

Contents

Contributors		ix
Preface		xi
Part I	Aetiology of Insulin Resistance and Type 2 Diabetes	
	Prevalence and Consequences of the “Diabesity” Epidemic	
Chapter 1	The Increasing Burden of Type 2 Diabetes: Magnitude, Causes, and Implications of the Epidemic	3
	<i>Edward W. Gregg, PhD; and Andrea K. Kriska, PhD</i>	
	Diabetes Prevalence and Incidence in Adults	3
	Type 2 Diabetes in Youths and Adolescents	7
	Risk Factors for Diabetes and Causes of the Epidemic	7
	Determinants of Recent Diabetes Trends	9
	Anticipated Consequences of Diabetes and the Outlook for Prevention	10
	Concluding Remarks	11
	References	11
Chapter 2	Waging War on Type 2 Diabetes: Primary Prevention Through Exercise Biology	15
	<i>Frank W. Booth, PhD; Manu V. Chakravarthy, MD, PhD; and Matthew J. Laye, BS</i>	
	Scope of the Problem	15
	Rationale for Action	16
	Role of Physical Inactivity in Diabetes	18
	New Ammunitions	19
	Future Battle Plans	20
	Concluding Remarks	21
	References	21
Part II	Defects in Metabolism and Insulin Resistance	
Chapter 3	Fatty Acid Uptake and Insulin Resistance	25
	<i>Arend Bonen, PhD; Adrian Chabowski, MD, PhD; Jan F.C. Glatz, PhD; and Joost J.F.P. Luiken, PhD</i>	
	Long-Chain Fatty Acids and Their Uptake Across the Sarcolemma	26
	Fatty Acid Transporters	27
	LCFA Transport and Transporters in Obesity and Type 2 Diabetes	32

	Concluding Remarks	37
	References	38
Chapter 4	Lipid Metabolism and Insulin Signaling	43
	<i>Jason R. Berggren, PhD; Leslie A. Consitt, PhD; and Joseph A. Houmard, PhD</i>	
	Lipid Metabolism in Skeletal Muscle	43
	Insulin Signaling	46
	Does Lipid Exposure Impair Insulin Action?	48
	Perturbations in Substrate Utilization With Type 2 Diabetes and Obesity	50
	The Exercise Paradox	51
	Effect of Weight Loss on Muscle Lipid Accumulation and Insulin Signaling	52
	Concluding Remarks	53
	References	53
Chapter 5	Metabolic Inflexibility and Insulin Resistance in Skeletal Muscle	59
	<i>Bret H. Goodpaster, PhD; and David E. Kelley, MD</i>	
	Substrate Utilization During Rest in Individuals Who Are Lean and Healthy	59
	Substrate Utilization in Individuals Who Are Insulin Resistant	60
	Effects of Weight Loss on Metabolic Flexibility in Obesity and Type 2 Diabetes	63
	Effects of Exercise Training on Metabolic Flexibility in Obesity and Type 2 Diabetes	64
	Concluding Remarks	66
	References	66
Chapter 6	Nutrient Sensing Links Obesity With Diabetes Risk	71
	<i>Sarah Crunkhorn, PhD; and Mary Elizabeth Patti, MD</i>	
	Nutrient Sensing and Control of Food Intake	71
	Cellular Nutrient Sensing	73
	PGC-1 as a Key Effector Responsive to Nutrition in Muscle	78
	Concluding Remarks	79
	References	79
Chapter 7	Inflammation-Induced Insulin Resistance in Obesity: When Immunity Affects Metabolic Control	83
	<i>Phillip James White, MS; and André Marette, PhD</i>	
	Obesity: A Chronic Low-Grade Inflammatory State	83
	Evolution of Inflammation in Obesity	85

