Subject Index

A

- ABCA1
cholesterol efflux and, 131–132
miR-33 targeting of, 227–229, 231
- ABCG1, 131–132
- ABCG5/8 transporters, 130. *See also*
Liver X receptors
- ACC (acetyl-CoA carboxylase), 241–243
- AceCS2, 270
- Acetylation
acetyl-CoA and
acetylation of proteins, 195–196
ACLY and regulation of histone
acetylation, 198
deacetylation of mitochondrial
proteins during fasting and,
269–270
protein acetylation regulation by
deacetylases, 196
protein acetylation regulation by
levels of acetyl-CoA, 196–197
purpose of histone acetylation, 199
apoptosis and, 381–383
conclusions, 288–289
glycolysis and gluconeogenesis regula-
tion by, 285–286
inhibition of PKM activity and promo-
tion of chaperone-mediated
autophagy, 286–287
lysine acetylation, 286, 381–382
nutrient-dependent controls (*see* PGC-
1 α acetylation)
promotion of ubiquitin-mediated
PEPCK degradation, 285, 286,
287–288, 302
pyruvate kinase regulation by, 285
- SIRT3 and
acetylation process and function,
267–268
activity induced during calorie
restriction, 270–271
deacetylation of mitochondrial
proteins during fasting,
269–270
down-regulation of expression dur-
ing high-fat feeding, 271–272
future questions, 273–274
mitochondrial deacetylase func-
tion, 268–269
mitochondrial dysfunction conse-
quences, 267
mitochondrial protein acetylation
and metabolic regulation,
272–273
- Acetyl-CoA (acetyl-coenzyme A)
about, 195, 404
acetylation of proteins, 195–196
ACLY and regulation of histone
acetylation, 198
cell proliferation support role, 331–332
conclusions, 200
deacetylation of mitochondrial proteins
during fasting and, 269–270
linking of cell growth and proliferation
to YMC, 197–198
purpose of histone acetylation, 199
regulation of apoptotic sensitivity by
metabolism and, 382
regulation of protein acetylation, 196–
199
role of acetylated proteins, 199
role of protein deacetylases, 199–200
TDH-mediated catabolism of threonine
and, 192
- Acetyl-CoA carboxylase (ACC), 241–243
- ACLY (ATP-citrate lyase), 26, 198, 382
- ACTR, 33
- Acute myeloid leukemia (AML), 243, 306
- Acute promyeloid leukemia (APL), 166–
168
- Acyclovir, 238
- AD (Alzheimer Disease), 10–11, 91, 95, 97
- Adenine nucleotide translocators (ANTs),
6, 379
- Adenosine diphosphate (ADP) binding, 406
- Adenosine monophosphate (AMP)-activat-
ed protein kinase. *See* AMPK
- Adenosine triphosphate. *See* ATP
- Adenylate kinase-1, 302
- Adipocyte differentiation
conclusions, 252
external signals inducing adipogenesis,
247–248
investigations of regulatory transcrip-
tional networks
chromatin remodeling during adi-
pogenesis, 249–250
cross talk between PPAR γ and
C/EBP α , 252
hotspots in early wave of adipo-
genic factors, 250–251
mapping of transcription factors,
248–249
potential cross talk between hot-
spots, 252
role of C/EBP β in establishment of
hotspots, 251–252
models of differentiation, 247
regulation by transcriptional
cascades, 248
- Adipogenesis
adiponectin functional analysis
about, 257
Ca²⁺ influx induction by AdipoR1,
258–260
decreased PGC-1 α and mitochon-
dria in muscle-R1KO mice, 258
insulin resistance in muscle-R1KO
mice, 258–259
epigenetic regulatory mechanisms and
adipocyte-specific FAIRE peaks
and PPAR γ binding sites, 262
analysis of PPAR γ and RXR α
binding sites, 261–264
genome-wide profiling of open
chromatin regions by FAIRE-
seq, 260–261
identification of mechanisms for,
260, 261f
identification of NF1 family tran-
scription factors, 262–264
- Adiponectin receptors (AdipoR), 257, 258
- ADP (adenosine diphosphate) binding, 406
- Aerobic glycolysis. *See also* Glycolysis
- cancer and cell proliferation (*see* Cell
proliferation support)
in cellular metabolism regulation, 26
stimulation by Myc, 370–371
- AFD thermosensory neurons, 94
- Age-related changes in cells
aging clock reset by gamete formation
(*see* Gametogenesis-induced
rejuvenation)
aging clock somatic mtDNA mutations
and, 10
mitochondrial genetics and diseases,
10–11
in muscles (*see* Muscle stem cells and
aging)
muscle stem cells and, 104
proteotoxic stress in aging and disease
(*see* HSR)
SIRT1 and slowing of aging, 84–85
- AICAR (5-Aminoimidazolecarboxamide-
R), 184, 192
- Akt
activation in cancer cells, 161, 217
activation of TOR, 26, 204, 358, 389
apoptosis and, 380–381
ENTPD5 and, 217, 218f
FOXO family regulation by, 106, 303
glucose uptake and, 25, 26
IGF-1 signaling and, 117
phosphorylation of SREBPs, 226
PI3K/Akt signaling (*see* PI3K/Akt
pathway)
- Akt1, 301–302
- Akt/PKB, 389–390
- ALS (amyotrophic lateral sclerosis), 91,
95, 97
- Alzheimer Disease (AD), 10–11, 85, 91,
95, 97
- 5-Aminoimidazolecarboxamide-R
(AICAR), 184, 192
- AML (acute myeloid leukemia), 243, 306
- AMP, 157–159
- AMP-activated protein kinase.
See AMPK
- AMPK (adenosine monophosphate (AMP)-
activated protein kinase)
about, 17, 155, 403, 406
activation by xenobiotics, 160
activation of signaling pathways and, 204
adipogenesis and, 257
binding of AMP or ADP at site 3,
158–159
cancer and viral infection roles, 160–161
conclusions, 161
control by miR-33, 229–230
cross talk between NR and AMPK, 20
described, 17, 19–20

