

Contents

Preface *XI*

Foreword *XIII*

1	Introduction	1
1.1	Historical Aspects	1
1.2	Yeast as a Eukaryotic Model System	2
2	The "Early Days" of Nucleic Acids	5
2.1	Molecular Biology of tRNA	5
2.2	Ribosomes, Ribosomal RNAs, and Ribosomal Proteins	9
2.3	Messenger RNAs	10
2.3.1	Structure of Yeast mRNAs	10
2.3.2	Introns and Processing of pre-mRNA	11
3	Genetic Engineering and Reverse Genetics	15
3.1	The Molecular Revolution	15
3.2	Transformation of Yeast Cells	16
3.3	More Genetic Tools from Yeast Cells	16
3.4	The Two-Hybrid System	17
4	Cell Structures and Functions	19
4.1	The Yeast Cell	19
4.2	Yeast Envelope and Cell Skeleton	19
4.3	Yeast Chromosome Structure and Function	21
4.3.1	Centromeres	21
4.3.2	Replication Origins and Replication	21
4.3.3	Telomeres	23
4.3.4	Retrotransposons in Yeast	25
4.3.4.1	Types and Structure	25
4.3.4.2	Ty Replication	27

4.3.4.3	Interactions between Ty Elements and their Host	28
4.3.5	Extrachromosomal Elements: Yeast Prions	29
5	Cellular Dynamics	33
5.1	Cell Propagation	33
5.1.1	Budding	33
5.1.2	Septins	34
5.1.3	Spindle Dynamics	34
5.2	Regulatory ATPases – AAA ⁺ Proteins	36
5.2.1	ATP-Dependent Proteases	36
5.2.2	Membrane Fusion Proteins	37
5.2.3	Cdc48	37
5.2.4	Peroxisomal AAA Proteins	38
5.2.5	Katanin and Vps4p	38
5.2.6	Dynein	39
5.2.7	DNA Replication Proteins	39
5.2.8	RuvB-Like Proteins	39
5.3	Protein Modification by Proteins and Programmed Protein Degradation	40
5.3.1	The Ubiquitin-Proteasome System	40
5.3.1.1	Ubiquitin and Factors in the Ubiquitin-Mediated Pathway	40
5.3.1.2	Yeast Proteasomes	43
5.3.1.3	Regulation of Yeast Proteasome Activity	46
5.3.2	More Functions for Ubiquitin	46
5.3.3	Ubiquitin-Like Proteins (ULPs) and Cognate Factors	47
5.3.3.1	SUMO	47
5.3.3.2	RUB1	49
5.3.3.3	Ubiquitin Domain Proteins	49
5.4	The Yeast Cell Cycle, Cell Division, and Chromosome Segregation	51
5.4.1	The Cell Cycle	51
5.4.2	Sister Chromatids: Cohesion and Separation	53
5.4.3	The Spindle Checkpoint	56
5.4.4	Chromosome Segregation During Meiosis	58
5.5	Intracellular Protein Sorting and Transport	58
5.5.1	The "Signal Hypothesis"	59
5.5.2	Central Role of the Endoplasmic Reticulum	60
5.5.3	Intracellular Protein Trafficking and Sorting	60
5.5.4	ER-Associated Protein Degradation	65
5.5.5	The Vacuolar Network	66
5.5.6	Endocytosis and the Multivesicular Body Sorting Pathway	67
5.5.7	Exocytosis	70
5.5.8	Nuclear Traffic	71
5.6	Membrane Transporters in Yeast	75
5.6.1	Channels and ATPases	76
5.6.1.1	H ⁺ -ATPases	76

5.6.1.2	Ca ²⁺ -Signaling and Transport Pathways in Yeast	76
5.6.2	Transition Metal Transport	79
5.6.2.1	Iron	79
5.6.2.2	Copper	80
5.6.2.3	Zinc	80
5.6.2.4	Manganese	81
5.6.3	Phosphate Transport	81
5.6.4	Nutrient and Ammonium Transport	82
6	Anatomy of the Transcription Machinery and Auxiliary Complexes: Chromatin Remodeling	85
6.1	Transcriptional Regulation and Transcription Factors	85
6.2	RNA Polymerases and Cofactors	86
6.2.1	RNA Polymerase I	86
6.2.2	RNA Polymerase III	86
6.2.3	RNA Polymerase II	89
6.2.4	General Transcription Factors	92
6.2.4.1	TBP	92
6.2.4.2	TFIIA	92
6.2.4.3	TFIIB	92
6.2.4.4	TFIIE and TFIIF	93
6.2.4.5	TFIIH	93
6.2.4.6	Transcription Activators	93
6.2.4.7	TFIID	94
6.2.4.8	SRB/Mediator	95
6.2.4.9	SAGA	98
6.2.4.10	Transcriptional Repressors	98
6.3	Coupling Transcription to Pre-mRNA Processing	99
6.4	DNA Repair Connected to Transcription	101
6.5	Modification of Chromatin During Transcription	102
6.5.1	Chromatin-Modifying Activities	104
6.5.2	Chromatin Remodeling Complexes	106
7	Molecular Signaling Cascades and Gene Regulation	109
7.1	MAP Kinase Pathways	109
7.1.1	Mating-Type Pathway	110
7.1.2	Filamentation/Invasion Pathway	110
7.1.3	Control of Cell Integrity	111
7.1.4	High Osmolarity Growth Pathway	112
7.1.5	Spore Wall Assembly Pathway	114
7.2	General Control by Gene Repression	115
7.2.1	Ssn6-Tup1 Repression	115
7.2.2	Activation and Repression by Rap1	117
7.3	Gene Regulation by Nutrients	117
7.3.1	The TOR System	117

