

INDEX

- Acetoacetate: *see* Ketone bodies
- Acetyl CoA carboxylase; *see also* AMPK; *and* Fatty acid biosynthesis
AMPK, 4, 5, 55, 57, 79, 96
BRCA1, 55
fatty acid oxidation, 232, 237; *see also* Fatty acid oxidation
“statin” agents, SREBP, 153, 154, 328
- Activator protein-1 (AP-1): *see* Nuclear factor κ B
- Adenine nucleotide translocase (ANT): *see* Mitochondrial energetics, VDAC
- Adenomatous polyposis coli (APC), 27, 30, 31, 33, 84-85, 97, 127, 315-316, 318, 366; *see also* Cancer
colon cancer, 27, 30, 33
glycogen synthase **kinase-3 β (GSK3 β)**: *see* PI3K/Akt/PKB
murine model, ^{Apc^{Min/+}}, 84, 127
PPAR δ , 85
wg/Wnt-like signaling: *see* PI3K/Akt/PKB signaling
- Adenosine diphosphate (ADP), ROS generation and, 147, 158, 285, 290-291, 363
- Adenosine monophosphate (AMP): *see* AMP-activated protein kinase
- Adenosine triphosphate (ATP) generation, stoichiometry, 58-60; *see also* Cell cycle
- Adenylate kinase and AMPK, 94, 96, 367
- Adherens junctions, 92, 306, 316, 366
- Adipocyte fatty acid binding protein (aP2): *see* Fatty acid binding proteins
- Adipose tissue; *see also* Diabetes mellitus; *and* Insulin resistance; *and* Obesity
visceral, 148, 179
- Advanced glycation endproducts (AGE), 147-148, 151; *see also* Hyperglycemia
- Affect: *see* Depression
- Aging, 8, 15, 82, 149, 158, 303, 307, 308, 314, 328, 362, 364
- Agouti-related peptide, 236
- Akt-protein kinase B (Akt/PKB): *see* PI3K/Akt/PKB signaling
- Alternative substrates, 124, 217, 260, 313-314
- Alzheimer disease, 6, 8, 9, 32-33, 155, 208, 225, 267, 277, 280, 303-330, 365; *see also*
Astrocyte; *and* Nicotine; *and* Synaptic function
 β amyloid, 33, 34, 152, 208, 223, 225, 240, 291, 304-306, 314-323, 328-329
cell cycle induction, 319

Alzheimer disease (*cont.*)

- amyloid precursor protein (APP), 306, 316, 317, 320, 323, 329
 - Swedish mutant APP, 306, 323
- apolipoprotein (a), 306
- apolipoprotein E (apoE), 305-306, 328
 - β amyloid and, 306, 320, 323
 - E2, E3 isoforms, 305
 - E4 isoform, 305-306, 308, 322-324
 - effects on neuronal repair, synaptic function, 305
- cerebral metabolism, 309-310
 - citric acid cycle, 305, 310, 311, 314, 316, 317, 319, 324
 - glucose-oxygen dissociation, 314; *see also* Neuronal activation
 - GLUT 3 adducts, 309, 324
 - insulin effects, 309-310
 - ketone body utilization and effects, 303, 309-314, 324, 326, 327, 329, 364
 - 2-oxo-glutarate dehydrogenase, 305, 310
 - regional differences, 310
- cerebrospinal fluid in diagnosis, 304, 308
- cholesterol
 - cholesterol-degrading enzyme, 305
 - risk factor, 309
 - “statins”, 15, 55, 147, 152-154, 328, 330, 367
 - synaptic function, 305
- diabetes mellitus, insulin resistance, 307-309
 - analogous retinal pathology, 308
- fatty acid metabolism, systemic manifestations, potential modulators, 327-330
 - nicotine, 322, 328-329
- insulin-degrading enzyme, 306, 322, 323
- neurofibrillary tangles, 32-33, 304, 306, 317, 318, 322, 324, 329
- PI3K/Akt/PKB, 304, 314-325, 328; *see also* PI3K/Akt/PKB signaling
 - GSK3 β** and, 314-324
 - Li*** effects and depression, 320-321
 - neurofibrillary tangles, 32-33, 304, 306, 317, 318, 322, 324, 329
 - neuronal death and the cell cycle, 319-320
 - presenilins (PS), 31-32, 306, 315-319, 324, 329
 - prion protein (**PrP^{sc}**) interactions, 321
 - τ phosphorylation, 317
 - “truncated” signaling, 316
- ROS, oxidative stress: *see* Reactive oxygen species
 - “vicious cycle” in pathogenesis, 321-326
- 5-Aminoimidazole-4-carboxamide ribonucleoside (AICAR): *see* AMP-activated protein kinase
- α -Amino-3-hydroxy-5-methyl-4-isoxazolepropionate** receptor (AMPA): *see* Synaptic transmission
- AMP-activated protein kinase (AMPK), 4-5, 54, 55, 57-59, 79, 94, 96, 97, 151, 179, 189, 264, 363, 367
 - adenylate kinase, 94, 96, 367
 - AICAR, 96-97
 - apoptosis and, 96-97

- AMP-activated protein kinase (AMPK), (*cont.*)
 fatty acid oxidation, 96-97, 151, 264
 regulation of growth, lipogenesis, 4-5
- Anandamide: *see* Cannabinoids
- Angiogenesis: *see* Hypoxia
- Apolipoprotein (a), 306; *see also* Alzheimer disease
- Apolipoprotein B, 150
- Apoptosis, 85-98, facing p. 85
 Bcl-2 protein family, 88-90
 caspase(s), 28, 34, 77, facing p. 85, 86, 87, 90, 93-96, 98, 125, 126, 144, 188, 239
 caspase 3 targets Akt/PKB, Bcl-2, β -catenin, cytokeratins 8/18, IKK β , p21^{Waf1/Cip1}, 95
 cell cycle and, 95-98
 AICAR, 96-98
 AMPK, 96-98
 carcinogenesis, 97
 hepatitis B and C, 97
 insulin, leptin, 97
 ceramide, 92-94, 144, 188, 239, 292
 ganglioside GD3, 92
 mitochondrial function, 77-98, facing p. 85
 apoptosome, 87
 apoptotic protease activating factor-1 (Apaf-1), 87
 inhibition by Hsp27, 90
 procaspase 9 activation, 87
 intermembrane protein release, 86, 89-90
 cardiolipin, 89
 cytochrome c, 89-90
 PI3K/Akt/PKB, 88-93
 ursodeoxycholic acid, 94, 126
 VDAC/permeability transition pore, 86, 91-92; *see also* Mitochondrial energetics, VDAC
 tumor necrosis factor receptor (TNFR) family, 85, facing p. 85, 86, 93-95; *see also*
 Proinflammatory cytokines
 Fas, Fas ligand (FasL), 85, 86, 92-95
 Fas mediation of butyrate-induced apoptosis, 123
 FasL-independent Fas signaling, 93-95
 AMPK, 94-95
 ATP, ROS, 94
 bile acids, menadione, UVB light, 93-94
 TNFR1, 85, 86
 PI3K/Akt/PKB-mediated signaling, 86, 91, 129, 185, 187, 188, 240, 287
- Apoptotic protease activating factor-1 (APAF-1), 87; *see also* Apoptosis, apoptosome
- Appetite: *see* Feeding behavior
- Arterial hypertension, 154
- Aspirin: *see* NSAIDs, salicylate
- Astrocyte: *see also* Alzheimer disease
 antioxidant defenses, 229, 231, 232, 239, 262, 266, 268, 326
 fatty acid binding protein, α -synuclein expression, 262
 fatty acid oxidation, 207-208, 210, 211, 262-264
 gluconeogenesis, 7, 211-212, 255-258, 324

