

Index

A

ABI1, 186
 AC. *See* Adenylyl cyclase
 ACC. *See* Acetyl-CoA carboxylase
 ACE. *See* Angiotensin-converting enzyme
 Acetylation, protein regulation mechanisms, 34–35
 Acetylcholine receptor, nicotinic, 267
 Acetyl-CoA, 170–171, 176–177, 393–394, 434–435
 Acetyl-CoA carboxylase (ACC), 287
 ACL. *See* ATP-citrate lyase
 Acrosome reaction, 336
 ActA, 399
 ACTH. *See* Adrenocorticotrophic hormone
 Actin
 cell migration and polymerization, 184–186
 pathogen modifiers
 elongation factors, 400
 nucleation factors, 399–400
 Activators of G-protein-mediated signaling (AGSs), 14
 ADAM1b, 336
 ADAM2, 336
 ADAM3, 336
 ADAM10, 111
 ADAM17 (TACE), 111
 Adenylyl cyclase (AC), 99–101, 335
 Adiponectin, energy homeostasis role, 281
 Adipose tissue triglyceride lipase (ATGL), 289
 Adrenocorticotrophic hormone (ACTH), energy homeostasis role, 278
 AF2, 130–131
 AGS proteins, 14
 AGSs. *See* Activators of G-protein-mediated signaling
 AKAPs. *See* A-kinase anchoring proteins
 A-kinase anchoring proteins (AKAPs), 43, 53–54, 101, 254, 335
 Akt
 cancer signaling, 408–416, 418–421
 glucose metabolism signaling
 G-protein-coupled receptor signaling, 13
 lymphocyte signaling, 321–323
 lymphocyte signaling, 322
 mTORC1 target, 175
 phosphoinositide, 3-kinase pathway overview, 87–89
 PI3K/Akt, 168, 170–171
 PIP₃ signaling, 57–59
 subcellular localization, 42
 ALDH1A1, 335
 α -Catenin, 20, 136
 AMBRA1, 378
 Amino acids, metabolism signaling cascades, 173, 175
 2-Amino-3-(3-hydroxy-5-methyl-isoxazol-4-yl) propanoic acid receptor (AMPA), learning and memory role, 249–251, 253, 256
 AMPAR. *See*, 2-Amino-3-(3-hydroxy-5-methyl-isoxazol-4-yl) propanoic acid receptor
 AMPK
 energy homeostasis role, 278–279, 283–284, 287, 289
 mTORC1 regulation, 176

Amyloid- β , 295
 Anaphase. *See* Mitosis
 Angiogenesis, cancer, 420
 Angiomotin, 135
 Angiotensin receptor, 273
 Angiotensin-converting enzyme (ACE), 273
 API, 318
 APAF1, 368, 376–377
 APC, 411
 Apoptosis
 cancer, 412
 caspases
 activation, function, and regulation, 367–368, 376
 caspase-1/-5/-11 activation in inflammasome pathway, 374
 caspase-2 activation in PIDDosome pathway, 374–375
 caspase-8 activation in death receptor pathway, 371, 373–374
 caspase-9 activation in mitochondrial pathway, 368–371
 kinases, 375
 overview, 366–367
 TNFR1 induction, 303
 Approximated, 134
 Arp2/3, 186, 255, 305, 399–400
 Arpp19, 155
 ASC, 300, 374
 ASK1, 351
 ATF1, 101
 ATF2, 349
 ATF4, 349
 ATF6, unfolded protein response, 347–349
 ATG proteins. *See* Autophagy
 ATM, 417
 DNA damage checkpoint, 158–159
 recruitment, 35
 ATP-citrate lyase (ACL), 414
 ATR, DNA damage checkpoint, 158–159
 Aurora B, 41
 Autophagy
 cell death role, 379
 signaling overview, 366, 377–379

B

Bacteria. *See* Infection
 Bad, 372, 378
 BAFF, 319–320, 322
 Bak, 369
 Bax, 369
 B-cell receptor (BCR)
 adaptor molecules, 316
 ITAM, 315–316
 signaling
 calcium, 316–317
 diacylglycerol, 316–318
 ERK1/2, 319
 inhibitory signals, 323
 nuclear factor of activated T cells, 317–318
 overview, 125–127, 317

 protein kinase C, 318–319
 Ras, 319
 structure and function, 314–315
 Bcl2, 356, 367, 369–371, 378–379, 412
 BCL6, 334
 Bcl10, 307, 319
 BCR. *See* B-cell receptor
BCR-ABL, 407
 Beclin, 1, 378–379
 BEN. *See* Biased excitable network
 β -Arrestin, G-protein-coupled receptor complex, 14, 107
 β -Catenin, 20, 104, 417
 β -TrCP, 370
 Biased excitable network (BEN), 193
 Bid, 370, 372
 BIK, 372
 Bim, 356, 370, 372, 412
 BK channel, 62
 BLNK, 316
 Bmf, 356, 373
 BMP. *See* Bone morphogenetic protein
 Bnip3, 373, 378
 BOC, 107
 Bone morphogenetic protein (BMP)
 BMPRII, 114
 embryonic patterning, 223, 225
 signaling overview, 113–114
 BRCA, 418
 Brinker, 226

C

Cadherins, signaling, 20
 Calcineurin, learning and memory role, 253–254
 Calcium
 binding motifs, 61
 buffering, 61–62
 channels and regulation of levels, 61
 history of study, 95–96
 lymphocyte signaling, 316–317
 signaling overview, 59–61, 95–97
 smooth muscle sensitization, 273
 spatiotemporal organization of signaling, 62
 termination of signal, 62
 Calcium/calmodulin-dependent protein kinase II (CaMKII), learning and memory role, 251–253, 258
 Calcium-induced calcium release (CICR), 62, 269
 Calcium release-activated channel (CRAC), 305, 316–317
 Calmodulin (CaM), calcium signaling, 97
 Calsequestrin (CSQ), 268–269, 271
 CaM. *See* Calmodulin
 CAMKII, caspase activation role, 375
 CaMKII. *See* Calcium/calmodulin-dependent protein kinase II
 cAMP. *See* Cyclic AMP
 CAMs. *See* Cell adhesion molecules
 Cancer
 cell polarity signaling, 210
 dysregulation
 angiogenesis, 420

