

---

# Contents

---

<b>Preface</b> . . . . .	ix
<b>Chapter 1. Historical Overview of Endocrinology, Neurology and Immunology</b> . . . . .	1
1.1. The history of endocrinology . . . . .	1
1.2. The history of neurology . . . . .	4
1.3. The history of immunology . . . . .	7
<b>Chapter 2. Regulatory Systems Integrating External and Internal Changes</b> . . . . .	11
2.1. Regulatory systems: endocrine, nervous and immune . . . . .	11
2.1.1. Endocrine system . . . . .	14
2.1.2. Nervous system . . . . .	18
2.1.3. Immune system . . . . .	19
2.2. Origin and diversity of signals and communication modes . . . . .	20
2.2.1. Origin . . . . .	20
2.2.2. Diversity . . . . .	27
2.2.3. Communication modes . . . . .	27
2.3. Integration of extracellular signals: plasma membrane receptors . . . . .	36
2.3.1. Chemical signals and mechanisms of action: receptor types and signaling modulation. . . . .	36
2.3.2. Integration of multiple signal inputs: ratio of stimulatory vs inhibitory signals. . . . .	58
2.3.3. Physical signals . . . . .	68
2.4. Nuclear receptors . . . . .	69
2.4.1. Chemical nature of signals and functional characteristics of nuclear receptors . . . . .	69
2.4.2. Molecular mechanisms underlying regulation of gene transcription . . . . .	72

---

<b>Chapter 3. Intracellular Events in Response to Signals</b> . . . . .	75
3.1. Signaling pathways . . . . .	75
3.1.1. General overview . . . . .	75
3.1.2. Signal termination . . . . .	76
3.1.3. Control of protein activities: allostery, covalent modifications and proteolytic cleavage . . . . .	88
3.1.4. Impaired cellular responses to extracellular signals . . . . .	93
3.1.5. Subcellular localization and sequestration . . . . .	100
3.1.6. Crosstalk. . . . .	108
3.2. Sensing of extracellular and intracellular cues . . . . .	114
3.2.1. Sensing of extracellular cues. . . . .	114
3.2.2. Sensing of intracellular cues . . . . .	121
3.3. Functional diversity of proteins. . . . .	130
3.3.1. Multifaceted “master regulators” . . . . .	130
3.3.2. Molecular motor proteins . . . . .	138
3.3.3. Interactional domains. . . . .	139
3.3.4. Carrier proteins . . . . .	142
3.3.5. Decoy molecules . . . . .	143
3.3.6. Heat shock proteins as molecular chaperones . . . . .	145
3.3.7. Hormone-like peptides: molecular mimicry . . . . .	146
3.3.8. Telomerase and integrity of linear chromosomes . . . . .	146
<b>Chapter 4. Integrative Aspects: From Cellular to Whole-Body Level</b> . . . . .	149
4.1. Homeostasis equilibrium: dynamic steady state. . . . .	149
4.1.1. Regulation of systemic glucose homeostasis . . . . .	150
4.1.2. Tissue homeostasis . . . . .	152
4.1.3. Muscle and bone mass homeostasis . . . . .	157
4.1.4. Whole-body energy homeostasis . . . . .	158
4.1.5. Metabolism and cellular energy homeostasis. . . . .	160
4.1.6. The gut microbiome and glucose homeostasis . . . . .	160
4.1.7. Synaptic homeostasis . . . . .	161
4.1.8. Open issues: membrane lipid homeostasis and acid–base homeostasis . . . . .	162
4.2. Homeostasis disruption . . . . .	162
4.2.1. Endocrine disorders: excess or impaired hormone secretion . . . . .	163
4.2.2. Muscle energy wasting . . . . .	165
4.2.3. Energy . . . . .	165
4.2.4. Cell number and activity . . . . .	165
4.3. Crosstalk between organs, tissues and regulatory systems . . . . .	168
4.3.1. Axis concept. . . . .	169
4.3.2. Crosstalk between neuroendocrine axes . . . . .	177
4.3.3. Crosstalks between organs and brain . . . . .	179
4.3.4. Crosstalk between immune, endocrine and nervous systems . . . . .	193

---

4.3.5. Immune system and cancer cell interactions . . . . .	199
4.3.6. Adjustments of intermediary metabolism: brain, skeletal muscle, cancer cells . . . . .	202
<b>Chapter 5. Epigenetics and Circadian Rhythms: Role of Environmental Factors . . . . .</b>	<b>213</b>
5.1. Epigenetics: general overview . . . . .	213
5.1.1. Epigenetic modifications of DNA and regulation of biological processes . . . . .	216
5.1.2. Genomic imprinting . . . . .	220
5.1.3. Setting and maintenance of DNA methylation . . . . .	222
5.1.4. Evidence for non-genomic inheritance: epigenetic mechanisms . . . . .	224
5.1.5. Nutritional influences on developmental epigenetics . . . . .	226
5.1.6. Gut microbiome and epigenetic changes . . . . .	231
5.1.7. Metabolites and epigenetic changes . . . . .	231
5.1.8. Social environment and endocrine disruptor: epigenetic changes . . . . .	232
5.1.9. Importance of epigenetics in the etiology of cancer . . . . .	234
5.1.10. <i>In vitro</i> reprogramming systems . . . . .	240
5.2. Circadian rhythms . . . . .	241
5.2.1. Circadian rhythms and the concept of a circadian clock. . . . .	242
5.2.2. Overview of the mammalian clock . . . . .	243
5.2.3. Mechanisms by which circadian clocks govern biological processes . . . . .	245
5.2.4. How is the SCN clock connected to tissue and cellular functions? . . . . .	246
5.2.5. Avian circadian clock. . . . .	254
5.3. Conclusion . . . . .	255
<b>Concluding Remarks . . . . .</b>	<b>257</b>
<b>References . . . . .</b>	<b>261</b>
<b>Index . . . . .</b>	<b>319</b>