- domain arrangement, 157–158
 energy metabolism and, 361–362
 functional domains, 156–157
 metabolic counter balances to, 303
 orthologs' role in nonmammalian eukaryotes, 155–156
 regulation by AMP, 157
 regulation by stresses, 159–160
 regulation of metabolism and circadian rhythm, 19–20, 67
 SIRT1 and, 34–35
 SREBP and, 226
- Amyotrophic lateral sclerosis (ALS), 91, 95, 97
- Anchorage independence in tumor growth consequences of ECM detachment, 315–316
 integrins and, 314
 models developed to study, 314–315
 tumor cells ability to survive without ECM attachment, 313–314
- Anoikis, 313, 315
- Anorexia nervosa, 126–127
- Antiotensin II, 206
- ANTs (adenine nucleotide translocators), 6, 379
- APAF-1 (apoptotic protease-activating factor-1), 376
- APL (acute promyeloid leukemia), 166–168
- ApoER2, 133
- Apoptosis and metabolism
 conclusions, 383–384
 core apoptotic machinery
 Bcl-2 family, 377–378
 caspase-activating complexes, 376
 caspases, 375–376
 mitochondrial role in caspase activation, 376
 mitochondrial function in apoptosis, 376
 overview of the integration of, 375
 regulation of apoptotic sensitivity by metabolism
 integration of mitochondrial metabolism and apoptotic sensitivity, 381–382
 metabolic control of protein lysine acetylation, 381–382
 metabolic factors directly involved, 380–381
 protein N - α -acetylation and, 382–383
 regulation of metabolism by apoptotic factors, 379–380
- Apoptosome in mammals, 376
- Apoptotic protease-activating factor-1 (APAF-1), 376
- Arachidonic acid, 96
- Arrest Defective 1 (ARD1), 382
- ATG* (autophagy-related genes), 397, 400
- ATP (adenosine triphosphate)
 enzymes and substrates and, 403
 generation of ATP energy in cancer cells
 aerobic glycolysis and, 299–300
 HIF-1 and, 301, 302–303
 metabolic counterbalances, 303
 metabolic flexibility, 303–304
 PI3K pathway, 301–302
 PMK2 and, 300–301
 PPP and, 300
 growth of proliferating cells and, 327–328
 hydrolysis activity and ENTPD5 (*see* ENTPD5)
- production of, 317–318, 325, 326f
- ATP-citrate lyase (ACLY), 26, 198, 382
- Autophagy
 about, 397, 398f
 adaptation to starvation and, 397–398
 cancer metabolism and
 autophagy addiction and cancer cell survival, 391–392
 cancer described as a metabolic disease, 389–390
 conclusions, 394
 mechanism of autophagy addiction, 392–394
 nutritionally hungry state of cancers, 390–391
 stress-responsive autophagy, 391
 therapeutic implications of autophagy, 394
 tumorigenesis and, 400
 conclusions, 400
 oocyte-to-embryo transition and, 398
 protein quality control by, 398
 quality control of mitochondria by, 399–400
 selective degradation of p62 by, 398–399
 tumorigenesis and, 400
- Autophagy-related genes (*ATG*), 397, 400
- ## B
- Bad (Bcl-2 associated death promoter), 379–380
- BAG6 (Bcl2-associated athanogene 6), 288
- Bak (Bcl-2 homologous antagonist/killer), 377–378, 383
- Basal autophagy, 398
- BAT3 (HLA-B-associated transcripts 3), 288
- Bax (Bcl-2 associated X protein), 377–378, 383
- B-cell lymphoma 2. *See* Bcl-2 family
- Bcl-2 associated athanogene 6 (BAG6), 288
- Bcl-2 associated death promoter (Bad), 379–380
- Bcl-2 associated X protein (BAX), 377–378, 383
- Bcl-2 family
 about, 377
 autophagy and, 399
 BH3-only proteins, 378
 cell metabolism and, 379–380
 multidomain proapoptotic members, 377–378
 prosurvival of members, 377
- Bcl-2 homologous antagonist/killer (Bak), 377–378, 383
- Beadle, GW, 403
- Beclin 1-interacting proteins, 400
- Bid, 377–378
- Bile acids, 139
- Bim, 377–378
- Bioenergetics
 anatomical perspective's dominance in medicine, 2, 3f
 animals' adaptation to the environment, 12f
 basic assumptions of Western medicine, 1
 energy and the environment, 11–12
 energy flow and the maintenance of complexity, 1–2
- entropy and, 1
 inherited mitochondrial variation, 8–10
 mitochondrial genetics complexes, 7–8
 mitochondrial genetics of age-related diseases, 10–11
 mitochondrial paradigm
 accumulation of somatic mtDNA mutations, 3
 apoptosis and, 4
 central energy transformation system, 2
 encoding of the genome, 2–3
 environmental impingements on OXPHOS, 3
 mitochondrial etiology of complex disease, 4f
 mtDNA encoding of genes, 2, 7, 9–10
 origin of
 bacterial origin of mitochondrion, 7
 body's organization according to energy use, 5
 evolution of nDNA and mtDNA genes, 5
 mitochondrial electrochemical gradient, 5–7
 mitochondrial metabolism's features, 6f
 mitochondrion self-destruct system, 7
 multicellular animals' capacity for adaption, 5
 OXPHOS complexes and, 7
 plant energy system, 5
 somatic mtDNA mutations and aging, 10
- BMAL1
 chromatin remodeling and, 33
 control of circadian rhythm, 19
 deacetylation by SIRT1, 34
 functional relationship with $ERR\alpha$ and $PROX1$, 59
 molecular organization, 31–32
 REV- $erb\alpha$ regulation of circadian recruitment of HDAC3, 52
- Body temperature rhythms, 44–45
- Bone. *See* Skeletal physiology
- Burst size, 42
- ## C
- Ca^{2+} influx induction by AdipoR1, 258–260
- cADP-ribose synthases (CD38 and CD157), 295
- Caenorhabditis elegans*
 apoptosis in, 375
 DAF-2 insulin-like receptor regulation experimental results, 114–115
 insulin/IGF-1 pathway function, 113
 materials and methods, 115–117
 results discussion, 115–117
 HSF-1 and, 95
 occurrence of gametogenesis-induced rejuvenation in, 78–79
- Calmodulin-dependent kinase kinases (CaMKK), 156, 242–243
- Caloric restriction (CR)
 activity induced by SIRT3 during, 270–271
 circadian clock response to reduced energy availability, 68
 deacetylation of mitochondrial proteins during fasting, 269–270