Index

- Cancer (*Continued*)
- apoptosis, 412
 - cell fate and differentiation, 417
 - cell migration, 415–417
 - cell polarity, 415–417
 - cell proliferation, 409–412
 - extracellular matrix, 418
 - genomic instability, 417–418
 - inflammation, 420–421
 - metabolism, 412–415
 - microenvironment, 418
 - fibroblasts, 421
 - gene mutations
 - overview, 407
 - signaling pathways, 407–408, 419
 - inflammation, 307
 - progression, 406–407
 - prospects for study, 421–422
- CAR. *See* Constitutive active/androstane receptor
- Carbohydrate. *See* Glucose, metabolism signaling
- Carbon monoxide (CO), signal transduction, 25
- Carboxy-terminal Src kinase (CSK), 315
- Cardiac muscle. *See* Muscle contraction
- Carma1, 319
- Carnitine:palmitoyl transferase (CPT), 284
- Casein kinase II (CK2), 370
- Caspases. *See* Apoptosis; Necrosis
- Catecholaminergic polymorphic ventricular tachycardia (CPVT), 271
- CATSPER, 336
- Caveolae, signaling, 43
- Cbl, 8
- Cdc2, 146, 153
- Cdc4, 145
- Cdc13, 146
- Cdc20, 148, 160–161
- Cdc25, 155, 157–159, 330
- Cdc34, 146
- Cdc42, 82, 354, 368, 98
 - cell migration role, 186, 188
 - cell polarity role, 200–201, 207
- CDKs. *See* Cyclin-dependent kinases
- CDO, 107
- Cdr2, 157
- C/EBP α , 131
- C/EBP β , 297
- CED3, 376
- CED4, 376
- CED9, 376
- Cell adhesion molecules (CAMs). *See also specific molecules*
- cadherin-dependent adhesions, 20
 - signaling, 19–21
- Cell cycle
- cancer, 409–412
 - cyclin-dependent kinase inhibitors
 - overview, 143–144
 - transcriptional regulation by inhibitors, 144–145
 - G₁ regulation
 - cyclin D, 141–142
 - cyclin E, 142–143
 - cyclin-dependent kinases, 141, 143
 - retinoblastoma protein, 140–141
 - ubiquitinylation, 145–147, 147–148
 - G₂/M transition. *See* Mitosis
 - meiosis. *See* Meiosis
 - overview, 140–141
- Cell fate. *See* Cancer; Embryonic patterning, *Drosophila*
- Cell migration
- actin polymerization, 184–186
 - adhesions, 186–188
 - cancer, 415–417
 - chemotaxis signaling
 - adaptation and excitation–global inhibition models, 193
 - excitability of networks, 192–193
 - myosin contraction, 186
 - overview, 184
 - polarization, 188
 - prospects for study, 193–195
 - signaling
 - focal adhesion kinase, 188–189
 - genetic analysis, 191–192
 - paxillin, 188–189
 - phosphoinositide, 3-kinase, 189–191
 - Rho GTPases, 188
- Cell polarity. *See also* Par proteins
- cancer, 415–417
 - cell migration, 188
 - machinery
 - intercellular junctions, 203
 - Par proteins, 202–203
 - symmetry breaking and positive-feedback loops, 200–202
 - Par protein localization
 - active exclusion, 205–207
 - membrane phospholipid attachment, 204
 - membrane protein anchoring, 204–205
 - messenger RNA localization, 205
 - oligomerization, 204
 - signaling
 - cancer, 210
 - Hippo pathway, 209–210
 - overview, 200
 - Par3–Par6–protein kinase C signaling, 207–209
 - Wnt signaling cross talk, 209
- Ceramide
- hydrolysis, 59
 - signaling overview, 56
 - stress response, 59
- cGMP. *See* Cyclic GMP
- CHBP, 400
- Chemotaxis. *See* Cell migration
- Chk1, 158–159, 417
- Chk2, 158–159, 417
- Cholecystokinin, receptor, 273
- Cholera toxin, 390
- Cholesterol
- Hedgehog coupling, 107
 - liver metabolism, 287–289
- CHOP, 350, 352
- CICR. *See* Calcium-induced calcium release
- Cif, 400
- CIN85, 316
- CK1, 317
- CKII. *See* Casein kinase II
- CKS1, 147
- Cks1, 434
- Clb5, 146, 434
- Cln2, 434
- CO. *See* Carbon monoxide
- Colony-stimulating factor, 1 (CSF1), 420
- Complement, C5A receptor in innate immunity, 304–305
- Computational models, signaling networks
- dynamical models, 71–72
 - graph theory for signaling network models, 69, 72–74
 - network models, 70–71
- Constitutive active/androstane receptor (CAR), 23–24
- Cortisol, energy homeostasis role, 278–279
- Cos, 107
- COX2, 297
- CPI-17, 273
- CPT. *See* Carnitine:palmitoyl transferase
- CPVT. *See* Catecholaminergic polymorphic ventricular tachycardia
- CRAC. *See* Calcium release-activated channel
- Crb2, 159
- CRE. *See* Cyclic AMP response element
- CREB, 274, 297, 334
- CRIB domain, 398
- Crk, 8
- CRL4, 148
- Crumbs, 135, 204, 416
- CSF. *See* Cytostatic factor
- CSF1. *See* Colony-stimulating factor, 1
- CSK. *See* Carboxy-terminal Src kinase
- CSL complex, 110–111
- CSQ. *See* Calsequestrin
- CTLA4, 319, 323
- Ctp1, 158
- Cyclic AMP (cAMP)
- G-protein-coupled receptor signaling, 13, 53
 - muscle relaxation, 265
 - phosphodiesterases, 55
 - protein kinase A as target, 53–54
 - signaling overview, 99–101
 - targets, 55
- Cyclic AMP response element (CRE), 287
- Cyclic GMP (cGMP)
- muscle relaxation, 265
 - phosphodiesterases, 55
 - protein kinase G as target, 55
 - targets, 55
- Cyclic GMP-dependent protein kinase (PKG), 55
- Cyclin B, mitosis entry role, 154–156
- Cyclin D
- G₁ regulation, 141–142
 - ubiquitinylation, 145–147
- Cyclin-dependent kinases (CDKs)
- activating kinase, 154
 - CDK1
 - activation in mitosis entry, 152–157
 - caspase activation, 375–377
 - oocyte maturation role, 331
 - G₁ entry regulation, 141
 - inhibitors
 - overview, 143–144
 - transcriptional regulation
 - INK4, 144–145
 - p21, 144
 - posttranscriptional regulation, 143
- Cyclin E, G₁ regulation, 142–143
- Cyclophilin D (CypD), 380
- Cyclosporin A, 318
- CYLD, 380
- CypD. *See* Cyclophilin D
- Cytochrome c, 376
- Cytokine receptor family, overview, 4, 6
- Cytokinesis, mitosis coordination, 161–162
- Cytostatic factor (CSF), 328
- D**
- Dachsous, 134
- DAI, 380
- Dcn1, 434
- DCP1, 376
- Death receptors. *See specific receptors*
- Deltex, 110
- Development. *See* Embryonic patterning, *Drosophila*
- Diabetes type, 2, overnutrition, 289–290
- Diaclyglycerol (DAG)
- lymphocyte signaling, 316–318
 - muscle calcium sensitization, 273