Astrocyte (*cont.*)

- glutamate, 255, 257, 259-262, 265, 268
- glutamine export, glutamine shuttle, 259-262
- ketogenesis, 6, 155, 208, 211, 212, 263-268, 325, 327, 364
 - cannabinoid effects, 264
- lactate export, 212, 255-258

Atherosclerosis

- ABCA1, 151
- C-reactive protein, 151-153
- CD36 scavenger receptor, 150-151
- cholesterol, 150-153
- endothelial lesion, 150-154
 - fatty acid binding protein (aP2), 151
 - fatty acid oxidation, 147-154
 - leptin, 151
 - trans fatty acids, 8, 144, 150, 151, 157, 362
 - peroxisome proliferator-activated receptors, 82, 84, 151-153; *see also* PPAR α , PPAR γ
- hypolipidemic drugs
 - fibrate peroxisome proliferators, 154
 - “statin” agents, 152-154
 - antiinflammatory, antiproliferative effects, 15, 152-154
 - fatty acid oxidation, 153
 - HMG CoA reductase, 152-153
 - LXR, 55, 92, 152, 154
 - SREBP, 152-154
- oxidized LDL, 149-150

Bipolar disorder: *see* Depression

Brain substrate utilization

- fatty acids: *see also* Feeding behavior
 - adverse effects on astrocyte, neuron, 263-268
 - astrocyte utilization and oxidation, 226-232; *see also* Astrocyte
 - ketogenesis, 6, 208, 211, 230, 263
 - MCFA, SCFA oxidation, 230
 - ROS generation, antioxidant defense, 231, 264-266
 - flow-independent uptake, 213, 226
 - neuronal SREBP, 232
 - PPAR expression and activity, 231
- glucose
 - flow-dependent uptake, 213
 - glucose transporters, GLUT 1, GLUT 3, 218
 - GLUT 3 adducts, 309, 324; *see also* Alzheimer disease, cerebral metabolism
 - glycolysis, 218
 - insulin, insulin receptor, 218, 235, 238, 309, 311, 315, 321, 322, 328
 - suppression by ketone bodies, 221, 222

ketone bodies

- flow-independent uptake, 213, 221, 310
- β -oxidation** in brain, 207, 208, 212, 220-225, 232, 261, 263, 264, 267, 268, 277-279, 282, 292, 309-314, 324, 326, 327

Brain substrate utilization (*cont.*)

- fasting-independent, 220-221
- inhibition of PDH, glycolysis, 222-223
- neuronal energetics, 6, 207, 208, 223-225
- neuronal utilization in preference to glucose, 207, 208, 221-225
- short term neuroprotection, 223-225
- uncoupling, uncoupling-like effects, 122, 123, 129, 208, 211, 222-224, 231, 263, 282, 324
- ROS generation, 208, 222-224, 264-268, 282, 292, 324
- synaptic function, 224-225
- neuroprotection vs. acute insults, 223-225

BRCA1 and acetyl CoA carboxylase, 55

Butyrate

- antiproliferative effects, 121-124, facing p. 123
- apoptosis, 123-124
- β -catenin**, 121
- colonic epithelium, 124
- fatty acid oxidation and ketogenesis, 122-124
- uncoupling, uncoupling-like effects, 122-123, 129, 222-223

C75, 237; *see also* Feeding behavior

E-Cadherin, 29, 32, 121, 125, 315, 318

P-Cadherin, 125

 α -Calcium-calmodulin-dependent protein kinase II (CaMKII), 287Calcium stimulation of mitochondrial dehydrogenases, 61, 287, 288; *see also* Mitochondrial energetics

Caloric restriction, 14, 146, 149, 328

Cancer, cancer cells, 15, 23-27, 29-31, 45, 47, 84, 365-367

cancer cachexia, 15, 47, 50, 52, 61-64

colon cancer

- butyrate, 124
- cell lines, 51, 84, 122, 127
- growth inhibition by MCT, ketone bodies, 49-50
- salicylate, NSAID effects, 127
- transplantable MAC-13/16, host and tumor metabolism, 49, 52, 61, 62
- fatty acid biosynthesis, 53-56

Cannabinoids, 59, 237, 292, 293, 365; *see also* Feeding behavior

cannabinoid receptor CB1, 59, 292

endocannabinoids, 292, 293, 365

anandamide, 292

fatty acid amide hydrolase, 292

tetrahydrocannabinol, 264, 292, 293, 365

Cardiac myocyte

- adverse effects of ketone bodies, 223
- fatty acid oxidation, 7, 58, 96, 97, 125, 151, 154, 232, 234
- TGF β** and mitochondria, 125
- oxidative stress, 154-155

Carnitine palmitoyltransferase-I (CPT-I): *see* Fatty acid oxidation **β -Catenin**; *see also* PI3K/Akt/PKB signaling

butyrate, 121

β -Catenin, (*cont.*)