- Caloric restriction (CR) (*continued*)
 enhancement of the function of satellite cells, 108
 insulin-like receptor DAF-2 and, 113–114
 mediation by sirtuins, 83–84
 SIRT1 and SIRT3 cooperation in, 87, 196
 starvation and autophagy, 397–398
 starvation and the ghrelin-growth hormone axis (*see* Ghrelin)
- CaMKK (calmodulin-dependent kinase kinases), 156, 242–243
- cAMP response element binding (CREB) protein, 42, 142, 204, 248
- Cancer
 activation of AMPK, 160–161
 altered metabolism inherent in (*see* Cancer and altered metabolism)
 anticancer target identification and metabolomics, 243–244
 ATP hydrolysis activity and ENTPD5 (*see* ENTPD5)
 energy metabolism and mRNA translation, 361–362
 insulin signaling pathway and, 25–26
 metabolism and, 406–408
 SIRT3 as a tumor suppressor, 86–87
 therapeutic targeting of Myc-reprogrammed cancer cell metabolism (*see* Myc and cancer)
- Cancer and altered metabolism
 cell proliferation support
 aerobic glycolysis and, 299–300, 325–326
 anabolic metabolism requirement, 326–328
 ATP production and, 325, 326f
 conclusions, 332–333
 by HIF-1 (*see* HIF-1)
 pyruvate kinase regulation, 329–331
 redirection of glucose carbon into serine biosynthesis, 331
 reductive metabolism of glutamine and, 331–332
 Eg1N prolyl hydroxylases as targets of mutations, 337–338
 HIF and oxygen availability, 335–336
 HIF role in cancer, 336–337
 non-Eg1N targets of mutations, 338
 2-oxoglutarate-dependent dioxygenases as therapeutic targets, 339–340, 407
 summary, 340
- Cancer cell metabolism
 altered metabolism inherent in (*see* Cancer and altered metabolism)
 autophagy and
 autophagy addiction and cancer cell survival, 391–392
 cancer described as a metabolic disease, 389–390
 conclusions, 394
 mechanism of autophagy addiction, 392–394
 nutritionally hungry state of cancers, 390–391
 stress-responsive autophagy, 391
 therapeutic implications of autophagy, 394
 tumorigenesis and, 400
 characteristics of, 299, 300f, 406–408
 conclusions, 307
 generation of ATP energy
- aerobic glycolysis and, 299–300
 HIF and, 302–303
 metabolic counterbalances, 303
 metabolic flexibility, 303–304
 PI3K pathway, 301–302
 PMK2 and, 300–301
 PPP and, 300
- metabolic alterations supporting
 balanced redox status
 DJ1, 305–306
 glutamine metabolism, 306
 IDH1, 306–307
 NADPH, 306–307
 ROS and, 304–305
 Myc and (*see* Myc and cancer)
- CAR (constitutive androstane receptor), 20, 45
- Carbohydrate-binding modules (CBMs), 157
- Carbohydrate response element binding protein (ChREBP), 408–409
- Cardiac function and PPAR γ . *See* PGC-1 α
- Carnitine *O*-octanoyltransferase (CROT), 229
- Carnitine palmitoyltransferase 1A (CPT1A), 229
- Carnitine palmitoyltransferase 1C (CPT1C), 303–304
- Caspase, 375–376
- Caspase-recruitment domain (CARD), 376
- CBMs (carbohydrate-binding modules), 157
- CCK (cholecystokinin), 140
- C/EBP family, 248, 251–252
- CED-4, 376
- Cell proliferation support. *See also* Cancer and altered metabolism
 aerobic glycolysis and cancer, 299–300, 325–326
 anabolic metabolism requirement
 ATP and growth of proliferating cells, 327–328
 efforts to understand the metabolic network of proliferating cells, 328
 metabolic needs other than ATP, 326–327
 ATP production and, 325, 326f
 conclusions, 332–333
 by HIF-1 (*see* HIF-1)
 pyruvate kinase regulation
 PGAM and conversion of PEP to pyruvate, 329–331
 PKM2 isoform expression in proliferating cells, 329
 proliferation without activity, 329
 redirection of glucose carbon into serine biosynthesis, 331
 reductive metabolism of glutamine and, 331–332
- Cellular metabolism regulation
 acetylation-mediated mechanisms (*see* PGC-1 α acetylation)
 aerobic glycolysis provision of a growth advantage to cells, 26
 by AMP kinase (*see* AMPK)
 cancer and the insulin signaling pathway, 25–26
 conclusions, 28
 de-acetylase enzymes, 404–405
 death by neglect, 24
 by ECM (*see* ECM regulation of metabolism)
 enzymes and substrates interactions, 403–404
- evolution of signal transduction and, 23
 glutamine's role in cell growth and proliferation, 26–28
 by HIF-1 (*see* HIF-1)
 metabolic pathway alterations supporting cell proliferation (*see* Cell proliferation support)
 metabolic specialization of mouse ES cells (*see* Mouse embryonic stem cells)
 metabolism and cancer (*see* Cancer cell metabolism)
 metazoan cell survival regulation considerations, 24–25
 monitoring of the metabolic state (*see* Acetyl-CoA)
 multicellular animals' regulation of shared nutrients, 23–24
 pivot points controlling sugar metabolism, 408–409
 reciprocity of metabolic and regulatory state, 405–406
- Central clock. *See* Circadian clock
- CFTR (cystic fibrosis transmembrane regulator), 97
- Chaperone-mediated autophagy, 286–287, 397
- Chaperones and heat shock response, 91–92
- Cholecystokinin (CCK), 140
- Cholesterol
 disease risk and, 129
 homeostasis regulation (*see* Liver X receptors)
 regulation by SREBPs, 226, 227
 Cholesterol 7 α -hydroxylase (CYP7A1), 139
- ChREBP (carbohydrate response element binding protein), 408–409
- Circadian clock
 AMPK involvement in circadian rhythm, 19–20
 chromatin remodeling and, 32–33
 circadian rhythm pattern in hepatic lipogenesis, 51–52
 conclusions, 37
 cross talk between NR and AMPK, 20
 energy homeostasis and (*see* Energy homeostasis and the circadian clock)
 feedback loop for circadian rhythm generation, 39–40
 HDAC3's role in
 circadian clock mechanism described, 49–50
 circadian rhythm pattern in hepatic lipogenesis, 51–52
 conclusions and perspectives, 52–54
 function as an epigenomic modifier controlling hepatic lipogenesis, 50–52
 molecular switch underlying hepatic lipogenesis, 52
 REV-erb α regulation of circadian recruitment of, 52
 impact on physiology, 32
 mechanisms of, 49–50
 model of the circadian clock, 31, 32f
 molecular organization, 31–32
 NAD $^{+}$ and, 35–37, 66–67
 regulation by ERR α (*see* ERR α)
 S-adenosyl methionine and, 37
 SCN and, 17, 31, 39–40

- SIRT1 and, 33–35
synchronization of peripheral clocks (*see* Peripheral clocks)
- Citrate, 392
- CLOCK-BMAL1
chromatin remodeling and, 33
control of circadian rhythm, 19
molecular organization, 31–32
REV-erb α regulation of circadian recruitment of HDAC3, 52, 67
- CMP (cytidine monophosphate)
kinase-1, 302
- Constitutive androstane receptor (CAR), 20, 45
- CPT1A (carnitine palmitoyltransferase 1A), 229
- CPT1C (carnitine palmitoyltransferase 1C), 303–304
- CR. *See* Caloric restriction
- CREB (cAMP response element binding) protein, 42, 142, 204, 248
- CREB/CRTC2, 84
- CROT (carnitine *O*-octanoyltransferase), 229
- Cyclopentenone prostaglandins, 96
- Cyclophilin D, 379
- CYP7A1 (cholesterol 7 α -hydroxylase), 139
- Cysteine proteases, 375–376
- Cystic fibrosis transmembrane regulator (CFTR), 97
- Cytidine monophosphate (CMP)
kinase-1, 302
- Cytochrome, 376
- D**
- DAF-2 insulin-like receptor regulation
DAF-2 regulation and expression, 117
experimental results
DAF-2 level regulation by environmental signals, 114–115
DAF-2 localization to neuronal processes and cell bodies, 114
molecular identification of *daf-1* null alleles, 114
expression in the XXX secretory cell, 115–116
IGF-1 signaling and, 116–117
insulin/IGF-1 pathway function, 113
localization to the nerve ring, 115
materials and methods, 118–119
- DDDP (differential display of DNA-binding proteins), 44
- Death by neglect, 24
- Death-inducing signaling complex (DISC), 376
- Dexamethasone, 247–248
- DHS (DNase I hypersensitive), 249–250
- Diabetes mellitus
metabolic regulation of muscle stem cells, 107
PGC-1 derangements and, 179–180
synthetic approaches to cell-signaling regulation, 150
- Dietary supplements and muscle cells, 108
- Differential display of DNA-binding proteins (DDDP), 44
- DISC (death-inducing signaling complex), 376
- DJ1, 305–306
- DNase I hypersensitive (DHS), 249–250
- Down syndrome patients with dementia (DSAD), 10–11
- Drosophila melanogaster*, 73, 375
- Drp1, 399
- Drug target discovery. *See* Metabolomics
- DSAD (Down syndrome patients with dementia), 10–11
- E**
- E1/2/3 enzymes, 134
- 4E-BPs binding proteins
aberrant cell proliferation and, 358–360
cancer and, 407
governing of eIF4E activity, 357–358
regulation of cell growth and proliferation and, 358–360
- ECM (extracellular matrix) regulation of metabolism
anchorage independence in tumor growth
consequences of ECM detachment, 315–316
integrins and, 314
models developed to study anchorage independence, 314–315
tumor cells ability to survive without ECM attachment, 313–314
- autophagy regulation, 317
conclusions, 320–322
modulation of cellular metabolism, 317
PDH flux modulation, 318–320
PDK4 and suppression of PDH flux, 320
ROS regulation of FAO and ATP production, 317–318
- Ectonucleoside triphosphate diphosphohydrolase 5. *See* ENTPD5
- Eg1N, 337–338, 339
- EGFR, 217
- eIF4B (eukaryotic initiation factor 4B)
4E-BP governing of eIF4E activity, 357–358
activity regulation, 357
cancer and, 407
direct binding of MNKs, 357
linking of MAPK and PI3K/AKT signaling, 361
role in mRNA translation, 141, 355–356
stimulation of translation of mRNA encoding factors, 356–357
- Electron transport chain (ETC), 5, 175
- Energy flow through organic systems. *See* Bioenergetics
- Energy homeostasis and the circadian clock
conclusions, 69
consequences of overabundance of nutrients, 68–69
experiments used in genetic analysis of clock function, 65–66
integration of clock, environment, and nutrient availability, 64–65
nutrient sensors linking metabolism to the clock
AMPK and, 67
NAD⁺-dependent sensors, 66–67
nutrient-sensitive transcription factors, 67
relationship to metabolic oscillators, 63–64
response to changes in nutrient availability, 67–68
transcription feedback clock loop, 63
- ENTPD5 (ectonucleoside triphosphate diphosphohydrolase 5)
about, 217–219, 408
control of growth factor receptors, 219, 221
degradation of EGFR through the ER-associated degradation pathway, 219
functional redundancy of ENTPD genes, 221–222
knockdown results, 219
materials and methods, 222–223
PI3K pathway and, 302
- ERK1/2, 318–320
- ERR α (estrogen-related receptor α)
circadian expression of ERR α and PROX1, 58
disruption of circadian physiology in knockout mice, 58
functional relationship with BMAL1 and PROX1, 59
regulation of diurnal expression of genes, 59
regulation of the circadian clock by, 58
role in circadian biology, 60
structure and function, 57–58
- ES. *See* Mouse embryonic stem cells
- ETC (electron transport chain), 5, 175
- Eukaryotic initiation factor 4B. *See* eIF4B
- Evolution and bioenergetics, 1
- Exercise and muscle function, 107–108
- Extracellular matrix. *See* ECM regulation of metabolism
- F**
- F2,6BP (fructose 2,6 biphosphate), 212–215
- FAIRE (formaldehyde-assisted isolation of regulatory elements), 260–261, 262
- FAO (fatty acid oxidation), 175, 177, 179, 317–318
- Farnesoid X receptor (FXR), 168
- FASN (fatty acid synthase), 225
- Fatty acid β -oxidation genes, 229
- Fatty acid oxidation (FAO), 175, 177, 179, 317–318
- Fatty acid synthase (FASN), 225
- FBA (Flux Balance Analysis), 146
- Feeding-fasting cycle
energy homeostasis and, 64–65
peripheral clocks and, 43–44
- FERM domain, 132, 134
- FGF19 (fibroblast growth factor 19)
about, 139
bile acid homeostasis regulation, 139–140
compared to insulin, 141–142
conclusions, 142–143
hepatic gluconeogenesis regulation, 142
hepatic protein and glycogen synthesis regulation, 140–142
- FGF21, 204–205
- FH (fumarate hydratase), 337–338, 369, 407
- Fibroblast growth factor 19. *See* FGF19
- Flux Balance Analysis (FBA), 146
- Flux profiling, 237
- Forkhead transcription factor. *See* FOXO transcription factor
- Formaldehyde-assisted isolation of regulatory elements (FAIRE), 260–261, 262