- protein kinase C as target, 55, 57
signaling overview, 57
- DIAP1, 376
- DISC, 374
- Discs large, 135
- DKK, 104
- Dlg, 204
- DLG1, 57
- DNA damage checkpoint, 157–159
- DNA-PK, DNA damage checkpoint, 158
- DNA replication checkpoint, 159
- DNMT1, 407
- DOCK180, 19
- Dock2, 305
- Dorsal, 217
- Double-strand break (DSB), 157–158
- Double-stranded RNA-dependent kinase (PKR), 349, 351
- DrrA, 398
- DSB. *See* Double-strand break
- DUSP, 355
- E**
- E2F, 141, 143
- E4orf6, 401
- E-cadherin, 20
- Ect1, 207
- EGF. *See* Epidermal growth factor
- eIF2, 349
- Electron microscopy, signaling studies, 430
- Elk1, 40
- Embryonic patterning, *Drosophila*
induction of cell fate, 216
signaling
bone morphogenetic protein, 223, 225
epidermal growth factor, 222–224, 229
fibroblast growth factor, 222–223, 229
Hedgehog, 222, 225
integration of pathways, 227–230
linear signaling, 226
long-range ligand distribution, 225–226
negative-feedback switches, 226
Notch, 220–222
overview, 216–218
threshold generation, 226–227
Wnt, 225
transcriptional cascade interactions with
signaling, 217, 219
- Emi2, 331, 338
- EMT. *See* Epithelial-to-mesenchymal transition
- Endoplasmic reticulum. *See* Unfolded protein response
- Endoplasmic reticulum stress element (ERSE), 347
- Endosomal sorting complex required for transport (ESCRT), 9, 111
- Energy homeostasis. *See also* Fatty acid metabolism;
Glucose, metabolism signaling
AMPK role, 278–279, 283–284, 287, 289
brown adipose tissue fatty acid oxidation, 289
diabetes type, 2 and insulin resistance, 289–290
hormonal control
adipose tissue, 281
adrenal gland, 278
hypothalamic-pituitary axis, 278
pancreas, 280
thyroid gland, 279–280
- liver
carbohydrate metabolism acute regulation,
284–286
gluconeogenesis long-term regulation, 286–287
lipid metabolism, 287–289
- muscle
exercise adaptation, 284
- fatty acid oxidation, 284
- glucose uptake and glycogen synthesis,
282–284
- glycogen breakdown, 281–282
- prospects for study, 290–291
- ENTPD5, 168
- EphB6, 8
- Epidermal growth factor (EGF)
embryonic patterning, 222–224, 229
receptor
cancer, 9
dimerization, 7
phosphorylation, 433
- Epithelial-to-mesenchymal transition (EMT),
cancer, 416–417
- EPSP. *See* Excitatory postsynaptic potential
- ERK. *See* Extracellular signal-regulated kinase
- ERO1, 349
- ERR. *See* Estrogen-related receptor
- ERSE. *See* Endoplasmic reticulum stress element
- ESCRT. *See* Endosomal sorting complex required
for transport
- E-selectin, innate immunity role, 303–304
- EspG, 398
- Estrogen-related receptor (ERR), 21, 23
- Ets, 334
- Excitatory postsynaptic potential (EPSP), 248
- ExoS, 396
- Extracellular signal-regulated kinase (ERK)
cancer signaling, 408–410, 412, 415–416, 418, 421
development role, 223, 226–227, 230
learning and memory role, 258
lymphocyte signaling, 319
lymphocyte signaling by ERK1/2, 319
overview, 81–82
stress signaling
activation cascade, 354–355
inactivation, 355
overview, 353–354
physiological roles
cell death, 356
inflammation, 356–357
metabolism, 357
scaffold protein function, 355–356
substrates, 41
- F**
- FADD, 16, 300, 302–303, 373–374
- FAK. *See* Focal adhesion kinase
- Far1, 146
- Farnesoid X receptor (FXR), 23
- Fas, 15
- Fat, 134
- Fatty acid metabolism
brown fat oxidation, 289
muscle oxidation, 284
- FBW7, 146
- Fbxo proteins, 146
- Fc receptors
FcεR1 and immunoglobulin E binding, 316
innate immunity
FcεRI, 305–307
FcγR, 307
- Fertilization. *See* Reproduction
- FGF. *See* Fibroblast growth factor
- Fibroblast growth factor (FGF)
cancer dysregulation, 417
embryonic patterning, 222–223, 229
receptor
dimerization, 7
stabilization, 40
- FIDOP domain, 397
- FIP200, 379
- FK506, 318
- FKBP12, 430
- FLIP, 303, 373–375, 380, 412
- Fluorescence resonance energy transfer (FRET),
signaling studies, 429
- FNDC5, 437
- Focal adhesion kinase (FAK), 18, 20, 188–189, 418
- Follicle-stimulating hormone (FSH), 334–335
- Formyl peptide receptor (FPR), innate immunity,
304–305
- 4E-BP1, 44
- Fos, 41, 274
- Foxo
cancer signaling, 414–415
FOXO1, 87
FOXO3A, 371
lymphocyte signaling, 322
- FPR. *See* Formyl peptide receptor
- FRET. *See* Fluorescence resonance energy transfer
- Frizzled, 10, 103, 209
- FSH. *See* Follicle-stimulating hormone
- FUNDC1, 379
- Fus3, 146
- FXR. *See* Farnesoid X receptor
- Fyb, 392
- Fyn, 20
- G**
- G protein
GTPase cycle, 37
heterotrimeric G proteins, 38–39
receptor specificity, 11–12
small G proteins, 37–38
- G-protein-coupled receptors (GPCRs)
activation, 11
classes and structure, 10–11
G-protein specificity, 11–12
guanine nucleotide exchange factors, 37, 39
innate immunity, 304–305
kinase networks, 13–14
ligand-induced conformational change, 12–13
lipid messengers, 57
overview, 10
pathogen signaling corruption in host
bacteria protein mimics
G proteins, 398
GTPase-activating proteins, 396
guanine-nucleotide exchange factors,
395–395
G-protein modifiers, 397–398
overview, 395
Yersinia, 396–397
protein–protein interactions, 14
second messengers, 13
sensory receptors. *See* Sensory receptors
signal integration, 15
signal termination, 14–15
- G₁. *See* Cell cycle
- G₂/M transition. *See* Mitosis
- GADD34, 350
- GADD45, 355
- GATA4, 269
- Gcn5, 176, 284
- GDNF. *See* Glial-derived neurotrophic factor
- Genomic instability, cancer, 417–418
- Germ-cell nuclear receptor, 24
- Germinal vesicle breakdown (GVBD), 330
- GFP. *See* Green fluorescent protein
- GFRA1, 334

