

Index

a

- AA *see* amino acid
- A β *see* amyloid β -peptide
- ABCA1 *see* ATP-binding cassette transporter-A1
- Abl 129–130
- actin remodeling 130–131
 - caveolin kinase 120, 129
 - caveolin phosphorylation 121
- acceptor, fluorescence correlation spectroscopy 59
- acceptor channels, FRET 146
- ACTH *see* adrenocorticotrophic hormone
- actin cytoskeleton
- attachment 127–129
 - dynamics of caveolin 199–200
 - dynamin 83
 - endocytosis 73
 - stabilisation 130
- actin/plasma membrane attachment sites, phosphorylation 128
- actin polymerization 131
- actin remodeling 127
- Abl 130–131
 - insulin-induced 131
- activation, Csk 125–127
- activation-induced cell death (AICD), lipid rafts 157
- acylation, signal transduction 92
- AD *see* Alzheimer's disease
- ADAM10, metalloprotease 214
- adaptor proteins, multifunctional 249
- adhesion complex, focal 198–199
- adhesion molecules, immunological synapse 151
- adipocytes
- caveolin 199
 - caveolin phosphorylation 117
 - signaling pathways 117
- adrenocorticotrophic hormone (ACTH) 256–257
- affinity conversion, lipid rafts 157
- AFM *see* atomic force microscopy
- aggregation, membrane proteins 32
- aging, gate theory 195
- aging process, caveolin 195
- AICD *see* activation-induced cell death
- Alzheimer's disease (AD) 205
- role of rafts 215–223
- amino acid (AA), caveolins domains 25
- amino-terminus, caveolin-1 123
- amphiphilic dye, LAURDAN 5
- amyloid β -peptide (A β) 215–217
- amyloid precursor protein (APP)
- cleavage 215–223
 - processing 205–223
- anchored protein (AP)
- GPI- 8, 54, 63, 92, 207, 214, 257
- angiogenesis, caveolin-eNOS interaction 241–242
- anisotropy, measurements 61
- annular lipids, transmembrane signaling 143
- anoikis, cellular resistance 253–254
- anomalous diffusion, immunological synapse 152
- antennopodia (AP) peptide 102
- anti-proliferative activity, caveolin-1 252
- antibodies, diffusion-based measurements 55
- antigen-presenting cell, immunological synapse *see* APC
- antisense suppression techniques, caveolin-1 253
- AP *see also* antennopodia, *see* anchored protein
- APC, immunological synapse 150
- apical membrane
- basolateral protein exclusion 14
 - epithelial cells 9–10