FOXO transcription factor
 metabolic counterbalances to, 303, 305
 metabolic regulation of muscle stem cells, 106–107
 regulation of gluconeogenesis and, 5, 84, 142
 Fructose 2,6 biphosphate (F2,6BP), 212–215
 Fumarate hydratase (FH), 337–338, 369, 407
 FXR (farnesoid X receptor), 168

G

G6Pase (glucose-6-phosphatase), 206, 211, 302
 G6P dehydrogenase (G6PDH), 300
 Galegine, 160
 Gallbladder, 139
 Gametogenesis-induced rejuvenation
 budding yeast used as a model system, 73–75
 conclusions, 79
 immortal germline-disposable soma theory, 73
 mechanisms of
 effects of aging on nucleolar physiology, 76–77
 histone modifications and, 77
 mitochondrial dysfunction and, 77–78
 nucleolar architecture and function and, 77
 transcription factor Ndt80 and, 75–76
 occurrence in other organisms, 78–79
 Ganciclovir, 238
 GAPDH (glyceraldehyde-3-phosphate dehydrogenase), 82
 Garrod, Archibald, 403
 GCN5, 205–206
 GDH (glutamate dehydrogenase), 85
 Gen5, 198–199
 Genome-wide association studies (GWAS), 1
 Ghrelin
 about, 121–122
 functional analysis of GOAT knockout mice
 hypoglycemia development, 123, 124f
 hypoglycemia prevention, 123, 124f, 125
 overview, 122
 protocol for chronic calorie restriction, 122–123
 gastric ghrelin-secreting cells' response to hypoglycemia, 125–126
 GOAT identification, 122
 mechanism for growth hormone production of hypoglycemia in CR GOAT mice, 125
 model illustrating mouse metabolic response to starvation, 126
 relevance to anorexia nervosa in humans, 126–127
 Ghrelin *O*-acyltransferase (GOAT), 122
 GlcNAcylation, 167–168, 171
 Glucocorticoid receptor (GR), 33, 250–251
 Gluconeogenesis, 84, 142, 285, 287–288
 Glucose-6-phosphatase (G6Pase), 206, 211, 302
 Glucose metabolism

Akt and glucose uptake, 25, 26, 302
 control of glucose/energy homeostasis regulators by miR-33, 229–230
 control through regulation of PFK-1 (*see* PFK-1)
 HIF, O₂ and glucose oxidation, 347
 hormonal response to starvation (*see* Ghrelin)
 link with cancerous transformation, 212–213
 Myc stimulation of glucose and glutamine metabolism, 370–371
 nutrient dependent acetylation and, 206
 PFK-1 and the glycolytic pathway, 211
 redirection of glucose carbon into serine biosynthesis, 331
 TCA and, 318–320
 Glutamate dehydrogenase (GDH), 85
 Glutaminase (GLS), 371
 Glutamine, 26–28, 306, 332, 390
 Glutathione (GSH), 85, 304
 Glyceraldehyde-3-phosphate dehydrogenase (GAPDH), 82
 Glycogen synthase (GS), 141
 Glycolysis
 aerobic (*see* Aerobic glycolysis)
 enhancement of in cancers, 299–300
 HIF-1 and cancer (*see* Cancer and altered metabolism)
 linking of protein acetylation and metabolism by sirtuins, 82–83
 regulation by acetylation of PKM, 285, 286–287
 regulation via PPP pathway, 408–409
 Glycolytic pathway and PFK-1 activity. *See* PFK-1
 GOAT (ghrelin *O*-acyltransferase), 122
 GPR109A, 294
 G-protein-coupled receptors (GPCRs), 257, 281–282
 GR (glucocorticoid receptor), 33, 250–251
 GS (glycogen synthase), 141
 GSH (glutathione), 85, 304
 GWAS (genome-wide association studies), 1

H

HADHB (hydroxyacyl-coenzyme A-dehydrogenase), 229
 Haplogroups, 9
 Hardie, Graham, 403
 HATs (histone acetyltransferases), 33, 404
 HCMV (human cytomegalovirus), 238, 240, 241
 HDAC3 (histone deacetylase 3)
 circadian clock mechanism described, 49–50
 circadian rhythm pattern in hepatic lipogenesis, 51–52
 conclusions and perspectives, 52–54
 function as an epigenomic modifier controlling hepatic lipogenesis, 50–52
 molecular switch underlying hepatic lipogenesis, 52
 REV-erba regulation of circadian recruitment of, 52
 HDAC-mediated deacetylation of histones, 33
 HDL (high-density lipoprotein), 130
 HDM. *See* HMTs/HDMs complexes
 Heat shock factor 1 (HSF-1), 44, 93, 406