Index

- GH. *See* Growth hormone
 Gli1, 107–108
 Gli2, 107
 Gli3, 107
 Glial-derived neurotrophic factor (GDNF), 8, 333–334
 Glucocorticoid response element (GRE), 286
 Glucose
 liver
 carbohydrate metabolism acute regulation, 284–286
 gluconeogenesis long-term regulation, 286–287
 metabolism signaling
 cancer, 412–415
 endoplasmic reticulum signals, 351–353
 hypoxia-inducible factor, 1, 171–173
 PI3K/Akt, 168, 170–171
 pyruvate kinase metabolic switch, 173–174
 muscle uptake and glycogen synthesis, 282–284
 transporters, 168, 282, 284
 Glycogen, muscle
 breakdown, 281–282
 glucose uptake and synthesis, 282–284
 Glycosylation, protein regulation mechanisms, 36–37
 GPCRs. *See* G-protein-coupled receptors
 GPR3, 329
 Graph theory, signaling network models, 69, 72–74
 Grb2, 18, 320
 GRE. *See* Glucocorticoid response element
 Green fluorescent protein (GFP), signaling studies, 428
 Growth hormone (GH), receptor dimerization, 7
 GRP78, 347, 351
 GRP94, 347
 GSK3, 104, 145–146, 284, 317, 370, 411, 433
 Guanylyl cyclase, 24–25
 Gustation. *See* Sensory receptors
 GVBD. *See* Germinal vesicle breakdown
- H**
 H2AX, 158–159
 HAT. *See* Histone acetyltransferase
 HCN. *See* Hyperpolarization-activated cyclic nucleotide-gated channel
 HDAC. *See* Histone deacetylase
 Hearing. *See* Sensory receptors
 Heart failure. *See* Muscle contraction
 Hedgehog (Hh)
 embryonic patterning, 222–223, 225
 signaling overview, 107–108
 Heme oxygenase (HO), 25
 Hemese, embryonic patterning, 219–220
 HES1, 227
 Hexokinase, 168
 Hh. *See* Hedgehog
 HIF1. *See* Hypoxia-inducible factor, 1
 Hippo
 cell polarity signaling, 209–210
 signaling overview, 131–136
 Histone acetyltransferase (HAT), 35
 Histone deacetylase (HDAC), 35, 130, 268
 HMG-CoA reductase, 287–288
 HMGB1, 294
 HNF4, 131
 Hormone-sensitive lipase (HSL), 289
 HRK, 373
 HSL. *See* Hormone-sensitive lipase
 HuR, 356
 2-Hydroxyglutarate aciduria, 176–177
 Hyperpolarization-activated cyclic nucleotide-gated channel (HCN), 55
 Hypoxia-inducible factor, 1 (HIF1)
 glucose metabolism signaling, 171–171
 oxygen signaling, 24
- I**
 ICAM. *See* Intercellular cell adhesion molecule
 ICPO, 400–401
 IDH. *See* Isocitrate dehydrogenase
 IKK, 45, 123, 297–299, 303, 307, 351, 393
 induced genes, 298
 Toll-like receptor activation, 295–297
 IL-2 receptor, 320–321
 IL-3
 metabolism regulation, 176
 receptor, 176
 IL-4 receptor, 321
 IL-7 receptor, 322
 IL-12 receptor, 320
 ILK. *See* Integrin-linked kinase
 Immunoreceptor tyrosine activation motif (ITAM), 303, 315–317
 Immunoreceptor tyrosine inhibition motif (ITIM), 323
 Infection
 actin modifiers
 elongation factors, 400
 nucleation factors, 399–400
 bacteria virulence factors, 390–392
 G-protein-coupled receptor signaling corruption
 overview, 395
 bacteria protein mimics
 G proteins, 398
 GTPase-activating proteins, 396
 guanine-nucleotide exchange factors, 395–395
 G-protein modifiers, 397–398
 Yersinia, 396–397
 lipid signaling highjacking, 398–399
 mitogen-activated protein kinase signaling corruption
 anthrax, 393
 overview, 392
 Shigella, 394
 Yersinia, 393–394
 oncoproteins of viruses, 390
 ubiquitylation disruption, 400–401
 Inflammation
 cancer, 307, 420–421
 caspase-1/-5/-11 activation in inflammasome
 pathway of apoptosis, 374
 mitogen-activated protein kinase stress signaling, 356–357
 unfolded protein response, 350–351
 Information flow, signaling networks
 computational models. *See* Computational models, signaling networks
 contextual nature of information, 75
 emergent properties of networks
 bistability, 74
 oscillations, 75
 redundancy, 75
 ultrasensitivity, 74
 graph theory models, 69, 72–74
 networks of pathways, 66, 68–69
 noise filtering, 76
 overview, 66–67
 versatility of responses, 75–76
 INK4, transcriptional regulation, 144–145
 Innate immunity. *See also specific receptors*
 E-selectin, 303–304
 Fc receptors
 FcεRI, 305–307
 FcγR, 307
 G-protein-coupled receptors, 304–305
 inflammation and cancer, 307
 integrin receptors, 303–304
 Nod-like receptors, 300
 pattern recognition receptor ligands, 294–295
 RIG-I-like receptors, 298–300
 TNFR1 signaling
 cell death induction, 303
 MAPK, 301–303
 nuclear factor-κB, 301–303
 Toll-like receptor
 interferon induction, 297–298
 ligands, 295
 TAK1 and IKK activation, 295–296
 TLR4 signaling, 296
 TRIF in signaling, 298
 Inositol hexaphosphate (IP₆), 57
 Inositol tetraphosphate (IP₄), 57
 Inositol-requiring enzyme, 1 (IRE1), unfolded protein response, 347–348, 350
 Inositol trisphosphate (IP₃)
 G-protein-coupled receptor signaling, 13, 57, 96
 receptors, 60, 273, 337
 Insulin
 energy homeostasis role, 280
 resistance and overnutrition, 289–290
 response unit, 287
 Insulin receptor substrate (IRS), 87
 Integrin receptors
 innate immunity, 303–304
 ligands, 18
 mechanosensing signaling, 17–19
 Integrin-linked kinase (ILK), 18–19, 189
 Intercellular cell adhesion molecule (ICAM), 17, 303
 IP₃. *See* Inositol trisphosphate
 IP₄. *See* Inositol tetraphosphate
 IP₆. *See* Inositol hexaphosphate
 IpgD, 398–399
 IRAK1, 123, 295, 298
 IRE1. *See* Inositol-requiring enzyme, 1
 IRF1, 298
 IRF7, 297–298, 401
 IRS. *See* Insulin receptor substrate
 IRS1, 351
 Ishihara test, 243
 Isocitrate dehydrogenase (IDH), 176, 178–179, 407, 415, 436
 ITAM. *See* Immunoreceptor tyrosine activation motif
 ITIM. *See* Immunoreceptor tyrosine inhibition motif
 IZUMO, 336
- J**
 JAK/STAT signaling
 cytokine signaling in lymphocytes, 320–321
 overview, 117–119
 JAM. *See* Junctional adhesion molecule
 Janus kinase. *See* JAK/STAT signaling
 JIP1, 356
 JIP2, 356
 JIP3, 356
 JIP4, 356
 JNK. *See* Jun N-terminal kinase
 Jun N-terminal kinase (JNK)
 overview, 82–83
 stress signaling
 activation cascade, 354–355
 inactivation, 355
 overview, 353–354
 physiological roles
 cell death, 356
 inflammation, 356–357
 metabolism, 357