- caspase 3, 95
- colonocyte, 30, 33, 84, 315
- liver regeneration, 180
- neuron, 32, 33, 306, 315-318, 320
- phosphorylation by **GSK3 β** , 28, 29, 31, 33, 315-320
- transcriptional regulation, 27-35, 92, 315-320
- PPAR γ** , **PPAR δ** , 84-85
- TGF β** , 125
- C. elegans*, 29
- Cell cycle
 - apoptosis and, 95-98, 319-320
 - energy (ATP) demands, 5, 6, 8, 13-15, 22-25, 30-32, 59, 361, 363, 364, 366-367
 - inhibition
 - butyrate, 121-122
 - cyclin-dependent kinase inhibitors
 - Cip/Kip family (**p21^{Waf1/Cip1}**, **p27^{Kip1}**), 29-30, 95-98, 366
 - p15^{INK4b}**, 29
 - p16^{INK4}**, 121
 - Forkhead transcription factors, 29
 - salicylate, NSAIDs, 127
 - TGF β** , 125
 - PI3K/Akt/PKB signaling, 27-31; *see also* PI3K/Akt/PKB signaling
 - inhibition by fatty acids, 31, 83, 86, 144, 145
 - ROS, 33-35
- Cell proliferation; *see also* Cell cycle; *and* Hypoxia; *and* Mitochondrial energetics
 - hypoxic, 14, 19, 26, 27, 30, 34-35, 50, 77, 81, 91, 93, 128, 158, 264, 361-363
 - requirements for model, 14-16
 - substrates
 - aerobic glycolysis and citric acid cycle, 14, 16, 20-23, facing p. 21, 25, 26, 32, 35, 55-58
 - fatty acids, 53-57
 - exclusion of fatty acid oxidation, 19, 59, 81-83, 144-145, 160, 181-184
 - fatty acid biosynthesis, 53-55
 - liver fatty acid binding protein, 49
 - PPAR α** , 81-83
 - glutamine, glutamate, 58, 124, 148
 - sterols, isoprenoids, 55-56, 363
- Ceramide, 92-94, 144, 188, 239, 292
- Cholesterol: *see* Alzheimer disease; *and* Atherosclerosis
- Citric acid cycle (tricarboxylic acid cycle): *see* Cell proliferation, substrates; *and* Mitochondrial energetics
 - effect of ω -3 fatty acids, 53
 - NSAIDs, 127, 129-131
 - PPAR γ** and **PPAR δ** , 84-85
- COX: *see* Cyclo-oxygenase
- CPT-I (Carnitine palmitoyltransferase-I): *see* Fatty acid oxidation
- Crabtree effect, 27, 148; *see also* Hyperglycemia
- C-reactive protein (CRP), 151-153; *see also* Atherosclerosis

- Cyclin D and PI3K/Akt/PKB, 28-30, 156
- Cyclo-oxygenase (COX, prostaglandin G/H synthase), 28, 53, 84, 85, 187, 240, 289; *see also* NSAIDs
- Cytochrome c: *see* Apoptosis, mitochondrial function; *and* Mitochondrial energetics
- Cytokeratins 8 and 18; *see also* Fatty acid oxidation, regulation of CPT-I
AMPK and CPT-I regulation, 54, 57-58, 95
caspase 3, 95
heat shock proteins, 156, 157
- Cytokines: *see* Proinflammatory cytokines
- Dementia: *see* Alzheimer disease; *and* HIV, dementia
- Depression, 239, 320-321, 365
- Docosahexaenoic acid (22:6, ω -3) (DHA): *see* Fatty acids
- Diabetes mellitus, 48, 80, 81, 126, 154, 155, 306, 362, 364
atherosclerosis, 147, 148, 150, 152
brain, 208, 224, 239, 307-310, 313, 323, 324, 327, 329, 362
cancer cachexia, 62, 366
diffuse organ injury, 126, 154, 155, 362, 365
plasma FFA and insulin resistance, 6, 8, 83, 143-148, 154, 208, 239, 264, 279, 292, 310, 324, 327, 329, 362-365
- Dicarboxylic fatty acids: *see* Fatty acids
- Eicosanoids, 14, 47, 53, 55, 57, 64, 80, 84, 127, 131, 179, 187, 269, 289
- Eicosapentaenoic acid (20:5, ω -3) (EPA): *see* Fatty acids
- Electron "leakage" and ROS generation: *see* Mitochondrial energetics; *and* Reactive oxygen species
- Electron transport chain: *see* Mitochondrial energetics
- Endothelium: *see* Atherosclerosis, endothelial lesion
- Enterocyte, 32, 148, 150, 260
- Epidermal growth factor (EGF), 22, 25, 28, 30, 32, 61, 127, 177
- Epithelial restitution, 32, 361
- Estrogens, 317, 325, 330
- Ethanol, protective effects, 156-157, 309, 325, 330
adverse effects, 94, 147
- Excitotoxicity: *see* Synaptic Transmission
- Extramitochondrial fatty acid oxidation: *see* Fatty acid oxidation
- Familial adenomatous polyposis (FAP): *see* Adenomatous polyposis coli (APC)
- Fas, FasL: *see* Apoptosis
- Fatty acid amide hydrolase, 292; *see also* Cannabinoids
- Fatty acid binding proteins (FABP), 81, 226, 231-233, 262, 292
adipocyte lipid binding protein (ALBP, aP2), 82, 151, 185, 238
astrocyte expression (brain, heart, keratinocyte, liver isoforms), 262
brain isoform (B-FABP), 233, 262
cutaneous isoform (C-FABP), 53
heart isoform (H-FABP), 262
keratinocyte isoform (K-FABP), 262
liver isoform (L-FABP), 49, 78, 180, 185, 262
cell proliferation, 49, 180, 185
 ω -6 fatty acids, 49

Fatty acid binding proteins (FABP), (*cont.*)

PPAR α , 78, 180

Fatty acid biosynthesis, 4, 20, 22, 25, 55, 78, 152-154, 232, 258, 363; *see also* Acetyl CoA carboxylase; *and* Lipogenesis

fatty acid synthase (FAS), 49, 53, 153, 237

Fatty acid oxidation; *see also* AMPK; *and* Brain substrate utilization; *and* Feeding behavior; *and* Reactive oxygen species; *and* **PPAR α**

adverse effects, various tissues, 143-160

cell growth, 5, 47, 49, 51, 53-55, 57-59, 62, 77, 361

growth inhibitor effects, 121, 123, 125-130

interaction with Bcl-2, 91

liver regeneration, 180-182, 184-189

mitochondria, carnitine palmitoyltransferase-I (CPT-I)-mediated, 7-8, 21-22

fatty acid override of, 21, 59, 83, 144, 145, 148, 181-182, 186, 212, 231, 238, 239, 362

long chain fatty acids, 20, facing p. 21, 22

medium, short chain fatty acids, 57; *see also* Fatty acids

ω -3 fatty acids, 51, 52, 57

regulation of mitochondrial fatty acid oxidation

activation by AMPK, 57, 58, 94

cytokeratins 8/18 (malonyl CoA-independent), 54, 57, 58, 95, 156, 157, 187

inhibition by fibrate peroxisome proliferators, 13, 49, 78, 80-82, 94, 151, 154, 180, 185