7.3.2	Regulation of Glucose Metabolism	121
7.3.3	Regulation of Galactose Metabolism	124
7.3.4	General Amino Acid Control	126
7.3.5	Regulation of Arginine Metabolism	127
7.4	Stress Responses in Yeast	129
7.4.1	Temperature Stress and Heat Shock Proteins	129
7.4.2	Oxidative and Chemical Stresses	134
7.4.2.1	AP-1 Transcription Factors in Yeast	134
7.4.2.2	The STRE-Dependent System	136
7.4.2.3	Pleiotropic Drug Resistance: ABC Transporters	136
7.4.3	The Unfolded Protein Response	139
7.5	Posttranscriptional Control of Gene Expression in Yeast	139
7.5.1	Translation	139
7.5.2	Control and Pathways of mRNA Decay	140
7.5.3	Exosome-Mediated Pathways in Yeast	140
7.5.4	Nonsense-Mediated mRNA Decay	142
7.6	Protein Splicing – Yeast Inteins	143
8	Yeast Organellar Biogenesis and Function	147
8.1	Mitochondria	147
8.1.1	Genetic Biochemistry of Yeast Mitochondria	147
8.1.2	Mitochondrial Functions Critical to Cell Viability	150
8.1.2.1	Superoxide Dismutase	151
8.1.2.2	Iron Homeostasis	151
8.1.3	Biogenesis of Mitochondria: Protein Transport	152
8.1.3.1	The Presequence Pathway and the MIA Pathway	154
8.1.3.2	The Membrane Sorting Pathway: Switch Between TIM22 and TIM23	155
8.1.3.3	The β -Barrel Pathway	156
8.1.3.4	The Endogenous Membrane Insertion Machinery	156
8.1.4	Mitochondrial Quality Control and Remodeling	156
8.2	Peroxisomes	158
9	Genome, Proteome, Transcriptome, Metabolome, and Regulatory Networks	165
9.1	The Yeast Genome Sequencing Project	165
9.2	Characteristics of the Yeast Genome	166
9.2.1	Gene Organization	168
9.2.2	Genetic Redundancy: Gene Duplications	169
9.2.3	Gene Typification and Gene Families	170
9.2.4	Functional Analysis of Yeast Genes	171
9.3	Functional Genomics	171
9.3.1	Yeast Transcriptome	171
9.3.1.1	Genomic Profiling	171
9.3.1.2	Protein–DNA Interactions	172

9.3.2	Yeast Proteome	174
9.3.2.1	Protein Analysis	174
9.3.2.2	Proteome Chips	175
9.3.2.3	Protein-Protein Interactions and Protein Complexes	175
9.3.3	Yeast Metabolome	177
9.3.4	Genetic Interaction Networks: Regulatory Networks and Oscillations	177
9.4	Hemiascomycetous Yeasts and Evolutionary Aspects	178
9.4.1	Model Genomes	178
9.4.2	Evolutionary Aspects	181
10	Disease Genes in Yeast	185
10.1	General Aspects	185
10.2	Trinucleotide Repeats and Neurodegenerative Diseases	187
10.3	Aging and Age-Related Disorders	190
10.4	Mitochondrial Diseases	191
11	Yeast in Biotechnology	197
11.1	Fermentation and Metabolic Engineering	197
11.1.1	"Typical" Fermentation Procedures	197
11.1.2	Food and Chemical Industries: Metabolic Engineering	198
11.2	Biopharmaceuticals from Health-Care Industries	201
11.3	Biomedical Research	204
11.4	Environmental Technologies: Cell-Surface Display	204
12	Epilogue: The Future of Yeast Research	207
	References	209
	Appendix: Online Resources Useful in Yeast Research	327
	Index	329