- scaffold protein function, 355–356
 Junctional adhesion molecule (JAM), 204–205
- K**
 KIP1, 147
 Kit, 9, 334
 KitL. *See* Stem cell factor
 KSR1, 356
 Ku70, 158
 Ku80, 158
- L**
 Lactate dehydrogenase (LDH), 414
 LAMP1, 378
 LAMP2, 378
 LAT, 126, 316
 LATS kinases, 162
 LC3, 379
 Lck, 315
 LDH. *See* Lactate dehydrogenase
 Learning and memory
 GTPases in synaptic plasticity, 257–259
 Hebbian behavior of synapses, 248–249
 postsynaptic density scaffold proteins, 254–256
 prospects for study, 259
 spine synapse signaling in brain
 2-amino-3-(3-hydroxy-5-methyl-isoxazol-4-yl)propanoic acid receptor, 249–251, 253, 256
 calcium-regulated signaling in postsynaptic density
 calcium/calmodulin-dependent protein kinase II, 251–253, 258
 calcineurin, 253–254
 N-methyl-D-aspartate receptor, 249–251
 overview, 249–251
 LEF/TCF, 114
 LEGI model, 193
 Leptin, 281
 Lethal factor, anthrax, 393
 Leukotrienes, signaling overview, 59
 Leydig cell, 332
 Lgl, 204–205, 210
 LGP2, 298–299
 LH. *See* Luteinizing hormone
 LIM kinase, 186
 Linear ubiquitin chain assembly complex (LUBAC), 295, 303
 Lipid raft, signaling, 43
 Lipids. *See* Fatty acid metabolism; *specific lipids*
 Liver X receptor (LXR), 23, 130–131
 LKB1, 415
 LMP1, 407
 Long-term depression (LTD), 249, 251–253
 Long-term potentiation (LTP), 249
 Lowfat, 134
 LRP4, 8
 LRP6, 228
 LTD. *See* Long-term depression
 LTP. *See* Long-term potentiation
 LUBAC. *See* Linear ubiquitin chain assembly complex
 Luteinizing hormone (LH), 334
 LXR. *See* Liver X receptor
- M**
 MAD, 134, 227
 Magnesium
 signaling overview, 59–60, 62–63
 transport, 63
 MAGUKS, 254
 MALT1, 307, 319, 420
 MAM. *See* Mitochondria-associated endoplasmic reticulum membrane
 MAML, 111
 Mammalian target of rapamycin (mTOR)
 complexes. *See* mTORC1; mTORC2
 G-protein-coupled receptor signaling, 13
 history of study, 92–93
 MAPK. *See* Mitogen-activated protein kinase
 Maturation promoting factor (MPF), 328, 330
 MCC. *See* Mitotic checkpoint complex
 Mcl1, 356, 369–370, 379, 412
 Mdc1, 158
 mDia1, 186, 305
 mDia2, 186
 MDM2, 43–44, 411
 Mechanosensation. *See* Sensory receptors
 MEF2, 219, 268
 Meiosis
 oocyte
 meiosis I, 328–331
 meiosis II arrest, 331–332
 spermatocyte meiosis and release, 335
 Memory. *See* Learning and memory
 MEN. *See* Mitotic exit networks
 Messenger RNA (mRNA), stability, 44
 Met1, 434
 Methylation, protein regulation mechanisms, 35–36
 MGA5, 298–300
 MHCK. *See* Myosin heavy-chain kinase
 MicroRNA, signaling, 44
 Microtubule-organizing center (MTOC), 188, 318
 Migration. *See* Cell migration
 Mitochondria-associated endoplasmic reticulum membrane (MAM), 346–347
 Mitochondrial outer membrane permeabilization (MOMP), 368–371, 376
 Mitogen-activated protein kinase (MAPK).
 See also specific kinases
 activation, 35
 cascade, 81
 classification, 81–83
 computational models, 72–73
 cyclin D transcription control, 141
 development role, 217
 embryonic patterning, 217
 G-protein-coupled receptor signaling, 13
 interacting kinases, 410–411
 learning and memory role, 258
 motifs, 40
 pathogen signaling corruption in host
 anthrax, 393
 overview, 392
 Shigella, 394
 Yersinia, 393–394
 scaffolds, 43, 85
 stress signaling
 activation cascade, 354–355
 inactivation, 355
 overview, 353–354
 physiological roles
 cell death, 356
 inflammation, 356–357
 metabolism, 357
 scaffold protein function, 355–356
 subcellular localization, 41
 synaptic plasticity role, 258
 TNFR1 signaling, 301–303
 unfolded protein response, 346
 Mitosis
 anaphase entry, 160
 CDK1 activation, 152–157, 160
 cytokinesis coordination, 161–162
 DNA damage checkpoint, 157–159
 DNA replication checkpoint, 159
 G₂/M transition regulation, 157
 network dissection, 160
 spindle assembly checkpoint, 160–161
 table of proteins in control, 154
 transitions, 152–153
 Mitotic checkpoint complex (MCC), 161
 Mitotic exit network (MEN), 161–162
 MLCK. *See* Myosin light-chain kinase
 MLCP. *See* Myosin light-chain phosphatase
 MLKL, 303, 380
 MMSET, 36
 Modularity, signaling studies, 431–432
 MOMP. *See* Mitochondrial outer membrane permeabilization
 Mos, 330–331
 M-phase promoting factor (MPF), 153
 MPE. *See* Maturation promoting factor; M-phase promoting factor
 Mrc1, 150
 MRN complex, 158
 mRNA. *See* Messenger RNA
 MscC, 238
 MscL, 238–239, 245
 MscS, 238–239
 MSK1, 303, 394
 MSK2, 394
 MTOC. *See* Microtubule-organizing center
 mTOR. *See* Mammalian target of rapamycin
 mTORC1, 88, 174–175
 activation and regulation, 88, 92–93, 176
 metabolic signaling, 178
 translational control, 44
 unfolded protein response studies, 350
 mTORC2, 92–93, 175
 Muscle contraction
 cardiac muscle
 contraction, 269
 heart failure, 271
 hypertrophy
 exercise-induced, 269–270
 pathophysiological, 270–271
 energy homeostasis
 exercise adaptation, 284
 fatty acid oxidation, 284
 glucose uptake and glycogen synthesis, 282–284
 glycogen breakdown, 281–282
 signaling overview, 264–266
 skeletal muscle
 contraction, 266–268
 fiber types and exercise response, 268–269
 malignant hyperthermia, 269
 smooth muscle
 calcium sensitization, 273
 contraction, 272–273
 types, 271
 vascular disease, 273–274
 Myc, 41, 173, 408, 411, 415, 418
 MyD88, 123, 295–298, 300
 Myopic, 134
 Myosin
 cell migration and contraction, 186
 myosin II, 186
 Myosin heavy-chain kinase (MHCK), 191
 Myosin light-chain kinase (MLCK), 186, 265, 268, 273, 304
 Myosin light-chain phosphatase (MLCP), 265, 273
 MYPT1, 273