- apical t-SNARE, syntaxin 3 16
 APP *see* amyloid precursor protein
 arachidonyl ethanolamine plasmalogens 94
 ARP2/3, actin polymerization 130
 artificial lipid membranes, DRM 50
 asialogangliosides, signal transduction 94
 asymmetric membrane protein, bending forces 33-35
 atomic force microscopy 149
 ATP-binding cassette transporter-A1 97
 autocorrelation function, FCS 147
 autofluorescence, FRET 146
 autophosphorylation, signal transduction 104
- b**
- baby hamster kidney, electron micrographs 80
 BACE *see* β -site APP cleavage enzyme
 basolateral proteins, exclusion from apical membrane 14
 bending energy, invaginated membrane domains 30
 bending forces, asymmetric membrane protein 33-35
 bending rigidity, biomembranes 27-28
 β -site APP cleavage enzyme (BACE) 215-218
 BHK cells *see* baby hamster kidney
 bilayer *see* lipid bilayer
 biomembranes
 – bending rigidity 27-28
 – *see* membranes
 blocked caveolin phosphorylation 119
 Bodipy-PC, fluorescence correlation spectroscopy 57
 breast cancer, caveolin-1 expression 252
 budding, coat-driven/domain-induced 15
 buds, formation 34-37
 bulb radius (preferred), caveolae 36-37
- c**
- C-terminal, caveolins 25, 177
 C-terminal region, endocytosis 70
 Ca²⁺ signal, voltage gated channels 154
 calciumbound calmodulin (CaM) 233
 – eNOS enzyme activity 236
 CaM *see* calciumbound calmodulin
 cancer progression, role of caveolin-1 249-259
 carboxyl terminal fragment (CTF), APP 215
 cardiac myocytes
 – caveolin-eNOS interaction 244-245
 – eNOS expression 234
 cargo sorting, membrane traffic 15
 caveola-cholesterol trafficking cycle, regulation 184-185
 caveolae 1-17, 131, 175-176
 – caveolin oligomer mixing 35
 – cholesterol localization 182-183
 – constitutively internalization 81-82
 – curvature 12
 – disruption 40
 – endocytosis 69, 75-81
 – endothelial nitric oxide synthase (eNOS) 233-246
 – FC 102-106
 – first observation 25
 – formation 30-31
 – function 199-200
 – invaginated lipid rafts 28-31
 – labeling 80
 – lipid composition 12
 – lipid rafts 206-207
 – lipids 93-95
 – membrane domains 71
 – membrane tension 38-42
 – membrane traffic 12-17
 – origin of name 10
 – preferred bulb radius 36-37
 – proteins 95-98
 – scaffold motif 99
 – scaffolded membrane domains 10-12
 – shaping forces 25-42
 – signal transduction 91-114
 – signaling 115-140
 – structure 96
 – subpopulations 84
 – thermodynamic phase separation of membrane proteins 35-38
 – water permeability 94
 – wave 74
 caveolar coat protein, caveolin-1 249
 caveolar endocytosis, consensus model 85
 caveolar function, dynamin 83
 caveolar invaginations 84-85
 caveolar-like domains (CLDs) 210
 caveolar proteins, FC depletion 102
 caveolar vesicles, free 73
 caveolin 11, 101-102, 175
 – contact site 99
 – contribution to cell-cycle regulation 40
 – homo-oligomers 33
 – insulin receptor 117-118
 – internalization 127
 – intracellular chaperone complexes 175-194
 – N-/C-Terminal 25
 – overexpression 176

- phosphorylation *see* caveolin phosphorylation
- protein acylation 186
- raft immobilization 84–85
- signal transduction 95
- signaling pathways 116–117
- caveolin-1
 - expression 251, 257–258
 - regulation 250
 - role in tumor cell survival and cancer progression 249–259
 - tyr14 phosphorylation 256–257
- caveolin-associated structures, intracellular 82–83
- caveolin binding motif (CBM) 235–236
- caveolin-eNOS interaction
 - angiogenesis 241–242
 - cardiac myocytes 244–245
 - lipoproteins 239–241
 - vasodilation and endothelial permeability 242–244
- caveolin-eNOS regulatory cycle 236–238
- caveolin family, endocytosis 70
- caveolin kinase 120
- caveolin localization, caveolae 182–183
- caveolin oligomers, mixing on caveolae 35
- caveolin phosphorylation 115–140
 - adipocytes 117
 - blocked 119
 - insulin-induced 119
 - signaling pathway 121
 - stress-induced 118–119
 - tyrosine *see* caveolin tyrosine phosphorylation
- caveolin protein structure 177–178
- caveolin rafts, morphology 40
- caveolin scaffolding domain (CSD) 235–236, 250
 - pro-survival action of caveolin-1 255
 - regulation of angiogenesis 242
 - signal transduction 98–101
- caveolin systems, mutant 37–38
- caveolin tyrosine kinases 123
- caveolin tyrosine phosphorylation 256–257
 - signaling pathways 116–123
- caveolins domains, amino acid 25
- caveosomes 82–83
- cbc *see* critical budding concentration
- CBM *see* caveolin binding motif
- CD36, scavenger receptors 187
- cell compartments *see* compartments
- cell-cycle regulation, contribution of caveolin 40
- cell death, activation-induced 157
- cell differentiation, caveolin-1 250
- cell fusion 155–156
- cell membrane
 - basic organization 1–3
 - mechanical regulation 41
 - phase separation 5–7
 - rafts 49–51
 - *see also* membranes
- cell migration, phosphorylation 130
- cell shape, roles of caveolae and caveolin 195–202
- cell-surface proteins, distribution patterns 144
- cell survival, caveolin-1 253–256
- cell types, caveolae 176
- cells in culture, physiological state 180–182
- cellular motility 196
- cellular organelles, membrane traffic 12
- cellular stresses, caveolin phosphorylation 118
- central supramolecular activation cluster *see* cSMAC
- ceramidase, signal transduction 95
- ceramide, signal transduction 94
- chaperone complexes 188
 - caveola-cholesterol trafficking cycle 184–185
 - intracellular 175–194
- chemical affinity, raft hypothesis 45
- chemical incompatibility, influence on lipid domain shape 29–30
- chemical interaction, lipid rafts 50
- cholera toxin
 - endocytosis 75–81
 - raft and caveolar endocytosis 14
- cholera toxin B, diffusion-based measurements 52
- cholesterol
 - APP processing 222
 - caveolin 183–184
 - cell membrane 2
 - DRM 50
 - fluorescence correlation spectroscopy 57
 - lipid rafts 205–206
 - low-density lipoprotein (LDL) 239–241
 - relative concentration, caveolae 175
 - signal transduction 91–114
 - ternary phase diagram 4
- cholesterol-binding drugs, endocytosis 77
- cholesterol-binding proteins, caveolae 115
- cholesterol-containing domains, raft hypothesis 45
- cholesterol depletion
 - PrP^C conversion 209

