

Contents

About the Author.....	ix
CHAPTER 1 General Introduction.....	1
References.....	4
CHAPTER 2 Adipose Tissue: A Major Secretory Organ	9
Mechanisms of Adipokine Release	13
Classical or Endoplasmic Reticulum/Golgi-Dependent Pathways.....	14
Adiponectin.....	14
Leptin.....	15
Nonclassical Protein Secretion	15
Transporter-Mediated Export of FGF2.....	15
Shedding of TNF α and DPP4	16
Multiple Export Routes of IL-1 β	17
Adiponectin and Leptin	20
Retinol-Binding Protein 4	21
Heme Oxygenase-1.....	22
WNT1-Inducible Signaling Pathway Protein 2.....	23
Secreted Frizzled-Related Proteins.....	23
Chemerin	24
The Fat–Muscle Crosstalk	25
TNF α and IL-6.....	27
MCP-1 and Vaspin.....	28
Adiponectin and Leptin	28
DPP4 and Visfatin Impact on Skeletal Muscle.....	29
The Fat–Liver Crosstalk.....	30
The Fat–Pancreas Crosstalk.....	32
Adiponectin and Leptin: Antagonist Effects on Pancreatic β -Cells.....	33
DPP4 and Visfatin: Potential Mediators of β -Cell Dysfunction?.....	34
Adiponectin and Leptin: Two Opposite Players in the Vascular Wall?	35
DPP4 and Visfatin: Promising Therapeutic Targets in Cardiovascular Diseases.....	36

	Perivascular Adipose Tissue	37
	Epicardial Adipose Tissue	39
	Physiological Function of Epicardial Adipose Tissue	40
	Crosstalk Between Epicardial Adipose Tissue and the Myocardium	41
	Brown Adipose Tissue	41
	Physiology and Regulation of Brown Adipose Tissue	43
	The Brown Fat Secretome	45
	References	47
CHAPTER 3	Skeletal Muscle: A Novel Secretory Organ	65
	The Myokine Concept and the Skeletal Muscle Secretome	66
	Myokines and Exercise Factors: A Definition	67
	Secretome Analysis	68
	IL-6 and Other Interleukins	70
	Novel Myokines With Potential Therapeutic Applications	73
	Follistatin-like 1: A Cardioprotective Myokine	74
	Fibroblast Growth Factor 21: A Potential Insulin Sensitizer	74
	Irisin: A Controversial Myokine	76
	Muscle—Adipose Tissue Crosstalk	79
	The Muscle—Bone Connection	82
	Conclusion and Future Directions	84
	References	84
CHAPTER 4	Adipomyokines: An Extended View on the Crosstalk Scenario	91
	Skeletal Muscle as the Source of Myokines and Adipomyokines After Acute and Chronic Exercise	93
	Exercise and the Production of Adipokines by Adipose Tissue	98
	Exercise-Induced Adipomyokines and Their Role in Bone Metabolism	102
	Conclusion and Future Directions	105
	References	107
CHAPTER 5	Secretory Malfunction: A Key Step to Metabolic Diseases	117
	Adipose Tissue Inflammation	118
	Obesity, Insulin Resistance, and Type 2 Diabetes	120
	Adipose Tissue Dysfunction and Cardiovascular Disease	124

DPP4 and DPP4 Inhibitors	124
DPP4 Inhibitors: Indirect Effects of DPP4	125
Direct Effects of Soluble DPP4	126
Lipocalin-2 and Visfatin	127
Lipocalin-2	127
Visfatin	128
Omentin and Apelin	130
Fatty Liver and Organ Crosstalk	131
Fibroblast Growth Factor 21	134
Fetuin-A	135
Selenoprotein P	136
Sedentary Lifestyle and Metabolic Diseases	137
The Antiinflammatory Effects of Exercise	137
Myokines and Antiinflammatory Effects	138
References	141
CHAPTER 6 Technical Annex	155
Cell Isolation and Culture Protocols	158
Isolation of Preadipocytes	158
Preadipocyte Proliferation	159
Isolation of Murine Preadipocytes	161
Mature Adipocyte Isolation	163
Preparation of Explants From Adipose Tissue	164
Culture of Human Adipocytes	165
Differentiation of Preadipocytes (Alternative Method)	167
Culture of Primary Human Skeletal Muscle Cells	168
Culture of C2C12 Myocytes	170
Culture of Primary Human Smooth Muscle Cells	171
Culture of Human Coronary Artery Endothelial Cells	173
Culture of HepG2 Liver Cells	174
Procedure	175
Culture of INS-1 Cells and Analysis of Insulin Secretion ...	175
Electrical Stimulation of Muscle Cells	177
Preparation of Solutions and Buffers	178
Measurement of Oxygen Consumption (Adipocytes)	
Using the Seahorse System	182
Metabolic Measurements	186
Staining and Microscopy	198
Oil Red O	198
Neutral Red Staining—Cytotoxicity Test	199

Nile Red Staining	200
Immunofluorescence Staining of Myotubes	202
Immunofluorescence—Human Adipocytes	205
Analytical Procedures	207
Isolation of RNA Using Qiagen RNeasy Mini Kit	207
Isolation of RNA Using TriPure in Combination With Qiagen RNeasy Mini Kit for Adipose Tissue	209
Isolation of RNA From Mouse White Adipose Tissue	210
RT-PCR Using GoTaq qPCR Master Mix (Promega)	211
Standard Program for QuantiTect Primer Assay	212
References	213
Index	217