Index

- Myristoylation, membrane proteins, 42
Myt1, 330
- N**
- NBR1, 379
Nbs1, 158
NCAM. *See* Neural cell adhesion molecule
Nck, 8, 189
NCS1, 271
Necrosis
 caspase control, 380
 excitotoxicity, 381
 Nox1 induction, 380–381
 overview, 366
 types, 379–380
Nedd4, 110, 113
Nedd8, 45
Nek2, 41
NEMO, 45, 123
Nerve growth factor (NGF), receptor dimerization, 7
Neural cell adhesion molecule (NCAM), signaling, 20–21
Neuromuscular junction (NMJ), 267
NF- κ B. *See* Nuclear factor- κ B
NF1, 411
NF2, 134
NFAT. *See* Nuclear factor of activated T cells
NGF. *See* Nerve growth factor
Nitric oxide (NO)
 muscle relaxation, 265
 signal transduction, 24–25, 37
Nitrosylation, protein regulation mechanisms, 37
NIX, 373, 379
NLR. *See* Nod-like receptor
NLRC4, 300, 303
NLRP1, 300, 303
NLRP3, 300, 303, 351
NMDAR. *See* N-Methyl-D-aspartate receptor
N-Methyl-D-aspartate receptor (NMDAR), learning and memory role, 249–251
NMJ. *See* Neuromuscular junction
NO. *See* Nitric oxide
Nod-like receptor (NLR), signaling, 300
NOD1, 300
NOD2, 300
Noise filtering, signaling networks, 76
Notch
 development role, 220–221
 embryonic patterning, 220–222
 intracellular domain, 111–112, 220
 proteolysis and activation, 9–10
 signaling overview, 109–111
Nox1, necrosis induction, 380–381
Noxa, 372
NPAS2, 25
NR4A receptors, 24
NR5A receptors, 24
NRF1, 284
NRF2, 284
NSK1, 303
Nuclear factor of activated T cells (NFAT), 127, 268, 274, 307, 317–318, 416
Nuclear factor- κ B (NF- κ B)
 induced genes, 298
 lymphocyte signaling, 127
 TLR signaling, 297
 TNFR1 signaling, 301–303
Nuclear receptors. *See also specific receptors*
 activation, 21
 classification, 21–22
 orphan receptors, 24
 overview, 21, 129–132
 promoter binding
 heterodimers, 22
 homodimers, 22
 monomers, 22–23
 structure, 21–22, 130
 types, 23–24, 130
Numb, cell polarity role, 207–207
- O**
- Oct4, 173
Odd paired, embryonic patterning, 219
Olfaction. *See* Sensory receptors
Omi, 369
Oocyte. *See also* Reproduction
 activation on fertilization, 336–338
 maturation
 meiosis I, 328–331
 meiosis II arrest, 331–332
 overview, 328
OSM, 356
OspF, 394
Oxidative stress, unfolded protein response, 349
Oxygen, signal transduction, 24
- P**
- p16, 144–145, 411
p18, 144–145
p21, 144, 143–144, 146–148, 411, 417
p27, 144, 411
p38 stress-activated protein kinase (SAPK)
 cell cycle checkpoint, 159
 overview, 84–85
 stress signaling
 activation cascade, 354–355
 inactivation, 355
 overview, 353–354
 physiological roles
 cell death, 356
 inflammation, 356–357
 metabolism, 357
 scaffold protein function, 355–356
p53, 43–44, 417, 420
p57, 144, 147
PAK, 113, 189, 258, 398
PAK2, 368
PAK3, 193
Palmitoyl acyltransferase (PAT), 42
Palmitoylation, membrane proteins, 42–43
Pals1, 204
PAR1. *See* Protease-activated receptor, 1
Par proteins
 cell polarity role, 202–203
 localization
 active exclusion, 205–207
 membrane phospholipid attachment, 204
 membrane protein anchoring, 204–205
 messenger RNA localization, 205
 oligomerization, 204
 Par1, 205
 Par2, 202
 Par3, 202–203, 205–208
 Par3–Par6–protein kinase C signaling, 207–209
 Par5, 205
 Par6, 202–208
Parvin, 189
PAT. *See* Palmitoyl acyltransferase
Patched, 107–108
Pathogens. *See* Infection
Patj, 204, 210
PAX2, 229
Paxillin, cell migration role, 188–189
PCNA, 411
PD-1, 319
PDEs. *See* Phosphodiesterases
PDGF. *See* Platelet-derived growth factor
PDK. *See* Pyruvate dehydrogenase kinase
PEA15, 355
Peli1, 298
PEPCK. *See* Phosphoenolpyruvate carboxykinase
PERK, 347–348, 350, 352
Perlipin1, 289
Permeability transition pore (PTP), 63
Peroxisome proliferator-activated receptor (PPAR), 23, 132
PFK. *See* Phosphofructokinase
PGC1 α , 268, 270, 274, 284
PHAPI, 371
PHD. *See* Prolyl hydroxylase
Phosphatidylinositol bisphosphate (PIP₂)
 bacteria hydrolysis, 398–399
 signaling overview, 55–57, 63
Phosphatidylinositol trisphosphate (PIP₃)
 Akt signaling, 57–59, 87
 lymphocyte signaling, 322–323
Phosphodiesterases (PDEs), 99
 oocyte PDE3, 329
 overview, 55
Phosphoenolpyruvate carboxykinase (PEPCK), 286–287
Phosphofructokinase (PFK), 168, 285–286
Phosphoinositide, 3-kinase (PI3K)
 activation, 52, 58, 87
 Akt pathway overview, 87–89
 cancer signaling, 408–416, 418–421
 cell migration role, 189–191
 G-protein-coupled receptor signaling, 13–14
 glucose metabolism signaling, 168, 170–171
 lymphocyte signaling, 126–127
 lymphocyte signaling, 321–323
 mTORC1 target, 175
 recruitment, 42
 subcellular localization, 42
Phospholamban, 269
Phospholipase A2 (PLA₂), isoforms, 432–433
Phospholipase C (PLC)
 activation, 52
 FcR signaling, 307
 feedback control, 9
 fertilization role, 337–338
 LAT recruitment, 316
 lymphocyte signaling, 126
 messenger generation, 56–57
 muscle calcium sensitization, 273
Phosphorylation, protein regulation mechanisms, 33–34
PI3K. *See* Phosphoinositide, 3-kinase
PIDD, 374–375
PIF, 429
Pins, cell polarity role, 205–206
PIP₂. *See* Phosphatidylinositol bisphosphate
PIP₃. *See* Phosphatidylinositol trisphosphate
PIX α , 305
PKA. *See* Protein kinase A
PKBR1, 191–192
PKC. *See* Protein kinase C
PKD. *See* Protein kinase D
PKG. *See* Cyclic GMP-dependent protein kinase
PKG. *See* Protein kinase G
PKI. *See* Protein kinase inhibitor
PKR. *See* Double-stranded RNA-dependent kinase
PLA₂. *See* Phospholipase A₂
Platelet-derived growth factor (PDGF)
 chemokine activity, 193
 receptor, 9