leptin, 58

malonyl CoA-dependent, 20, 22, 51, 54, 57, 58, 92, 154, 185, 186, 228, 232, 237, 238, 328, 363

malonyl CoA decarboxylase, 59

peroxisomes, **β -oxidation**, 7, 8, 51-52, 54, 78-80, 83, 144, 182

ROS generation, 54, 83, 144, 148, 150, 151, 155, 182, 264, 362

smooth endoplasmic reticulum, **ω -oxidation**, 78-80, 144, 148, 180, 182, 232

Fatty acids

adverse effects on mitochondrial function, 143-145

cell growth, 47-64

dicarboxylic fatty acids, **PPAR α -induced** peroxisome proliferation, 78, 180, 232

medium chain fatty acids (MCFA), 49, 57, 79, 143, 230

oleic acid, 262

omega-3 (**ω -3**) unsaturated fatty acids

brain, 262, 286, 327

cell growth, 15, 47, 52-53, 57, 160, 187, 361, 367

metabolic effects, 6, 51-52

antioxidant, uncoupling effects, 6, 15, 51, 53, 129, 131, 144, 152

fatty acid oxidation, 6, 47, 51-52, 143, 145

glycerolipid/lipoprotein synthesis, 51-52

omega-6 (**ω -6**) unsaturated fatty acids, 47-50, 55, 57

brain, 262, 327

cell growth, 47-50, 52, 53, 55, 57, 179, 180, 187, 189, 361

metabolism, 51, 52

ROS generation, 48, 55, 57

PI3K/Akt/PKB activation, 48

saturated fatty acids, 49, 144, 309

- Fatty acids, (*cont.*)
short chain fatty acids (SCFA), 50, 57, 230, 318, 319, 361; *see also* Butyrate
trans fatty acids, 8, 144, 150, 151, 157, 362
- Feeding behavior, hypothalamic regulation, 6-7, 233-237, 365; *see also* Cannabinoids
cannabinoids, 237
fatty acid oxidation, 233-236
fatty acid synthase and C75, 237
leptin and insulin effects, 234-236
relationship to plasma [FFA], 234-235
- Fibrate hypolipidemic agents: *see* Atherosclerosis; and Fatty acid oxidation, CPT-I; and
PPAR α
- Forkhead transcription factors, 28, 29, 33, 34, 84, 93, 158
- Free (unesterified) fatty acids (FFA); *see also* Diabetes mellitus; and Fatty acid oxidation,
CPT-I override; and Human immunodeficiency virus; and Insulin resistance
advanced glycation products, 147-148, 151
brain: *see* Brain substrate utilization
effects in various tissues, 143-160
endothelial lesion of atherosclerosis, 148-154
nicotine, 148, 155, 239, 328, 329, 365
visceral adipose tissue, 148, 179
- Fructose-2,6-bisphosphate (-phosphatase) [F2,6BP(ase)], 20, 21, 25; *see also*
Gluconeogenesis; and Glycolysis
- Gamma-aminobutyric acid (GABA)
mitosis, 319
neurotransmission, 259, 262, 282, 284, 319
- Germ-free animals, 124, 185
- Glia: *see* Astrocyte
- Gluconeogenesis, 7, 21, 22, 145-148, 313; *see also* Astrocyte
cancer cachexia, 50, 62, 64
growth regulatory factor effects, 25, 126
kidney, 7, 62, 64, 179, 182
liver regeneration, 16, 50, 177-182, 184, 187, 189
- Glucose transporters (GLUT 1, 3, 4), 23, 30, 34, 55, 218, 309, 324, 366
ROS-induced GLUT 3 adducts, 309, 324
- Glutamate; *see also* Synaptic transmission; and Mitochondrial energetics, VDAC
impairment of cystine uptake and glutathione balance, 91, 283, 285-286, 288-289
neurotransmission, 256, 259, 282-293
postsynaptic neuronal uptake: *see* Synaptic transmission
respiratory substrate and source of ROS, 54, 124, 148; *see also* Cell proliferation,
substrates
ROS inhibition of uptake by astrocyte, 265
- Glutamine and intestinal epithelium, 124; *see also* Astrocyte
- Glutamine export, shuttle: *see* Astrocyte
- Glutathione and apoptosis, 91
- Glycogen storage disease, type I, 13, 14, 189
- Glycogen synthase **kinase-3 β (GSK3 β)**: *see* PI3K/Akt/PKB signaling
- Glycolysis
aerobic, and cell proliferation, 14, 16, 20, facing p. 21, 23, 25, 26, 32, 35, 55-58
anaerobic, 20

Glycolysis, (*cont.*)

neuronal activation, 209, 210, 212-214, 218

GSK3 β (Glycogen synthase **kinase3 β**): *see* PI3K/Akt/PKB signaling

Heart: *see* Cardiac myocyte

Heat shock factor (HSF1), 156

Heat shock proteins (Hsp27, Hsp70, Hsp90)

attenuation of **TGF β** effect (Hsp70), 157

induction by ethanol, thermal stress (Hsp27, Hsp90), 156-157

inhibition of apoptosis (Hsp27, Hsp90), 90

interaction with intermediate filaments (Hsp27, Hsp90), 156

ischemic preconditioning (Hsp27, Hsp90), 156

stabilization of Akt/PKB (Hsp27, Hsp90), 34, 93, 156, 157

Hep G2 cells, 53, 153

Hepatectomy: *see* Liver regeneration

Hepatic tumors, 127; *see also* Glycogen storage disease, Type I

Hepatitis: *see* Apoptosis, cell cycle; *and* Nonalcoholic steatohepatitis

Hepatocellular carcinoma, 28, 62, 79, 155

Hepatocyte growth factor (HGF)

activation of adipocyte lipolysis, 55, 177-178

glycolysis, 25

liver regeneration, 177

PI3K/Akt/PKB, 28, 31, 55, 89

SREBP signaling, 55

Hexokinase

glycolysis, 20, 23

hexokinase II, 23; *see also* Mitochondrial energetics, membrane contact sites, VDAC

activation by PI3K/Akt/PKB, 27, 30, 89, 92, 157

cell proliferation, 23-27, 30, 366

HIF1 α activation, 26

inhibition of Bax-induced cytochrome c release, 24, 27, 89

neuronal activation, 209-211, 213, 216, 218-219

VDAC, 22-24, 218-219

fatty acid-induced dissociation, 59-60, 144

kinetic advantages, 24

Hexose monophosphate shunt (pentose phosphate pathway), 20, 22, 25, 158, 184, 239, 255, 313