- strong 216
 - cholesterol homeostasis
 - endocytosis 185
 - regulation 187
 - cholesterol localization, caveolae 182–183
 - cholesterol recognition amino acid consensus *see* CRAC
 - cholesterol/sphingolipid-rich microdomains 91
 - cholesterol transport, specialized tissues 188
 - chronotropic effects, negative 244–245
 - clathrin-coated pits
 - endocytosis 76
 - internalization of PrP^c 209–210
 - clathrin-mediated endocytosis, caveolae 69, 176
 - CLDs *see* caveolar-like domains
 - CLSM 165
 - cluster size, lipid microdomains, ERB2 164
 - clustered cell-surface distribution, immunological synapse 152
 - clustered raft domains 8–9
 - cmc *see* critical micelle concentration
 - co-clustering 154
 - co-immunoprecipitation, caveolins 117
 - co-localization
 - endocytosis 78
 - immunological synapse 153
 - lipid rafts 159, 162
 - membrane proteins 142
 - co-mobility, protein 147
 - coat-driven budding, cargo sorting and vesicle formation 15
 - coat proteins, caveolae 115
 - coats, protein 13
 - columnar epithelia 9
 - compartments, intracellular 208–210, 215–217
 - confluent human umbilical vein endothelial cells 181
 - confocal laser scanning microscopy, domain size 144
 - conformational diseases 205
 - conformational transition, PrP^c-PrP^{Sc} 211–214
 - consensus model, caveolar endocytosis 85
 - constitutively internalization, caveolae 81–82
 - contact site, proteins 99
 - cooperative interactions, lipid microdomains 163
 - coronary arteries, endothelial cells 234
 - correlation spectroscopy, fluorescence 57–58
 - CRAC 98
 - CRAC-1 101
 - critical budding concentration (cbc) 34, 37
 - critical micelle concentration 34
 - cross-correlation coefficient, fluorescence distributions 145
 - CSD *see* caveolin scaffolding domain
 - Csk 127, 257
 - activation 125–127
 - phosphocaveolin 124–125
 - Src-family kinases 125
 - cSMAC, immunological synapse 150
 - CT
 - endocytosis 75–76, 78
 - internalization by caveolae 81
 - CT-B, internalization 79, 84
 - CT-B-gold, endocytosis 76
 - CT-B-HRP conjugate, incubated BHK cells 80
 - CTF *see* carboxyl terminal fragment
 - CTL, immunological synapse 150
 - CtxB *see* cholera toxin B
 - curvature
 - caveolae 12
 - spontaneous 27
 - cyclodextrin, FC depletion 104
 - cyclosporine, chaperone complexes 184
 - cysteines
 - caveolin 178
 - protein acylation 186
 - cytofacial leaflet, endocytosis 183
 - cytokine receptor assembly, lipid rafts 156–162
 - cytoskeleton mesh, single-molecule tracking 53
 - cytotoxic T cell *see* CTL
- d**
- Danielli-Davson model 1
 - deformable fluid membranes, physical modeling 26–29
 - dehydroergosterol, signal transduction 94
 - depletion, cholesterol 209, 216
 - FC 102–104
 - detergent-free isolation, caveolae 93
 - detergent-insoluble glycolipid (DIG) 46
 - detergent-resistant membranes (DRM) 2, 46, 49–51, 206, 209, 215–217
 - dialkylcarbocyanine *see* DiI
 - 1,1'-dieicosanyl-3,3,3',3'-tetramethylindocarbocyanine perchlorate *see* DiI-C20
 - differentiated primary cells, signal transduction 91
 - diffusion-based measurements, raft hypothesis 52–58
 - diffusion constants, FRAP 56

