.5 | Loss of Heterozygosity and Formation of Chimeras | 410 |
| 16.1.6 | Asymmetrical Growth of Clonal Populations | 411 |
| 16.2 | Gene Duplication Mechanisms and their Evolutionary Consequences | 412 |
| 16.2.1 | Gene Clusters | 412 |
| 16.2.2 | Whole-Genome Duplication | 413 |
| 16.2.3 | Segmental Duplications | 414 |
| 16.2.4 | Retrogenes and Dispersed Paralogues | 414 |
| 16.3 | Other Mechanisms of Gene Formation and Acquisition of Novel Functions | 415 |
| 16.3.1 | Introgression | 415 |
| 16.3.2 | Horizontal Gene Transfer from Bacterial Origin | 416 |
| 16.3.3 | <i>De Novo</i> Gene Formation | 417 |
| 16.3.4 | Integration of Other Sequences in Yeast Chromosomes | 418 |
| | Further Reading | 419 |

17 Epilog: The Future of Yeast Research 421

Appendix A: References 423

Appendix B: Glossary of Genetic and Taxonomic Nomenclature 425

Appendix C: Online Resources useful in Yeast Research 427

Appendix D: Selected Abbreviations 429

Index 433