Heat shock response. *See* HSR
 HEK293 cells, 293
 HeLa cells, 186–187, 190–191
 Hepatic lipogenesis
 circadian rhythm pattern in, 51–52
 conclusions regarding HDAC3 role in, 52–54
 HDAC3's role in controlling, 50–52
 Hepatitis C, 160–161
 Heterochronic parabiosis, 108
 HFD (high-fat feeding), 271–273
 HIF-1 (hypoxia-inducible transcription factor 1)
 about, 406
 activation in cancer, 183, 214, 348–349
 cancer and altered metabolism and, 335–337, 339
 generation of ATP energy, 301, 302–303
 induction of LOX expression, 339
 O₂ and glucose oxidation, 347
 O₂ homeostasis and, 347–348
 role in cancer metabolism, 335–337, 349–350
 SIRT3 as a tumor suppressor, 86–87
 High-density lipoprotein (HDL), 130
 High-fat feeding (HFD), 271–273
 Histone acetylation, 199
 Histone acetyltransferases (HATs), 33, 404
 Histone deacetylase 3. *See* HDAC3
 Histone demethylase (HDM). *See* HMTs/HDMs complexes
 Histone methyltransferase (HMT). *See* HMTs/HDMs complexes
 HLA-B-associated transcripts 3 (BAT3), 288
 HMGR (3-hydroxy-3-methylglutaryl-coenzyme A reductase), 225
 HMTs/HDMs complexes (histone methyltransferases/histone demethylases)
 about, 165–166
 activation of MLL5, 166–168
 conclusions, 172
 GlcNAcylation of MLL5, 171
 HDM activation in response to fasting signals, 168–170
 as NR co-regulators, 165
 regulation of NR transcriptional activities via PTMs, 171–172
 Hormesis, 91
 Hormone therapy and muscle cells, 108
 HSF-1 (heat shock factor 1), 44, 93, 406. *See also* HSR
 Hsp104, 74, 75–76
 HSR (heat shock response)
 chaperones and, 91–92
 conclusions, 97
 function of, 92–93
 heat shock transcription factors, 93
 inducement situations, 94
 organization and domains structure, 93
 proteostasis network and, 91, 96
 proteotoxic stress in aging and disease, 94–95
 regulation of HSF-1 by small molecules, 95–97
 stress-inducible regulation of chaperone networks, 93–94
 Human cytomegalovirus (HCMV), 238, 240, 241
 Huntington Disease, 91, 95
 3-hydroxy-3-methylglutarylcoenzyme A reductase (HMGCR), 225

Hydroxyacyl-coenzyme A-dehydrogenase (HADHB), 229
 Hypertensive heart disease, 178
 Hypoxia-inducible transcription factor.
See HIF-1

I

IDH1/2/3 (isocitrate dehydrogenase)
 activation of IDH2 by SIRT3, 85
 cancer cell metabolism and, 306–307,
 369, 407
 Eg1N prolyl hydroxylases as targets of
 IDH mutations, 337–338
 non-Eg1N targets of IDH mutations,
 338
 TCA cycle and, 28, 243
 Idol (inducible degrader of the LDLR),
 132–134
 IGF-1 (insulin/IGF), 106–107
 Immediate early transcription factors
 (IETFs), 42, 44
 Indomethacin, 96
 Inducible degrader of the LDLR (Idol),
 132–134
 Inflammasomes, 376
 INSIG/SCAP complex, 226
 Insulin
 cancer and the insulin signaling path-
 way, 25–26
 compared to FGF19, 141–142
 DAF-2 in *C. elegans* (*see* DAF-2 insu-
 lin-like receptor regulation)
 insulin-like receptor and calorie re-
 striction, 113
 SREBP accumulation and, 226
 stimulation of adipogenesis and, 248
 Insulin growth factor 1 receptor (IGF1R),
 94–95
 Insulin receptor substrate 2 (IRS2),
 229–230
 Integrins, 314
 Interleukin-3 receptor α (IL-3R α), 306
 Isocitrate dehydrogenase. *See* IDH1/2/3

J

Jacob, F., 403
 JAK2, 340

K

K120, 382
 K1F1B β , 338
 KDM2/3/4/5, 339–340
 Keap1, 398–399
 Kidney cancers, 337
 K_m of sirtuins (Michaelis constant), 291,
 292, 404
 Kuhn, Thomas, 1

L

LC3-p62 interaction, 399
 LCAD (long-chain acyl-CoA dehydroge-
 nase), 269, 272
 LDHA (lactate dehydrogenase A), 369,
 370–371, 372
 LDLR (low density lipoprotein receptor),
 225
 Leptin, 280
 Lipotoxic cardiomyopathy, 179

Liver

cholesterol homeostasis control (*see*
 Liver X receptors)
 FGF19 regulation of metabolism (*see*
 FGF19)
 HDAC3's role in hepatic lipogenesis
 (*see* HDAC3)
 Liver kinase B1 (LKB1), 156, 406
 Liver X receptors (LXRs)
 about, 129–130
 cholesterol and disease risk, 129
 LXR-Idol pathway and human metab-
 olism, 134
 LXR-Idol pathway function, 132–133
 LXR-Idol pathway regulation of LDLR
 family members, 133
 regulation of cellular cholesterol efflux,
 131–132
 regulation of systemic cholesterol ho-
 meostasis, 130
 results of loss of Idol expression, 133
 sterol metabolism and, 129
 therapeutic implications of the LXR
 pathway, 134–135
 ubiquitin ligase complex for LDLR
 degradation, 134
 LKB1 (liver kinase B1), 156, 406
 Long-chain acyl-CoA dehydrogenase
 (LCAD), 269, 272
 Low density lipoprotein receptor (LDLR),
 129, 225
 LOX, 339
 LXRs. *See* Liver X receptors
 Lysine acetylation, 286, 381–382

M

Macroautophagy. *See* Autophagy
 Male fertility regulation by bone. *See*
 Skeletal physiology
 Malic enzyme (ME), 306
 Malonyl-CoA decarboxylase (MCD), 272
 Mammalian target of rapamycin. *See*
 mTOR
 MAPK (mitogen activated-protein kinase),
 357, 361, 407
 MAPK signal-integrating kinases
 (MNKs), 357
 Mauro, Alexander, 102
 MBOATs (membrane bound *O*-acyltrans-
 ferases), 122
 MCD (malonyl-CoA decarboxylase), 272
 Mcl-1, 381
 MDI cocktail, 247
 ME (malic enzyme), 306
 Membrane bound *O*-acyltransferases
 (MBOATs), 122
 Mendel's laws of inheritance, 2
 Metabolic syndrome
 down-regulation of SIRT3 expression
 during high-fat feeding, 271–272
 mitochondrial dysfunction conse-
 quences, 267
 Metabolism and circadian clock. *See*
 Circadian clock
 Metabolomics
 anticancer target identification and,
 243–244
 background to study of, 235–236
 challenge of identifying metabolites by
 concentration differences, 238,
 240
 conclusions and outlook, 244
 expansion of the range of novel antiviral
 targets, 241–243
 finding antiviral targets through,
 237–238, 239f
 flux measurements, 237
 identification of *N*-acetyl-aspartate in
 HCMV infection, 238, 240
 identification of unexpected or novel
 compounds, 236–237
 probing of TCA cycle fluxes, 240–241
 quantitation of known metabolites, 236
 recognition that metabolic enzymes are
 drug targets, 236
 systems-level flux quantitation in
 HCMV-infected cells, 241
 Metformin, 160
 1-Methyl-3-isobutyl Xanthine (MIX),
 247, 248
 Methyl-tetrahydrofolate (mTHF), 184
 Michaelis constant (K_m of sirtuins), 291,
 292, 404
 Microautophagy, 397
 miR-33a/b (microRNAs)
 about, 226–227
 biogenesis pathway, 227f
 cholesterol regulation by SREBPs and,
 225–226
 conclusions, 230–231
 experimental results
 control of glucose/energy homeo-
 stasis regulators, 229–230
 SREBP function as a host gene, 227
 targeting of ABCA1, 227–229
 targeting of fatty acid β -oxidation
 genes, 229
 SREBP control at the transcriptional
 level, 226
 Mitochondrial ATP, 6
 Mitochondrial outer membrane permeabil-
 ization (MOMP), 377, 378, 379
 Mitofusin, 399, 400
 Mitogen activated-protein kinase (MAPK),
 357, 361, 407
 Mixed-lineage leukemia 5 (MLL5),
 166–168, 171
 MIX (1-methyl-3-isobutyl xanthine),
 247, 248
 MLL5 (mixed-lineage leukemia 5),
 166–168, 171
 MNKs (MAPK signal-integrating kinases),
 357
 MOMP (mitochondrial outer membrane
 permeabilization), 377, 378, 379
 Monod, J., 403
 Mouse embryonic stem cells (ES)
 changes in metabolite abundance during
 cell differentiation, 184–185
 conclusions, 193
 discovery of Qc compounds, 189–190
 effect of Qc1 inhibitor on cell growth,
 192–193
 effect of TDH inhibitors on cell growth,
 190–192
 experiment overview, 183–184
 expression of TDH mRNA, 185–186
 utilization of threonine as a metabolic
 fuel, 186–189
 mRNA translation
 4E-BP governing of eIF4E activity,
 357–358
 aberrant cell proliferation and, 358–360
 about, 355
 conclusions, 362
 eIF4E activity regulation, 357

