

Contents

1 Human Genome, Development, Evolution and Aging	1
1.1 The Human Genome and Its Variation	2
1.2 Principles of Development and Aging	9
1.3 Evolutionary Perspective on Aging	13
1.4 Hallmarks of Aging	15
Bibliography	18
2 Principles of Gene Expression and Epigenetics	19
2.1 Gene Regulation	19
2.2 Chromatin Structure and Epigenetics	22
2.3 Information Storage by Chromatin Modifications	24
2.4 Epigenetics Enables Gene Expression	33
Bibliography	39
3 Epigenetics, Memory and Aging	41
3.1 Transgenerational Epigenetics	41
3.2 Epigenetics of Aging	46
3.3 Epigenetics and Time: The Circadian Clock	51
Bibliography	56
4 Biochemistry of Aging	57
4.1 Principles of Metabolism	57
4.2 Aging and Conserved Nutrient Sensing Pathways	59
4.3 Neuroendocrine Regulation of Energy Metabolism and Aging	65
Bibliography	71
5 Molecular and Cellular Basis of Aging	73
5.1 Mitochondria and Endoplasmatic Reticulum Dysfunctions	73
5.2 Apoptosis, Autophagy and the Loss of Proteostasis	80
5.3 Stem Cell Exhaustion and Cellular Senescence	84
5.4 Long- and Short-Lived Cells	88
Bibliography	91

6	Immunity and Aging	93
6.1	Innate and Adaptive Immunity	93
6.2	Relation of Epigenetics and Immunity	98
6.3	Inflammation and Aging	103
6.4	The Aging Immune System	108
6.5	The Microbiome in Aging	112
	Bibliography	116
7	Chronic Diseases and Aging	117
7.1	The Global Burden of Diseases	117
7.2	The Metabolic Syndrome: Obesity, T2D and CVD	118
7.3	Cancer	124
7.4	Neurodegenerative Diseases	128
	Bibliography	133
8	Premature Aging	135
8.1	DNA Repair Mechanisms	135
8.2	Premature Aging Syndromes Associated with Genomic Instability	139
8.3	Laminopathies	145
	Bibliography	148
9	Healthy Aging and Longevity	151
9.1	Impact of Energy Balance and Dietary Macronutrient Composition	151
9.2	Impact of Physical Activity	158
9.3	Aging Clocks	160
9.4	The Socio-Economic Need of Healthy Aging	163
	Bibliography	167
	Glossary	169