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 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 *S. cerevisiae* 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 Ca^{2+}-Signaling and Transport Pathways in Yeast *227*
8.3.3.1 Ca^{2+} Transport *227*
8.3.3.2 Ca^{2+} -Mediated Control *228*
8.3.3.3 Ca^{2+} 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 TFIIS *247*
9.2.4.7 TFIID *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) adeninivorans* – 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 Paralogs *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 *De Novo* 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*