- mRNA translation (*continued*)
 eIF4E direct binding of MNKs, 357
 eIF4E linking of MAPK and PI3K/
 AKT signaling, 361
 eIF4E stimulation of translation of
 mRNA encoding factors,
 356–357
 energy metabolism and cancer and,
 361–362
 initiation step, 141, 355–356
 regulation of cell growth and prolifera-
 tion, 358–360
- mtDNA (mitochondrial DNA)
 bioenergetics and, 1, 7–10
 encoding of non-Mendelian genes, 2
- mTHF (methyl-tetrahydrofolate), 184
- mTOR (mammalian target of rapamycin)
 4E-BP governing of eIF4E activity and,
 357–358
 aberrant cell proliferation and, 360–361
 activation of signaling pathways and,
 204–205
 Akt1 phosphorylation and, 302
 blocking of HCMV replication, 243
 cancer described as a metabolic disease
 and, 389–390, 407
 gametogenesis-induced rejuvenation
 and, 76
 glycolytic metabolism pathway and, 26
 metabolic regulation of muscle stem
 cells, 106–107
 muscle repair and, 104
 regulation of cell growth and prolifera-
 tion and, 358–360
 signaling pathway and SREBP func-
 tion, 226
 stress-responsive autophagy and, 391
- Murine 3T3-L1 cell line, 247
- Muscle-R1KO mice, 258
- Muscle stem cells and aging
 age-related changes in cells, 104
 conclusions, 108–109
 enhancement of the function of satellite
 cells, 107–108
 extrinsic changes in aging muscle stem
 cells, 106
 intrinsic changes in aging muscle sat-
 ellite cells, 104–106
 mechanisms leading to sarcopenia, 101
 metabolic regulation of muscle stem
 cells, 106–107
 muscle-resident nonmyogenic cell
 populations, 102
 regulators of muscle regeneration,
 103–104
 satellite cells defined, 101
 satellite cells purpose, 102, 103f
- Myc and cancer
 about, 306, 406
 conclusions, 372
 deregulated Myc expression and
 nutrient addiction, 371
 function in ribosome biogenesis and
 biomass accumulation, 370
 Myc-induced glutaminolysis, 26
 MYC oncogene as a master regulator,
 369–370
 new focus on altered metabolisms, 369
 stimulation of glucose and glutamine
 metabolism, 370–371
 targeting of LDHA and GLS in cancer
 therapies, 372
- Myelomatosis viral oncogene (Myc). *See*
 Myc and cancer
- Myostatin, 103–104
- MYST, 33
- ## N
- NA (nicotinic acid), 293
N- α -acetylation, 382–383
N-acetyl-aspartate, 238, 240
N-acetyltransferase protein complexes
 (NATs), 382
- NAD⁺ (nicotinamide adenine
 dinucleotide)
 about, 404
 conclusions and future perspectives, 295
 discovery of, 291
 metabolism linked to the circadian
 clock and, 35–37, 66–67
 negative regulation of SREBPs and, 226
 protein acetylation and, 196, 203–204
 role in deacetylase activity of sirtuin
 proteins, 207
 sirtuins and energy metabolism and, 33,
 35–37, 268
 sirtuins as sensors of, 291–294
 strategies to modulate sirtuin activity
 through, 293–295
- NADPH (nicotinamide adenine dinucleo-
 tide phosphate)
 anabolic processes and, 326–327
 apoptotic regulations and, 380–381
 cancer cell metabolism and, 300, 306–
 307
 glutamine and production of, 26, 27
 production in mitochondria through, 85
- NADPH-oxidase (nicotinamide adenine
 dinucleotide phosphate-oxi-
 dase), 390
- NAM (nicotinamide), 35–36
- NAMPT (nicotinamide phosphoribosyl-
 transferase enzyme), 36, 293
- NA phosphoribosyltransferase (NAPT), 293
- Narcolepsy, 65
- NASH-CRN study, 272
- NATs (*N*-acetyltransferase protein com-
 plexes), 382
- Natural selection and bioenergetics, 2
- NCoR (nuclear receptor corepressor), 50
- nDNA (nuclear DNA), 2–3, 7, 9–10
- Ndt80, 75–76, 78
- NF1 family transcription factors, 262–264
- NF- κ B signaling pathway, 107
- NHRs (nuclear hormone receptors), 67
- Niacin, 294
- Nicotinamide (NAM), 35–36
- Nicotinamide adenine dinucleotide.
See NAD⁺
- Nicotinamide adenine dinucleotide phos-
 phate. *See* NADPH
- Nicotinamide phosphoribosyltransferase
 enzyme (NAMPT), 36, 293
- Nicotinamide riboside (NR), 293
- Nicotinic acid (NA), 293
- NMNAT (NMN adenylyltransferase), 293
- NMR (nuclear magnetic resonance), 235
- Nonsteroidal anti-inflammatory
 (NSAID), 96
- Notch signaling, 104, 106
- NR (nicotinamide riboside), 293
- Nrf2 (nuclear respiratory factors), 175,
 398–399
- NR kinases (NRKs), 293
- NRs (nuclear receptors)
 about, 17
- cross talk between NR and AMPK, 20
- ERR α and (*see* ERR α)
- HMT/HDM and, 165, 171–172
- involvement in circadian rhythm, 19
- liver X (*see* Liver X receptors)
- ring of physiology, 18–19
- NSAID (nonsteroidal anti-inflammatory),
 96
- Nuclear DNA (nDNA), 2–3, 7, 9–10
- Nuclear hormone receptors (NHRs), 67
- Nuclear magnetic resonance (NMR), 235
- Nuclear receptor corepressor (NCoR), 50
- Nuclear respiratory factors (Nrf2), 175,
 398–399
- Nucleic acids and energy flow, 1–2
- Nutraceuticals, 160
- ## O
- Obesity
 adiponectin and molecular causes of
 (*see* Adipogenesis)
 PGC-1 derangements and, 179–180
- Octamer transcription factor 1 (OCT1),
 303
- Octanoyleated peptide hormone. *See*
 Ghrelin
- O-linked *N*-acetylglucosamine (GlcNAc)
 transferase (OGT), 167, 404
- Orexin/hypocretin, 65
- Osteocalcin hormonal functions, 280–282
- 2-Oxoglutarate-dependent dioxygenases,
 339–340, 407
- OXPHOS (oxidative phosphorylation), 2,
 5, 7, 83, 175, 285, 335
- Oxygen homeostasis regulation by HIF-1.
See HIF-1
- ## P
- p53 family of transcription factors, 78,
 305, 408
- p62/SQSTM1, 398–399, 400
- p90 Ribosomal S6 kinase (p90RSK), 141
- Paired box transcription factor 7 (Pax7),
 102. *See also* Satellite cells
- Parangangliomas, 337–338
- Parkin, 399–400
- Parkinson Disease (PD), 10–11, 91, 95,
 97, 399–400
- PARPs (poly(ADP)-ribosyl polymerases),
 294–295
- Pasteur effect, 335
- Pax7 (paired box transcription factor 7),
 102. *See also* Satellite cells
- PCSK9 (proprotein convertase subtilisin/
 kexin type 9), 132, 133, 135
- PD. *See* Parkinson Disease
- PDH flux modulation, 318–320
- Pentose phosphate pathway (PPP), 300,
 326–327
- PEP (phosphoenolpyruvate), 300–301, 329
- PEPCK (phosphoenolpyruvate carboxyki-
 nase), 206, 285, 287–288, 302
- PER2, 44
- Peripheral clocks
 body temperature rhythms and, 44–45
 circadian clock and, 32
 conclusions, 45
 differences between SCN neurons and
 peripheral cell types, 40
 feedback loop for circadian rhythm
 generation, 39–40