Hippocampus, 228, 306, 310

HMG CoA reductase: *see* **β -hydroxy- β -methyl-glutaryl** CoA reductase

Human immunodeficiency virus (HIV) infection, 94, 240

apoE4, Alzheimer disease, 306, 327, 330, 365; *see also* Alzheimer disease, apoE dementia, 208, 267-268

proinflammatory cytokine activation, 267-268; *see also* Liver regeneration, proinflammatory cytokines

fatty acid metabolism, 6, 8, 9, 144, 145, 208, 238, 239, 264, 267-268, 279-280, 292, 365

Hydrogen peroxide (**H₂O₂**): *see* Reactive oxygen species (ROS)

β -Hydroxy-butyrate: *see* Ketone bodies

β -Hydroxy- β -methyl-glutaryl CoA reductase (HMG CoA reductase), 57, 152-153

4-Hydroxynonenal (HNE), 324

- Hypercholesterolemia: *see* Alzheimer disease, cholesterol; *and* Atherosclerosis, cholesterol
- Hyperglycemia, 126, 147, 148, 151, 155, 310
 advanced glycation endproducts (AGE), 147-148, 151
 Crabtree effect, 27, 148
- Hypoxia, 14, 19, 26, 27, 34-35, 50, 77, 81, 91, 93, 158, 181, 264, 291
 angiogenesis, 26, 34, 59, 84, 361
 hypoxia-inducible **factor-1 α /aryl** hydrocarbon nuclear translocator (**HIF1 α /ARNT**), 26-27, 34-35, 81, 93, 158, 362
 ROS activation of PI3K/Akt/PKB, 34, 128, 362, 363
 vascular endothelial growth factor (VEGF), 34, 93, 362, 366
 von Hippel-Lindau (VHL) protein, 34-35
- Insulin, 6, 8, 28, 129, 362, 364, 365; *see also* Diabetes mellitus; *and* Feeding behavior; *and*
 Insulin resistance
 apoptosis, 89, 97
 brain, 218, 222, 223, 234-236, 238, 239, 255, 264, 279, 287, 292
 Alzheimer disease, 306-311, 313-318, 320-324, 327-330
 cancer cachexia, 62, 63
 growth regulation, 22, 25, 27, 28, 30-34, 48, 49, 51, 54, 55, 57, 58, 81, 83, 160
 liver regeneration, 177, 179, 180, 182, 185-189
 contrast with **TNF α** , 187, 189
- Insulin-degrading enzyme (IDE) and Alzheimer disease, 306, 322, 323
- Insulin-like growth factor-1 (IGF-1), 27, 28, 30, 94, 188, 218, 317
 IGF-2, 62
- Insulin receptor, 25, 185, 188, 218, 235, 238, 309, 311, 315, 321, 322, 328
- Insulin receptor substrate-1 (IRS-1), 23, 28, 30, 89, 315, 316, 321
 expression in early hepatocellular carcinoma, 25
 PI3K/Akt/PKB signaling, 28, 30, 89, 315, 316, 321
- Insulin resistance; *see also* Alzheimer disease; *and* Diabetes mellitus; *and* Obesity
 plasma FFA, 6, 8, 144, 145, 147, 148, 152, 154, 208
 visceral adipose tissue, 148, 179
- Insulin secretion, 14, 27, 62, 154, 155, 364
- Interleukin-1, -6 (IL-1, -6): *see* Proinflammatory cytokines
- Intermediate filaments: *see* Cytokeratins 8, 18
- Ischemia/reperfusion injury, 8, 15, 86, 155-157, 362
- Ischemic preconditioning, 156, 157, 362
- Islet cell: *see* Pancreatic islet β cell
- Isoprenoids (farnesyl-, geranyl-geranyl-pyrophosphate), 22, 55, 57, 64, 152-154, 158, 232, 366
- Ketogenesis: *see* Ketone bodies
- α -Ketoglutarate**: *see* Cell proliferation, substrates; *and* 2-Oxoglutarate; *and* Synaptic transmission
- Ketone bodies (acetoacetate, **β -hydroxybutyrate**); *see also* Alzheimer disease, cerebral metabolism; *and* Astrocytes; *and* Brain substrate utilization
 cell proliferation, 48-50, 123, 130, 145, 268
 ketogenesis, 21, 83
 decrease in regenerating liver, 50, 181, 185
 mitochondrial fatty acid oxidation, 6, 21, 22, 58, 59, 121, 123, 126, 130, 145, 211, 230, 263

Ketone bodies (*cont.*)

mitochondrial oxidation

ROS, oxidative stress generation, 123, 129, 208, 222-224, 264-268, 282, 292, 324
 uncoupling, uncoupling-like effects, 122, 123, 129, 208, 211, 222-224, 231, 263, 282, 312, 324

Kupffer cells: *see* Macrophages

Lactate

astrocyte gluconeogenesis, export, 255-259
 glycolysis, 7, 20, 25, 26, 209, 213, 214, 218
 ketone body inhibition of hepatocyte uptake, 256
 neuronal uptake, utilization, 212, 224, 256, 278, 326

Leptin, 7, 58, 97, 151, 234-237, 365; *see also* Feeding behaviorLipid-mobilizing factor (LMF), 52, 61-62; *see also* Cancer, cancer cachexiaLipogenesis; *see also* Fatty acid biosynthesis

cancer cachexia, 49, 64
 cell proliferation, 4, 5, 20-22, 53-56, 77, 78, 81, 92, 158, 185-187, 238, 363
 fatty acid oxidation, 22, 58, 232
 SREBP regulation, 55-56, 92, 152-154, 232
 suppression by AMPK, 4, 57, 58
 suppression by ω -3 fatty acids, 51