- PLC. *See* Phospholipase C
 Plk1. *See* Polo-like kinase, 1
 Plx1, 338
 Plzf, 334
PML-RAR fusion, 417
 Polarity. *See* Cell polarity
 Polo-like kinase, 1 (Plk1), 40–41, 338
 Pom1, 157
 Pop1, 146
 Postsynaptic density (PSD)
 calcium-regulated signaling
 calcineurin, 253–254
 calcium/calmodulin-dependent protein kinase II, 251–253, 258
 scaffold proteins, 254–256
 PP1. *See* Protein phosphatase, 1
 PP2A. *See* Protein phosphatase, 2A
 PPAR. *See* Peroxisome proliferator-activated receptor
 PRAS40, 88
 Pregnane X receptor (PXR), 23–24
 Prex1, 305
 Prolyl hydroxylase (PHD), 171–173
 Prostaglandins, signaling overview, 59
 Protease-activated receptor, 1 (PAR1), 10
 Protein kinase A (PKA)
 cyclic AMP target, 53–54, 101
 isozymes, 57
 myristoylation, 43
 regulation, 101
 substrates, 101
 Protein kinase B. *See* Akt
 Protein kinase C (PKC)
 atypical PKC, 135, 188, 202–203, 205–208
 diacylglycerol target, 55, 57
 feedback control, 9
 lipid messengers, 57
 lymphocyte signaling, 318–319
 muscle calcium sensitization, 273
 Par protein localization, 205–207
 polarity signaling, 207–209
 receptor feedback, 9
 Protein kinase D (PKD), 318
 Protein kinase G (PKG), cyclic GMP target, 55
 Protein kinase inhibitor (PKI), 101
 Protein levels, equation, 45
 Protein phosphatase, 1 (PP1)
 learning and memory role, 254
 PKA as substrate, 101
 Protein phosphatase, 2A (PP2A)
 CDK1 as substrate, 155
 learning and memory role, 254
 oocyte maturation role, 331
 PKA as substrate, 101
 PSD. *See* Postsynaptic density
 PSD93, 254
 PSD95, 254–256
 P-selectin, 303
 PSG1, 303
 PTB domain, protein–protein interactions, 39–40
 PTEN, 59, 89, 176, 189–191, 407–408, 418
 PTP. *See* Permeability transition pore
 Puma, 372
 PXR. *See* Pregnane X receptor
 Pyk2, 18
 Pyrin domain, 368
 Pyruvate dehydrogenase kinase (PDK), 284, 414
 Pyruvate kinase, 173–174, 415, 431
- Q**
 Q30, 400
- R**
 RA. *See* Retinoic acid
 Rab, 104, 387, 431, 82, 141, 188–189, 396–398
 cell migration role, 188–189
 G-protein-coupled receptor signaling, 13
 Rac1, 354, 368
 RACK1, 350
 Rad17, 159
 Raf1, synaptic plasticity role, 258
 Rag, 175
 RAIDD, 374–375
 RAMPs. *See* Receptor activity-modifying proteins
 Rap
 learning and memory role, 259
 synaptic plasticity role, 258–259
 Rap1, 318
 RAR. *See* Retinoic acid receptor
 Ras
 cancer signaling, 408–410, 412, 415–416, 418, 421
 innate immunity, 305
 learning and memory role, 259
 lymphocyte signaling, 319
 prenylation, 42–43
 synaptic plasticity role, 257–259
 RasC, 192
 Rb. *See* Retinoblastoma protein
 Receptor activity-modifying proteins (RAMPs), 14
 Receptor tyrosine kinases (RTKs)
 cell adhesion molecule interactions, 21
 coreceptors, 8
 dimerization, 5–7
 downstream signaling, 8
 endocytosis, 9
 feedback and amplification, 9
 mutations and disease, 9
 overview, 4–5
 proteolysis, 10
 Regulators of G-protein-coupled receptor signaling (RGS), 15
 Replication protein A (RPA), 158
 Reproduction. *See also* Meiosis; Oocyte; Sperm fertilization
 acrosome reaction, 336
 gamete fusion and egg activation, 336–338
 prospects for study, 339
 zygote formation, 338
 Ret, 333–334
 Retinoblastoma protein (Rb)
 cancer, 408
 cell cycle control, 140–141
 Retinoic acid (RA), sperm maturation role, 335
 Retinoic acid receptor (RAR), 22, 317
 Retinoid X receptor (RXR), 21–22, 130
 REV-ERB, 24–25
 RGS. *See* Regulators of G-protein-coupled receptor signaling
 Rheb, 175, 322
 RHIM, 298, 303, 380
 Rho, G-protein-coupled receptor signaling, 13
 Rho1, 207
 RhoA, 396
 cell migration role, 188
 cytoskeleton regulation, 188
 Par6 regulation, 208
 Rhodopsin, 239–240
 RhoG, 305
 RIG-I-like receptor (RLR), signaling, 298–300
 RIP1, 298, 300, 303, 355, 373–374, 380
 RIP2, 300
 RIP3, 303, 366, 373, 379–380
 RIPK, 380
 RLR. *See* RIG-I-like receptor
- ROCK, 186
 Ror, 106
 RPA. *See* Replication protein A
 RSK, 330–331, 411
 Rsr1, 200
 RTKs. *See* Receptor tyrosine kinases
 Rub1, 434
 Rum1, 147
 RXR. *See* Retinoid X receptor
 Ryanodine receptor (RyR), 264–265, 267–269, 271, 274
 Ryk, 8, 105
 RyR. *See* Ryanodine receptor
- S**
 S6 kinase, 88
 S144, 205
 SAP102, 254
 SAP97, 254
 SAPK. *See* p38 stress-activated protein kinase
 SARA. *See* Smad anchor for receptor activation
 SCF. *See* Stem cell factor
 Scribble, 135, 204, 210, 416
 SDF1, 37
 Second messengers. *See also specific molecules*
 cyclic nucleotides, 53–55
 ions, 59–83
 lipids, 55–59
 overview, 52–53
 Secretion systems, bacteria, 391–399
 Sensory receptors
 evolution, 242–244
 G-protein-coupled receptors, 234–235, 238–239, 241
 olfaction, 242
 photoreceptors, 239, 241, 243
 prospects for study, 244–245
 receptor activation, 238–240
 signaling overview, 234–238
 thermosensation, 242
 Septation initiation network (SIN), 161–162
 SERCA, 62, 268–270, 274
 Serine/threonine kinase receptors
 activation, 7
 downstream signaling, 8
 mutations and disease, 9
 overview, 4, 6
 Serpent, embryonic patterning, 219
 Sevenless, 230
 SF. *See* Sperm cytosolic factor
 SH2 domain
 motifs, 40–41
 protein–protein interactions, 39–40
 SH3 domain
 motifs, 41
 protein–protein interactions, 39–40
 SHANK, 254–256
 Shc, 8
 SHIP, 323, 338
 Ship1, 190
 SHP1, 323
 Sic1, 146, 434
 SIK1, 287
 Sildenafil, 55
 SIN. *See* Septation initiation network
 SIRT1, 284, 287, 375
 Skeletal muscle. *See* Muscle contraction
 Ski, 113
 SKP2, 146–147
 SLP76, 128, 316
 SMAC. *See* Supramolecular activation cluster
 Smac, 369
 Smad, transforming growth factor- β signaling, 113–114