	Mechanisms Linking Inflammation to Insulin Resistance in Obesity	89
	AMPK: From a Gauge of Energy Status to a Novel Target for Alleviating Inflammation in Obesity	96
	Concluding Remarks	97
	References	98
Part III Prevention of Type 2 Diabetes Through Exercise Training		
Chapter 8	Transcription Factors Regulating Exercise Adaptation	107
	<i>David Kitz Krämer, PhD; and Anna Krook, PhD</i>	
	Activation of MAPK Signaling	107
	Nuclear Factor of Activated T Cells	110
	Regulation of GLUT4 Expression	110
	Myocyte Enhancer Factor 2 and GLUT4 Enhancer Factor	111
	Mitochondria Biogenesis and Increased Lipid Oxidation	111
	Exercise-Mediated Regulation of PPARs	112
	Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1	113
	Myogenic Development and Adaptation	113
	Concluding Remarks	114
	References	115
Chapter 9	Exercise and Calorie Restriction Use Different Mechanisms to Improve Insulin Sensitivity	119
	<i>Gregory D. Cartee, PhD</i>	
	Effects of Exercise and Calorie Restriction on Skeletal Muscle Energy Status	119
	Insulin Signaling for Glucose Transport	120
	Exercise- and Contraction-Stimulated Signaling Pathway for Glucose Transport	120
	Insulin Signaling and Action After Acute Exercise	121
	Effects of Exercise Training on Insulin Sensitivity and Signaling	124
	Effects of Calorie Restriction Distinct From Weight Loss	127
	Effects of Calorie Restriction on Insulin Signaling in Skeletal Muscle	127
	Combined Effects of Exercise and Calorie Restriction	129
	Concluding Remarks	130
	References	131
Chapter 10	Mitochondrial Oxidative Capacity and Insulin Resistance	135
	<i>Kevin R. Short, PhD</i>	
	Mitochondrial Structure and Function	135
	Evidence of a Role for Mitochondria in Insulin Resistance and Diabetes	135

	Evidence That Mitochondria Are Not Responsible for Insulin Resistance	138
	Concluding Remarks	142
	References	142
Chapter 11	Effects of Acute Exercise and Exercise Training on Insulin Action in Skeletal Muscle	147
	<i>Erik A. Richter, MD, DMSci; and Jørgen F.P. Wojtaszewski, PhD</i>	
	Exercise and Contraction Signaling in Muscle	147
	Insulin Signaling: A Web	150
	Effects of a Single Exercise Bout on Insulin Sensitivity	152
	Effects of Exercise Training on Insulin Action	153
	Concluding Remarks	156
	References	156
Chapter 12	Resistance Exercise Training and the Management of Diabetes	161
	<i>Jørgen F.P. Wojtaszewski, PhD; Henriette Pilegaard, PhD; and Flemming Dela, MD</i>	
	Resistance Training and Insulin Sensitivity	162
	Mechanisms Behind Resistance Training-Induced Improvements in Insulin Sensitivity	166
	Training-Induced Gene Expression	169
	Concluding Remarks	170
	References	170
Part IV	Prevention of Type 2 Diabetes	
	Identification of Novel Molecular Targets and Pathways	
Chapter 13	AMPK: The Master Switch for Type 2 Diabetes?	177
	<i>W.W. Winder, PhD; and D.M. Thomson, PhD</i>	
	Discoveries Suggesting AMPK Could Be Important for Prevention and Treatment of Type 2 Diabetes	177
	Could Type 2 Diabetes Result From a Deficiency in AMPK Signaling?	178
	How Can AMPK Activation Help Prevent Type 2 Diabetes?	179
	Can Chemical AMPK Activation Prevent Diabetes?	181
	Feasibility of Using AMPK Activators	181
	Future Directions	182
	Concluding Remarks	182
	References	183

Chapter 14	Protein Kinase C and Insulin Resistance	187
	<i>Carsten Schmitz-Peiffer, PhD</i>	
	PKC Family of Serine and Threonine Kinases	187
	Roles for PKC in Normal Glucose Homeostasis	189
	PKC and Defective Glucose Disposal	190
	Concluding Remarks	195
	References	196
Chapter 15	Evidence for Prescribing Exercise as a Therapy for Treating Patients With Type 2 Diabetes	203
	<i>Sarah J. Lessard, PhD; and John A. Hawley, PhD, FACSM</i>	
	Options for Treating Insulin Resistance and Type 2 Diabetes	203
	Molecular Evidence for Prescribing Exercise Training	204
	Exercise and Drug Combination Therapy	207
	Exercise-Like Effects of Current Antihyperglycemic Drugs	209
	Prescribing Exercise Training: Practical Considerations	209
	Concluding Remarks	210
	References	211
Index		215
About the Editors		219