Lipotoxicity, 144, 155

Lithium (**Li**^{*}), 6, 19, 33, 92, 208, 290, 314, 320-323, 325, 330, 365

Liver regeneration, 14-16, 177-189, 364

adipocyte lipolysis, plasma FFA, 177

 ω -6 fatty acids, 180

visceral adipose tissue, 179

cancer cachexia, comparison, 47, 50, 63-64

counterregulatory hormones, plasma glucose, and insulin, 177

fatty acid oxidation

extramitochondrial oxidation, 180, 182

ketogenesis, 181

mitochondrial, 180-184

PPAR α , 180, 182

gamma-aminobutyric acid (GABA), 319

gluconeogenesis, liver and kidney, 178-180

glycolysis, 180

liver fatty acid binding protein (L-FABP), 49, 180

mitochondrial energetics and redox balance, 181-187

uncoupling protein-2, 129, 187

mitosis, acinar gradient, 78

DNA synthesis, 184

NF κ B, 187-189

nitric oxide synthase (NOS), 188

proinflammatory cytokines, 78, 184-188, 239

TNF α vs. insulin, 187, 189

steatosis, 184

TGF β , 60

Liver transplantation, 182, 184

- Liver X receptor (LXR), 55, 92, 152, 154
- Long-term potentiation (LTP): *see* Synaptic transmission
- Low density lipoprotein (LDL), 55, 149-153, 267, 305
- LRP: LDL receptor-related protein, 305
- LXR: *see* Liver X receptor
- MAC-13, MAC-16: *see* Cancer, colon cancer
- Macrophages
 - atherosclerosis, 149-154
 - brain, 267-268
 - endothelial, adipocyte fatty acid binding protein (aP2), 82
 - ω -3 fatty acid uncoupling effect, 51
 - ICAM, scavenger receptor expression, 51
 - Kupffer cell **NF κ B** activation, cytokine secretion, 78, 82, 184, 185, 364
 - mitochondrial ROS and UCP expression, 82, 156
 - PPAR expression: *see* PPARs
- Malic enzyme, 78, 258
- Malonyl CoA; *see also* Acetyl CoA carboxylase
 - decarboxylase, 57, 59, 144
 - inhibition of CPT-I, 20, 22, 51, 63, 92, 144, 363
 - AMPK vs., 54, 56-59, 79
 - atherosclerosis, 153-154
 - brain, 228, 232, 237-238, 328
 - liver regeneration, 181, 185-186
- Medium chain fatty acids (MCFA): *see* Fatty acids
- Medium chain triacylglycerols (MCT), antiproliferative effect, 49-50
- Melanocortin, 236
- Mesenteric adipose tissue: *see* Adipose tissue, visceral
- Metabolic syndrome, 152
- Mitochondrial energetics, 21-22, facing p. 21, 24
 - calcium stimulation of mitochondrial dehydrogenases, 61, 287, 288
 - electron transport chain, 21-22, facing p. 21, 24
 - electron "leakage" and ROS generation, 59, 127-130; *see also* ROS
 - inner membrane potential ($\Delta\Psi_m$), 21, facing p. 21, 24
 - membrane contact sites, 23, 24, 59-60, 89, 144, 218-220
 - oxidative phosphorylation, 21
 - Alzheimer disease, 304, 310, 311, 314, 316, 317
 - cell proliferation, 22-26
 - cytoplasmic diffusion barriers, 23
 - uncoupling, and uncoupling proteins, 6, 14, 22, 49, 51, 53, 59, 62, 82, 83, 123, facing p. 123, 127, 129-131, 144, 154-155, 157, 159, 181, 211, 222, 223, 231, 233, 240, 286, 289, 290, 362, 367
 - uncoupling-like effects, 122, 123, 129, 208, 211, 222-224, 231, 263, 282, 324
 - voltage-dependent anion channel (VDAC), 23-27, 59-60, 89, 218-220
 - components and structure, 23, 24; *see also* Hexokinase II
 - adenine nucleotide translocase (ANT), 23, 24, 59, 219
 - disruption by fatty acids, 59-60, 89, 144
 - modulation by glutamate, 219-220, 284, 291
 - permeability transition pore opening by fatty acids, 59-60, 89, 144

Mitogen-activated protein kinase (MAPK), 81, 317

- Monocarboxylate carrier, 221, 224
 Muscarinic acetyl choline receptor, 305, 328
- NAD(P), NAD(P)H: *see* related processes
 NADPH oxidase and ROS, 34, 154
 Neural progenitor cells, 268-269
 Neuritic plaques, 304, 305
 Neurodegenerative disease, 6, 15, 149, 239, 267, 280, 291, 292, 307, 308, 321, 322, 328, 330, 362, 365
 Neuronal activation, 6, 8, 31, 32, 207-215; *see also* Alzheimer disease; *and* Brain substrate utilization
 energetics, 207-214
 oxidative phosphorylation, 214, 218, 304, 310, 311, 314, 316, 317
 glucose utilization and citric acid cycle, 207-214, 218-220
 ketone bodies, 220-225
 cerebral blood flow (CBF) and glucose uptake, 207, 208, 213; *see also* Alzheimer disease
 glucose-oxygen dissociation, 208, 225, 278-279, 314
 substrate efficiency, 278, 314
 Neuropeptide Y, 236, 237
NFκB: *see* Nuclear factor κB
 Nicotine, nicotine receptor, 148, 155, 239, 322, 328-329, 365; *see also* Alzheimer disease
 N-methyl-D-aspartate (NMDA), 282, 286-290, 292; *see also* Synaptic transmission
 Nitric oxide (NO), 86, 94, 125, 158, 182, 187, 188, 213, 239, 240, 266, 313
 Nitric oxide synthase (NOS), 57, 86, 125, 129, 131, 187, 188, 238-240, 289
 Nonalcoholic steatohepatitis, 15, 94, 150, 155
 Nonsteroidal antiinflammatory drugs (NSAIDs), 14, 85, 93, 121, 127-131, 143, 145, 160, 320, 325, 328, 330
 antiproliferative effects, 127-131
 colon tumors, 127
 COX2, eicosanoid independence, 127, 129-131, 320, 325
 insulin, 129
 mitochondrial effects, facing p. 123, 127-131
 electron transport chain inhibition, 130
 uncoupling, antioxidant effects, 127-131
 NFκB and AP-1 activation, 128-131
 salicylate, 15, 121, 127-131, 145, 240, 290, 325, 367
 sulindac, 130
 Nuclear factor κB (**NFκB**)
 activation by **TNFα**, 86, 187, 188
 AP-1, 34, 48, 129
 excitotoxicity, 289, 290
 liver regeneration, 187-189
 ROS, 34, 48, 51, 82, 94, 126, 129-131, 152, 157, 158
 salicylate, 129-130, 290
 survival/protective effects, 28, 34, 129, 199
 neuroprotection, 240, 325, 362
TGFβ, 125