SUBJECT INDEX

421

- feeding-fasting cues used to deal with redundancy, 43–44
- properties of peripheral oscillators, 40–42
- signaling pathways able to synchronize clocks, 42–43
- Permeability transition (PT) pore, 379, 380
- Peroxisome proliferator-activated receptor γ (PPAR γ)—coactivator 1 α . *See* PGC-1 α
- PFK-1 (phosphofructokinase-1)
- F2,6BP regulation and cancer cell metabolism, 213–214
 - F2,6BP role in cell metabolism, 212–213
 - glycolysis and, 300, 302, 408–409
 - hormonal regulation of PFK-2 activity, 213
 - link between glucose metabolism and cancerous transformation, 213–214
 - role and regulation, 211–212
 - TIGAR and, 214–215
- PFKFB (6-phosphofructo-2-kinase/fructose-2,6-biphosphatase), 213. *See also* PFK-1
- PGAM (phosphoglycerate mutase), 300–301, 330–331
- PGC-1 α (PPAR γ coactivator)
- about, 175–176
 - acetylation of (*see* PGC-1 α acetylation)
 - adipogenesis and, 261–264
 - analysis of binding sites in 3T3-L1 adipocytes, 261–264
 - conclusions, 180
 - fuel switches in hypertrophied and failing heart, 177
 - gene regulatory circuit derangements, 178
 - metabolic derangements in heart disease and obesity, 178–180
 - mitochondrial derangements in the heart, 178
 - regulation by Gen5 and Sirt1, 198–199
 - regulation of adipocytes, 248–249
 - role in cardiac metabolic maturation, 176–177
 - stimulation by adiponectin, 257
 - transcriptional activity of ERR α and, 57
- PGC-1 α acetylation
- about, 203, 404
 - conclusions, 208
 - decreased PGC-1 α and mitochondria in muscle-R1KO mice, 258
 - NAD⁺ regulation of, 196
 - purpose of protein acetylation, 203–204
 - regulation by Gen5 and Sirt1, 198–199
 - regulation by protein acetylation, 205
 - relationship with GCN5 and, 205–206
 - relationship with Sirt1 and, 206–208
 - signaling pathways activated by external stimuli, 204–205
 - signals contributing to metabolic switching, 204
 - transcriptional coactivator role in metabolic remodeling, 205
- Phagophores, 391
- PHD (prolyl hydroxylases, Eg1N), 337–338, 339
- PHD3 (prolyl hydroxylase-3), 301
- PHGDH (phosphoglycerate dehydrogenase), 300–301
- PHGDH* gene, 331
- Phosphatase tensin homolog (PTEN), 217, 357, 407
- Phosphatidylcholine, 226
- Phosphoenolpyruvate (PEP), 300–301, 329
- Phosphoenolpyruvate carboxykinase (PEPCK), 206, 285, 287–288, 302
- 6-Phosphofructo-2-kinase/fructose-2,6-biphosphatase (PFKFB), 213. *See also* PFK-1
- Phosphofructokinase-1. *See* PFK-1
- 3-Phosphoglycerate (3-PG), 331
- Phosphoglycerate dehydrogenase (PHGDH), 300–301
- Phosphoglycerate mutase (PGAM), 300–301, 330–331
- Phosphoinositide-3 kinases. *See* PI3Ks pathway
- Phospholipid phosphatidylcholine, 225
- Physiologic hypertrophy, 178
- PI3K/Akt pathway
- activation of signaling pathways and, 204–206
 - ENTPD5 and, 219, 221
 - FOXO family regulation by, 106
 - growth factor signaling and ECM and, 314, 317, 320
 - IGF-1 signaling and, 106
 - induction by insulin, 141–142
 - linking of MAPK and PI3K/AKT signaling, 361
- PI3Ks (phosphoinositide-3 kinases) pathway
- activation of signaling pathways and, 204–205
 - cancer and, 25–26, 217, 389, 407
 - generation of ATP energy, 301–302
 - linking of MAPK and PI3K/AKT signaling, 361
 - metabolic counterbalances to, 303
- PIDDosome, 376
- PINK1 (PTEN-induced putative kinase), 8, 302, 399
- PK (pyruvate kinase)
- PGAM and conversion of PEP to pyruvate, 329–331
 - PKM2 isoform expression in proliferating cells, 329, 349–350
 - proliferation without activity, 329
 - regulation by acetylation, 285
 - regulation by growth signals, 328
- PKA (protein kinase A), 168, 204, 408–409
- PMK2 (pyruvate kinase M2)
- cancer and, 407
 - generation of ATP energy and, 300–301
 - PKM2 isoform expression in proliferating cells, 329, 349–350
 - redirection of glycolytic metabolism and, 331
- PN (proteostasis network), 91. *See also* HSR
- Poly(ADP)-ribosyl polymerases (PARPs), 294–295
- PolyQ proteins, 95
- Posttranslational modifications (PTMs), 165
- PPAR γ coactivator. *See* PGC-1 α
- PPARs (proliferator-activated receptors), 175. *See also* PGC-1 α
- PPP (pentose phosphate pathway), 300, 326–327
- Preiss-Handler pathway, 293
- Prolyl hydroxylase-3 (PHD3), 301
- Proprotein convertase subtilisin/kexin type 9 (PCSK9), 132, 133, 135
- Prospero-related homeobox 1 (PROX1), 57, 59
- Protein acetylation. *See* PGC-1 α acetylation
- Protein kinase A (PKA), 168, 204, 408–409
- Proteostasis network (PN), 91. *See also* HSR
- Proteostasis regulators (PRs), 96
- PROX1 (prospero-related homeobox 1), 57, 59
- Psoriasis, 318
- PT (permeability transition) pore, 379, 380
- PTEN (phosphatase tensin homolog), 217, 357, 407
- PTEN-induced putative kinase (PINK1), 8, 302, 399
- PTMs (posttranslational modifications), 165
- Puma, 377–378
- pVHL-defective renal carcinomas, 337
- Pyruvate, 392
- Pyruvate kinase. *See* PK
- Pyruvate kinase M2. *See* PMK2
- ## Q
- Quinazolinecarboxamide (Qc), 189–190, 192–193
- ## R
- R-2HG, 338, 339
- Rapamycin, 243
- Ras/MAPK pathway, 391–394
- RBP2, 340
- Reactive oxygen species (ROS), 81, 304–305
- Reelin, 133
- Restricted feeding (RF), 67–68
- Resveratrol, 160
- Retinoid X receptor (RXR), 129
- REV-erb α , 52, 67
- Ribosomal RNAs (rRNAs), 7
- Ribosomal subunit S6 (rpS6), 141
- RNA-based synthetic devices, 149–150
- ROS (reactive oxygen species), 81, 304–305
- rpS6 (ribosomal subunit S6), 141
- rRNAs (ribosomal RNAs), 7
- RXR (retinoid X receptor), 129
- ## S
- S-adenosyl methionine (SAMe), 37, 225
- SAGA (Spt-Ada-GCN5 acetyltransferase), 404
- Sarcopenia, 101
- Satellite cells
- about, 101
 - enhancement of the function of, 107–108
 - extrinsic changes in aging muscle stem cells, 106
 - intrinsic changes in aging muscle satellite cells, 104–106
 - purpose, 102, 103f
 - regulators of satellite-cell mediated muscle regeneration, 103–104
- SCD (stearoyl coenzyme A desaturase), 225
- SCN (suprachiasmatic nucleus), 17, 31, 32, 39–40