Index

- Smad anchor for receptor activation (SARA), 113
 Smo, 107
 Smooth muscle. *See* Muscle contraction
 SNAREs, 62, 336
 SNARK/NUAK2, 283
 SNoN, 113
 SOCE. *See* Store-operated calcium entry
 Sodium/potassium ATPase, 59
 Sopc, 395–396
 Sperm cytosolic factor (SF), 338
 Sperm. *See also* Reproduction
 capacitation and calcium channels, 335–336
 maturation
 overview, 332–334
 stem cell proliferation and maintenance, 334–335
 spermatocyte meiosis and release, 335
 Sphingomyelin, signaling, 56
 Sphingosine, hydrolysis, 59
 Spindle assembly checkpoint, 160–161
 SPIRE, 399
 SptP, 396
 Src, 19, 189, 315, 411
 SREBP. *See* Sterol response element-binding protein
 SRF, 274
 STATS. *See* JAK/STAT signaling
 Stem cell factor (SCF), 145, 147, 333
 Sterol response element-binding protein (SREBP),
 288, 414
 STIM1, 307, 316
 STIM2, 316
 STING, 436
 Store-operated calcium entry (SOCE), 337
 Stress-activated protein kinase. *See* p38 stress-activated
 protein kinase
 SuFu, 107
 SUMO, 45, 131
 Supramolecular activation cluster (SMAC), 318
 Swe1, 157
 Syk, 4, 315–316
 SynGAP, 258
- T**
- TAB2, 355
 TAB3, 355
 TACE. *See* ADAM17
 TAK1, 45, 295–297, 300, 303, 355
 Talin, 18, 187
 TAO1, 135
 Target of rapamycin. *See* Mammalian target of rapamycin
 Taste. *See* Sensory receptors
 TAZ, 115, 230
 TBC1D1, 283
 TBC1D4, 282
 TBK1, 123, 298, 300
 T cell
 classification, 314
 costimulatory molecules, 319–320
 cytokine signaling, 320–321
 PI3K/Akt signaling, 321–323
 receptor. *See* T-cell receptor
 T-cell receptor (TCR)
 adaptor molecules, 316
 ITAM, 315–316
 signaling
 calcium, 316–317
 diacylglycerol, 316–318
 ERK1/2, 319
 inhibitory signals, 323
 nuclear factor of activated T cells, 317–318
 overview, 125–127, 317
 protein kinase C, 318–319
 Ras, 319
 structure and function, 314–315
 TCF, 227, 319
 TCF/LEF, 103–104
 TCR. *See* T-cell receptor
 Tel1, 158
 Tem1, 162
 TET1, 407
 TGF- β . *See* Transforming growth factor- β
 Thrombospondin (Tsp1), 420
 Thyroid hormone
 energy homeostasis role, 279–280
 receptor, 22
 TIGAR, 415
 TIMP3, 420
 Tinman, 219
 Tip60, 35
 TLR. *See* Toll-like receptor
 TNFRs. *See* Tumor necrosis factor receptors
 Toll-like receptor (TLR)
 interferon induction, 297–298
 ligands, 295
 signaling overview, 121–123
 TAK1 and IKK activation, 295–296
 TLR4 signaling, 296
 TRIF in signaling, 298
 TopBP1, 159
 TorC2, 191–192
 Torso, development role, 217
 Tp12, 297
 TRADD, 16, 298, 300, 302, 371, 373–374
 TRAF, 15
 TRAF2, 59, 350–351, 355, 374
 TRAF3, 123, 297–298
 TRAF6, 45, 114, 295, 297, 307
 TRAIL, 373, 412
 Transcriptional regulation, protein levels, 43–44
 Transforming growth factor- β (TGF- β)
 receptor types, 8
 signaling overview, 114–115
 Translational regulation, protein levels, 44
 TRB3, 350
 TRIF; Toll-like receptor signaling, 298
 Troponin C, 62
 TRPA1, 242
 TRPC6, 272
 TRPM6, 63
 TRPM7, 63
 TRPM8, 239, 242
 TRPV1, sensory role, 237, 239, 242, 244
 TSC1, 93, 350
 TSC2, 88, 93, 350, 411, 413, 416
 Tsp1. *See* Thrombospondin
 TTR, 356
 Tumor necrosis factor receptors (TNFRs)
 activation, 15
 caspase-8 activation in death receptor pathway,
 371, 373–374
 ligand diversity, 15
 pathology, 17
 signaling, 15–17
 structure, 15–16
 TNFR1 signaling
 cell death induction, 303
 MAPK, 301–303
 nuclear factor- κ B, 301–303
 TXNIP, 351
- U**
- Ubch proteins, 295, 301
 Ubiquitylation
 G₁ regulation
 CIP/KIP degradation, 147–148
 cyclin degradation, 145–147
 pathogen disruption, 400–401
 protein degradation, 44–47
 UCP. *See* Uncoupling protein
 ULK1, 378–379
 Uncoupling protein (UCP), 289
 Unfolded protein response (UPR)
 canonical signaling, 346–349
 noncanonical aspects, 349
 physiological roles
 cell survival and death responses, 350
 inflammation, 350–351
 metabolic responses, 351–353
 overview, 349–350
 UPR. *See* Unfolded protein response
- V**
- VAMP8, 378
 Vascular cell adhesion molecule (VCAM), 17, 303
 Vascular endothelial growth factor (VEGF)
 cancer angiogenesis, 420
 hypoxia signaling, 24
 VCAM. *See* Vascular cell adhesion molecule
 VEGF. *See* Vascular endothelial growth factor
 VHL, 171–172, 420
 Vinculin, 18
 VirG, 399
 Virus. *See* Infection
 Vision. *See* Sensory receptors
 VOCC. *See* Voltage-operated calcium channel
 Voltage-operated calcium channel (VOCC), 59, 62, 337
 VopA/P, 394
 VopS, 397
 VPA0450, 399
 Vps15, 378
 Vps34, 378
- W**
- WASP, 398
 WAVE, 186, 40
 Wee1, 155, 157, 329–330
 WH2 domain, 399–400
 WIP1, 355
 Wnt
 canonical signaling, 104
 cell polarity signaling cross talk, 209
 embryonic patterning, 225
 noncanonical signaling, 104–105
 signaling overview, 103–105
 WTS, 134
- X**
- XBP1, 347, 349–351, 353
 XIAP, 369, 375, 412
- Y**
- YAP, 115, 230
 YK1. *See* Yorkie
 YopE, 396
 YopH, 392
 YopI, 393–394
 YopT, 396
 Yorkie (YKI), 134, 143, 298, 230
 YpkA, 396
- Z**
- Zap70, 4
 ZO1, 20
 ZO2, 20

Signal Transduction

Principles, Pathways, and Processes

CELLS MUST RESPOND TO A WIDE variety of signals. These include hormones, growth factors, morphogens, and environmental stress, as well as signals from internal regulators and checkpoints. A complex network of signal transduction pathways within the cell ensures that these signals are relayed to the correct molecular targets and that the cell responds appropriately.

This textbook provides a comprehensive and up-to-date view of signal transduction, covering both the fundamental mechanisms involved and their roles in key biological processes. Taking a novel approach, it first lays out the basic principles of signal transduction, explaining how different receptors receive information and transmit it via signaling proteins, ions, and second messengers. It then surveys the major signaling pathways that operate in cells, before examining in detail how these function in processes such as cell growth and division, cell movement, metabolism, development, reproduction, the nervous system, and immune function.

The book is essential reading for students learning about signal transduction for the first time. It will also be a vital reference for all cell, molecular, and developmental biologists and pharmacologists, neurobiologists, and immunologists studying processes regulated by cell signaling.



COLD SPRING HARBOR
LABORATORY PRESS

ISBN 978-0-879699-01-7