- Obesity, 6, 8, 31, 83, 143-145, 148, 150-152, 154, 155, 185, 208, 235, 237-239, 264, 279, 288, 292, 327-329 365; *see also* Adipose tissue, visceral; *and* Diabetes mellitus; *and* Insulin resistance
- Oxaloacetate, 256, 258, 259
- Oxidative phosphorylation: *see* Mitochondrial energetics
- Oxidative stress: *see* Reactive oxygen species (ROS)
- Oxidized LDL: *see* Atherosclerosis
- 2-Oxo-glutarate, 26, 35, 58, 124, 146, 148, 259, 278, 284, 285, 289, 291; *see also* Cell proliferation, substrates; *and* Mitochondrial energetics; *and* Synaptic transmission
- 2-Oxo-glutarate dehydrogenase (2-OGDH), 61, 83, 305, 310
- Oxysterols, 55, 152
- P450 2E1, 182
- P450 4A, 78, 180, 182, 232
- P450 4X1, 232
- p53, 26-28, 90-93; *see also* Apoptosis, mitochondrial function
 apoptosis, 26, 27, 90-93, 96, 97, 121, 125, 319, 320, 366
 cell cycle, 90-93, 96, 97, 121, 125, 319, 366
 mitochondria, 90-93, 145
 telomerase, 91-93
- Pancreatic islet β cell, 14, 27, 154, 155, 234, 235, 364
- Pentose phosphate pathway: *see* Hexose monophosphate shunt
- Peroxisome proliferator-activated receptor α , γ , δ (β) [PPAR α , γ , δ (β)
PPAR α , 78-83, 92, 122
 activator ligands, 49, 78-83, 130, 151, 180, 232
 antioxidant effects, 77, 81-83, 145
 apoptosis, 79-80, 94
 atherosclerosis, 82, 84, 151, 153
 COX2, prostaglandins, NSAIDs, 130-131
 dicarboxylic fatty acids, 78, 180, 232
 fatty acid oxidation, 51, 55, 63, 78-83, 92, 122, 145, 159
 peroxisomes and SER, 7, 8, 51, 52, 59, 63, 78, 80, 83, 122, 144, 148, 150, 151, 155, 182, 230-232, 266, 362
 mitochondrial ROS generation, 145-148; *see also* Fatty acid oxidation, mitochondria; *and* Mitochondrial energetics
 fibrates and rodent hepatocarcinogenesis, 78, 79
 contrasts vs. regeneration, 78, 82
 hepatocyte proliferation, liver regeneration, 13, 54, 78-83, 180, 182
 human liver, 83
 hypoxia, 81
 L-FABP, 180
 MAPK, 81
NF κ B, 188
 SREBP, 55
 tissue and macrophage expression, 82, 84, 231, 268
 absence from human astrocytes, 231, 264, 268, 327
 absence from Kupffer cells, 82
 arterial endothelium, 82
TNF α , 82, 186
 transcriptional regulation, 78-83

Peroxisome proliferator-activated receptors (*cont.*)**PPAR γ** , 84-85

activator ligands

fatty acids, 84

PPAR γ -independent effects, 85, 291

15dPGJ2, thiazolidinediones, 85

antiproliferative, differentiating effects, 84

antitumor effects, 84-85

induction by butyrate, NSAIDs, **TGF β** , 84, 122, 125, 126, 130

atherosclerosis, 84, 151-153

PPAR γ -coactivator-1 α (PGC-1 α), 155

tissue expression, 84, 231

PPAR δ (β), 85, 131, 231Peroxisome proliferators: *see* **PPAR α**

Peroxynitrite (ONOO), 158, 239, 313

Phosphatase and tensin homolog deleted on chromosome ten (PTEN): *see* PI3K/Akt/PKB signaling, PTENPhosphatidyl-inositol-3-kinase (PI3K): *see* PI3K/Akt/PKB signalingPhosphoenolpyruvate carboxykinase (PEPCK): *see* Gluconeogenesis

Phosphofructokinase-2 (PFK2), 25, 30, 180

Phosphoinositide-dependent kinase-1 (PDK1), 27, 31

Phospholipase A2, 151, 289, 328

PI3K/Akt/PKB signaling (wg/Wnt-like signaling); *see also* **β -Catenin**

Alzheimer disease, 304, 314-325, 328

APC, 30, 31, 33, 315, 316, 318, 366

axin, 30, 31, 315, 316, 318

Bcl-2 family, 88-93

epithelial restitution, 32-33

epithelial-to-mesenchymal transition, 125

GSK3 β , 27-33

HSF1 activation, 156, 158

inhibition of

caspase 3, 95

butyrate, 121

fatty acids, 31, 83, 86, 144, 155, 188

p53, 90-93

PTEN, 27, 28, 31, 48, 90, 97, 269, 366

TGF β , 125-126leptin, 236: *see also* Feeding behaviorlithium (**Li $^+$**), 6, 19, 33, 92, 208, 290, 314, 320-321, 325, 330, 365neuronal activation and synaptic function, 6, 207, 285, 287-288, 290, 292, 304, 316, 317, 324, 325, 328; *see also* Cannabinoids

nicotine, 155, 322, 328-329

proliferative and survival effects, 5, 6, 15, 27-35, 48, 54, 55, 86, 90-94, 155-158, 182, 240, 269, 313-321, 361-364, 366

signaling by CD40, EGF, HGF, IGF-1, Wnt, 30-31

TNF α , 86, 91, 187, 188, 364

ROS activation of, 33-35, 158, 362, 363

stabilization by Hsp27 and Hsp90, 93, 157

- PI3K/Akt/PKB signaling, (*cont.*)
 telomerase, 90-93
- Placenta, 14, 26, 365
- Porin: *see* Mitochondrial energetics, VDAC
- Portal hypertension, 230
- Pre-eclampsia, 365
- Presenilin 1, 2 (PS1, 2), 31-32, 306, 315-319, 324, 329
- Prion protein (PrP): *see* Alzheimer disease, PI3K/Akt/PKB
- Procaspase(s): *see* Apoptosis
- Programmed cell death: *see* Apoptosis
- Proinflammatory cytokines; *see also* Apoptosis; *and* Human immunodeficiency virus infection; *and* Liver regeneration
 brain, 237-240, 267-268
 interleukin-1 (IL-1), 78, 184, 185, 237-239, 340
 interleukin-6 (IL-6), 78, 184, 185, 237-239
 tumor necrosis factor (**TNF α**), 28, 29, 31, 55, 61-63, 78, 82, 85, facing p. 85, 86, 89, 91, 92, 95, 129, 145, 157, 160, 184-189, 237-240, 287, 291, 317, 328, 364
TNF α receptor (TNFR), 31, 85, 86, 91, 129, 185, 187, 188, 240, 287
 PI3K/Akt/PKB, 86, 91, 187, 188, 240, 287
- Prostaglandins (PG), 52, 53, 83, 85, 127, 130, 131
 PGD, PGE, 52, 53, 130, 131
 15-deoxy-delta-12,14-PGJ2, 83, 85
- Protein kinase A (PKA), 151, 287
- Protein kinase C (PKC), 31, 53, 60, 317
- Proteolysis-inducing factor (PIF), 61-62
- p53-upregulated modulator of apoptosis (PUMA): *see* Apoptosis, Bcl-2 family
- Pyruvate carboxylase (PCB), 256, 258, 259
- Pyruvate dehydrogenase (PDH), 20, facing p. 21, 22, 28-30, 32, 33, 62, 81, 83, 91, 120, 122, 124, 130, 144, 145, 148, 180, 182, 209, 212, 220, 222, 223, 231, 256, 261, 263, 264, 279, 281, 282, 284, 292, 310, 311, 314, 317, 318, 323-325
- Pyruvate kinase (PK), increased activity in human cancers, 25, 180, 366
- Randle cycle, 211, 223
- Reactive oxygen species (ROS), hydrogen peroxide (**H₂O₂**), and superoxide anion (**O₂⁻**); *see also* Hypoxia; *and* Mitochondrial energetics
 beneficial/protective effects of low level transient ROS, 8, 19, 33-35, 156-159, 362-364
 ethanol, ischemic preconditioning, heat stress, 156-157
 ROS at peak mitochondrial energization, 158-159
- oxidative stress, injurious effects, 362-365
 apoptosis, 89-91, 94, 96, 124
 atherosclerosis, 149-154
 brain and Alzheimer disease, 208, 212, 220, 224, 231, 233, 234, 238, 240, 264, 265, 267, 268, 279, 282, 284-287, 289-291, 303, 304, 310-313, 319, 322-324, 327, 328
 glutamate, glutamine, 148
 hyperglycemia and, 147-148
 Crabtree effect, 27, 148
 ischemia/reperfusion injury, 8, 15, 86, 155-157, 362
 mitochondria, 77, 82, 127-131, 145-148
 cardiac myocyte, 154-155
 fatty acids, 5, 7, 8, 14, 22, 48, 55, 57, 83, 144, 148-149