- diffusion process, membranes 58
diffusion time, FCS 148
2-(4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diazas-indacene-3-pentanoyl)-1-hexadecanoyl-sn-glycero-3-phosphocholine *see* Bodipy-PC
DIG *see* detergent-insoluble glycolipid
diglyceride, signal transduction 94
DiI-C20, fluorescence correlation spectroscopy 57
dilauroyl phosphatidylcholine (DLPC), fluorescence correlation spectroscopy 57
dimerization
– lipid microdomains 163
– signal transduction 104
1,2-dioleoyl-sn-glycero-3-phosphoethanolamine-fluorescein *see* FL-DOPE
dipalmitoyl phosphatidylcholine (DPPC), fluorescence correlation spectroscopy 57
1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine-fluorescein *see* FL-DPPE
dipole moment, molecular 5
diseases
– Alzheimer's *see* Alzheimer's disease
– conformational 205
– prion 205–223
distributions
– clustered cell-surface 152
– fluorescence 144–145
– GM1 gangliosides 160
DLPC *see* dilauroyl phosphatidylcholine
domain energy, in relation to domain shape and membrane tension 39
domain-induced budding, cargo sorting and vesicle formation 15
domain shape
– in relation to domain energy and membrane tension 39
– lipid 29–30
domain size, determination 144–145
domains
– caveolin 25, 177–178
– caveolin scaffolding *see* caveolin scaffolding domain
– macro- 143
– membrane 30, 45, 71
– MHC I molecules 152
– micro- *see* microdomains
– raft 8–9
donor, fluorescence correlation spectroscopy 59
donor channel, FRET 146
donor photobleaching *see* pbFRET
downstream signaling cascades, tyrosine phosphorylation 123
DPPC *see* dipalmitoyl phosphatidylcholine
DRM *see* detergent-resistant membranes
Duchènne muscular dystrophy, caveolae number 40
dynamain
– caveolar function 83
– transendothelial transport 74
dynamin-1 mutant, endocytosis 81
- e**
Echovirus 1 75
ECM *see* extracellular matrix
effective membrane temperature 27
EGF 117
– receptor, lipid microdomains 163
– signal transduction 96
electron microscopy, lipid rafts 51
EM *see* electron microscopy
endocytic machinery 69
endocytic marker, constitutively internalization 81
endocytic pathways, caveolae 176
endocytic vesicles, free 83
endocytosis 69
– caveolae-mediated 85, 200–201
– cholera toxin 75–81
– independent pathways 84
endoplasmic reticulum (ER), PrP^c-PrP^{Sc} transconformation 208
endoplasmic reticulum-Golgi-intermediate-compartment *see* ER-GIC
endosomes
– APP cleaving pathways 218
– caveosomes communication 82
endothelial cells, coronary arteries 234
endothelial nitric oxide synthase *see* eNOS
endothelial permeability, caveolin-eNOS interaction 242–244
endothelial tube formation, stimulation by statins 241
endothelin receptor-A, scaffold sequence 99
endothelium-dependent vascular relaxation 242–243
energy, bending 30
energy barrier, between flat and budded caveolae states 37–39
energy transfer process, fluorescence 59
eNOS (endothelial nitric oxide synthase) 70
– and caveolae 233–246
– protein acylation 186
– signal transduction 98
eNOS-caveolin interaction