- SDH (succinate dehydrogenase)
 cancer and, 369, 407
 Eg1N prolyl hydroxylases as targets of mutations, 337–338
 non-Eg1N targets of mutations, 338
 Second Law of Thermodynamics, 1
 Signal transduction evolution, 23
 Silencing mediator for retinoid and thyroid receptors (SMRT), 50
 Single-nucleotide polymorphisms (SNPs), 1
 SIRT1. *See also* Sirtuins
 about, 291–292
 circadian clock and, 33–35, 66–68
 control of protein acetylation, 205
 down-regulation of PARP-1 and, 294
 enhancement of the function of satellite cells, 108
 mechanism of modulation, 207
 mediation of calorie restriction, 83–84
 negative regulation of SREBPs, 226
 posttranslational mechanisms regulating, 207–208
 proteins modulating the activity of, 208
 regulation of PGC-1 α by Gen5 and, 198–199
 relationship with PGC-1 α acetylation, 206–208
 Ser434 phosphorylation and, 208
 signaling pathways able to synchronize clocks and, 42–43
 slowing of aging and diseases by, 84–85
 SIRT2, 288, 291. *See also* Sirtuins
 SIRT3. *See also* Sirtuins
 about, 268
 acetylation process and function, 267–268
 activity induced during calorie restriction, 270–271
 deacetylation of mitochondrial proteins during fasting, 269–270
 down-regulation of expression during high-fat feeding, 271–272
 future questions, 273–274
 mitochondrial deacetylase function, 268–269
 mitochondrial dysfunction consequences, 267
 mitochondrial protein acetylation and metabolic regulation, 272–273
 protection against oxidative damage on mitochondria, 85–87
 tumor suppressor role, 86–87
 SIRT6, 229–230, 231. *See also* Sirtuins
 Sirtuins. *See also specific sirtuins*
 about, 81, 268, 291–292, 404–405
 conclusions, 87
 linking of protein acetylation and metabolism
 activation of cellular proteins, 81–82
 glycolysis and, 82–83
 oxidative phosphorylation and, 83
 protein acetylation and, 83
 mediation of calorie restriction, 83–84
 metabolic regulation of muscle stem cells, 106–107
 mitochondrial matrix and, 85–87
 regulation of PGC-1 α by Gen5 and Sirt1, 198–199
 regulation of protein acetylation and, 196
 Skeletal muscle precursor cells (SMPs), 102, 103f
 Skeletal physiology
 conclusions, 282
 genetic basis for endocrine control of bone and energy metabolism, 279–280
 hormonal functions of osteocalcin, 280–282
 Small molecules regulation of HSF-1, 95–97
 SMPs (skeletal muscle precursor cells), 102, 103f
 SMRT (silencing mediator for retinoid and thyroid receptors), 50
 SNAP23, 242
 SNPs (single-nucleotide polymorphisms), 1
 SOD2 (superoxide dismutase), 85–86, 302, 318
 Sodium salicylate, 96
 Somatic mtDNA mutations, 10
 Spt-Ada-GCN5 acetyltransferase (SAGA), 404
 SRC-3 (steroid receptor coactivator protein), 206
 SREBP-2 transcription factor. *See also* Liver X receptors
 cholesterol regulation, 133
 miR-33a/b and, 225–230
 START checkpoint, 358
 Starvation and autophagy, 397–398
 Starvation and the ghrelin-growth hormone axis. *See* Ghrelin
 Stearoyl coenzyme A desaturase (SCD), 225
 Stem cells. *See* Muscle stem cells and aging
 Steroid receptor coactivator protein (SRC-3), 206
 Sterol regulatory element-binding protein. *See* SREBP-2 transcription factor
Structure of Scientific Revolutions, The (Kuhn), 1
 Succinate dehydrogenase (SDH)
 cancer and, 369, 407
 Eg1N prolyl hydroxylases as targets of mutations, 337–338
 non-Eg1N targets of mutations, 338
 Sugar metabolism, 408–409
 Superoxide dismutase (SOD2), 85–86, 302, 318
 Suprachiasmatic nucleus (SCN), 17, 31, 32, 39–40
 Synthetic biology
 about, 145
 cell-signaling regulation systems, 150
 conclusions and outlook, 151–152
 metabolic engineering and, 145–147
 synthetic devices for metabolic dysfunction, 147, 148f
 tool delivery challenges, 150–151
 transcriptional regulation systems, 147, 149
 translational regulation systems, 149–150
 Systems biology, 279
 T
 Tangier disease, 132
 Tap63 α , 78
 Tatum, EL, 403
 TCA (tricarboxylic acid)
 ERR α and, 57
 glucose metabolism and, 318–320
 IDH3 and, 28, 243
 investigations of cycle fluxes, 240–241
 proliferation of tumor cells and, 390
 pyruvate metabolism and, 285, 331–332
 TDH (threonine dehydrogenase), 185–186, 190–192
 Telomere homeostasis, 79
 Testosterone production and osteocalcin, 281–282
 Testosterone supplementation, 108
 TET2 (Tet methyl cytosine dioxygenase 2), 243–244, 338, 407
 TGF signaling, 103–104
 Thioredoxin (TRX), 304, 318
 Thr172, 156, 157
 3T3-L1 adipocytes, 260–264
 Threonine dehydrogenase (TDH), 185–186, 190–192
 TIGAR (Tp53-induced glycolysis and apoptosis regulator), 214–215, 408
 Toll-like receptor 4 (TLR4), 180
 TOR (target of rapamycin). *See* mTOR
 Transfer RNAs (tRNAs), 7
 Tricarboxylic acid. *See* TCA
 Triose phosphate isomerase (TPI), 300–301
 Triterpenoid celastrol, 96
 tRNAs (transfer RNAs), 7
 TRX (thioredoxin), 304, 318
 Tryptophan, 293
 Tuberculosis sclerosis complex (TSC), 336
 Type 2 diabetes, 160
 U
 UBE2D family, 134
 UDP-glucose, 217. *See also* ENTPD5
 Unc-51-like kinase (ULK) complex, 391
 Uridine 5' diphosphate (UDP), 217, 218f, 302. *See also* ENTPD5
 Uridine 5' monophosphate (UMP), 217, 218f, 302. *See also* ENTPD5
 V
 VDAC (voltage-dependent anion channel), 379, 381–382, 399
 Viral infection activation of AMPK, 160–161
 VLDLR, 133
 W
 Warburg effect, 217, 219, 285, 299, 300–301, 303, 320, 336
 Wnt signaling, 104
 X
 Xenobiotic detoxification, 20, 45
 XXX secretory cell, 115–116
 Xylulose-5-phosphate, 408
 Y
 Yeast metabolic cycles (YMC), 197–198

Cold Spring Harbor Symposia on Quantitative Biology

Subject Index

Cold Spring Harb Symp Quant Biol 2011 76: 414-422

Access the most recent version at doi:[10.1101/sqb.2011.76.SI](https://doi.org/10.1101/sqb.2011.76.SI)

License

Email Alerting Service

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article or [click here](#).

To subscribe to *Cold Spring Harbor Symposia on Quantitative Biology* go to:
<http://symposium.cshlp.org/subscriptions>