- Reactive oxygen species, (*cont.*)
- hepatocarcinogenesis, 155
 - liver regeneration, 181, 182, 187
 - mitigation by uncoupling, 51, 82, 123, 129-131, 240
 - nonalcoholic steatohepatitis, 155
 - pancreatic β cell, 154-155
 - pathological consequences, 149-160
 - plasma FFA, in obesity, insulin resistance, type II diabetes mellitus, HIV, 144, 145, 148; *see also* Diabetes mellitus; *and* HIV; *and* Insulin resistance; *and* Obesity
 - peroxisomes, 83, 144
 - pyruvate, 147
 - TGF β , 125-126
- Retinal neurodegeneration in diabetes mellitus, 308; *see also* Alzheimer disease
- Retinoblastoma protein (pRb), 96, 122, 189
- Retinoid X receptor- α (RXR α), 78, 84
- Rho/Ras/Raf, 153 (Raf), 153 and 287 (Ras), 193 (Rho)
- ROS: *see* Reactive oxygen species
- Saccharomyces cerevisiae (S. cerevisiae), 3, 4, 14, 23, 57, 189
- Secretase (α , β , γ), 306, 317, 320, 323, 325
- Short chain fatty acids (SCFA): *see* Fatty acids
- Smads, 93, 125
- Smoking: *see* Nicotine
- Smooth endoplasmic reticulum (SER); *see also* Atherosclerosis, oxidized LDL
- redox conditions, 149-150
 - fatty acid oxidation, 78, 144; *see also* Fatty acid oxidation
- SNF1, 4, 5, 57, 189
- Sterol regulatory element binding protein (SREBP), 28, 55, 90, 92, 152-155, 232, 328, 366
- “Statin” hypolipidemic agents: *see* Acetyl CoA carboxylase; *and* Alzheimer disease, cholesterol; *and* Atherosclerosis, hypolipidemic drugs
- Streptozotocin, 23, 48, 147, 309, 324
- Superoxide anion (O₂⁻): *see* Reactive oxygen species
- Superoxide dismutase (SOD), 29, 128, 145, 151, 182, 266, 286, 325
- Synaptic transmission, 282-293; *see also* Glutamate; *and* Mitochondrial energetics
- glutamate removal from synaptic cleft, 282-285
 - augmented neuronal exposure to glutamate, 285-293
 - long-term potentiation, 285-288
 - AMPA expression, 282, 286-288
 - excitatory postsynaptic current (EPSC), 286, 287
 - PI3K/Akt/PKB, 287-288
 - excitotoxicity, 288-293
 - neuroprotection, 289-293
 - ketone body and cannabinoid effects, 292-293
- Tau (τ) isoform of microtubule-associated protein, 32, 304, 306, 315
- Telomerase, 28, 90-93, 317
- Tetrahydrocannabinol: *see* Cannabinoids
- Thiazolidinedione, 84, 85
- Thioredoxin, 128

- Tobacco: *see* Nicotine
- Transforming growth **factor- α** (TGF α), 94
- Transforming growth **factor- β** (TGF β)
- antiproliferative, pro-apoptotic effects, 60, 80, 84, 93, 121, 125-127, 157, 366
 - metabolic effects, 125-126
 - association with mitochondria, 125
 - brain, 313, 320, 324, 325
 - fatty acid and glucose metabolism, 25, 53, 126, 145, 160
 - ROS generation, 125
 - signaling, 93, 125
- Triacylglycerol, triglyceride (TG), 20, 51-53, 150, 180, 182, 186, 211, 238, 256
- Tumor necrosis **factor- α** (TNF α) and receptor (TNFR): *see* Apoptosis; *and* Proinflammatory cytokines
- Tumorigenesis, 13, 14, 25, 33, 52, 53, 84, 98, 127, 130, 155, 189, 268, 269, 315, 318
- Ubiquinone, 24, 128, 183, 220, 224, 290
- Ultraviolet light: *see* Apoptosis, FasL-independent Fas signaling
- Uncoupling, Uncoupling proteins (UCP), 49, 62, 82, 129, 157, 233, 286, 362; *see also* Mitochondrial energetics, oxidative phosphorylation
- Uncoupling-like effect: *see* Butyrate; *and* Ketone bodies; *and* Mitochondrial energetics, oxidative phosphorylation
- Ursodeoxycholic acid: *see* Apoptosis, FasL-independent Fas signaling
- Vascular endothelial growth factor (VEGF), 34, 93, 362, 366; *see also* Hypoxia
- Very low density lipoprotein (VLDL), 53, 149, 150, 182, 186, 238, 305
- “Vicious cycle” in Alzheimer disease pathogenesis: 304, 321-326; *see also* Alzheimer disease
- Visceral adipose tissue: *see* Adipose tissue, visceral
- Voltage-dependent anion channel (VDAC): *see* Mitochondrial energetics
- von Hippel-Lindau protein (VHL), 34; *see also* Hypoxia
- Wingless(wg)/Wnt-like signaling pathway: *see* PI3K/Akt/PKB signaling
- Yeast: *see* *S. cerevisiae*