- angiogenesis 241–242
 - cardiac myocytes 244–245
 - lipoproteins 239–241
 - vasodilation and endothelial permeability 242–244
 - eNOS interacting protein (NOSIP) 237–238
 - eNOS traffic inducer (NOSTRIN) 237–238
 - epithelia, columnar 9
 - epithelial cells, apical membrane 9–10
 - epitope accessibility, caveolae determination 179
 - ER *see* endoplasmic reticulum
 - ER-associated degradation (ERAD) 208
 - ER-GIC 182
 - ERAD *see* ER-associated degradation
 - ErbB2, lipid microdomains 163
 - estrogen uptake, caveola 185–186
 - exclusion, due to phase separation 15
 - exofacial leaflet, endocytosis 183
 - expression
 - caveolin-1, heterologous 252–254
 - caveolin-1, in human cancer 251
 - caveolins 178–182
 - extracellular matrix (ECM) 198–199
 - extracellular signals, caveolin phosphorylation 124
 - extracytoplasmic proteins, raft hypothesis 48
 - ezetimibe, cholesterol transport 188
- f**
- FAK *see* focal adhesion kinase
 - fatty-acid linked proteins 48
 - FC
 - caveolae 102–104
 - changes 104–106
 - interactions 94
 - FC binding
 - proteins 101–102
 - structural aspects 101
 - FC depletion, effects on caveolar proteins 102
 - FC recognition sites, signal transduction 99
 - FC-rich vacuoles, increased endocytosis 103
 - FCCS *see* fluorescence cross-correlation spectroscopy
 - FCS *see* fluorescence correlation spectroscopy
 - fibroblasts
 - phase separation 10
 - signaling pathways 125
 - fibronectin, phosphorylation 128
 - filamin 127
 - identification 199
 - filipin, cholesterol localization 182
 - filopodia, focal adhesion complex 198–199
 - fission-fusion processes, endocytosis 73
 - FL-DOPE 52
 - fl-PE 52
 - FLIP, endocytosis 72
 - flotillins, signal transduction 96
 - flow cytometric FRET, lipid rafts 162
 - fluid membranes, physical modeling 26–29
 - fluid-mosaic model 45–46
 - fluorescein phosphatidylethanolamine *see* fl-PE
 - fluorescence correlation spectroscopy (FCS) 57–59, 147
 - diffusion-based measurements 52
 - mobility measurements 161
 - fluorescence cross-correlation spectroscopy (FCCS) 147
 - mobility measurements 161
 - fluorescence distributions, overlap 144–145
 - fluorescence lifetime, FRET 147
 - fluorescence loss in photobleaching *see* FLIP
 - fluorescence microscopy 144–145
 - fluorescence recovery after photobleaching (FRAP) 10, 16, 55–57
 - endocytosis 72
 - fluorescence resonance energy transfer 59, 145
 - focal adhesion complex, caveolin 198–199
 - focal adhesion kinase (FAK) 199, 256–257
 - Foerster's resonance energy transfer *see* FRET
 - formation
 - buds 34–37
 - caveolae 30–31, 37–38
 - endothelial tube 241
 - PrP^{Sc} 210–211
 - stress fiber 195–202
 - supramolecular protein complexes 141–174
 - vesicle 15
 - Förster distance 146
 - Förster's resonance energy transfer *see* FRET
 - FRAP *see* fluorescence recovery after photobleaching
 - free-cholesterol-binding sites, peptide contributions 100
 - free endocytic vesicles, caveolar function 83
 - free energy (F), physical modeling of lipid membranes 26
 - FRET 4, 6–7, 16, 145
 - efficiency 145
 - flow cytometric 162
 - immunological synapse 151
 - lipid rafts 157
 - pb *see* pbFRET

- proximity measurements 60
- frustration, bilayer order 31–32
- Frye-Edidin experiment 155
- functional multiprotein complexes 103
- functional suppression, caveolin-1 in cancer cells 252–254
- functional unit 142
- Fyn
 - activation 132
 - caveolin phosphorylation 121
 - expression 119
 - inhibition 125–127
 - overexpression 122
- Fyn-Abl, interaction 122–123

g

- gangliosides 93
- gate theory of aging 195
- gel state, lipids in membranes 49–50
- genetic suppression, caveolin-1 in cancer cells 252–254
- GFP 6
 - proximity measurements 60
- GFP-tagged caveolin 71
- giant unilamellar vesicle (GUV)
 - fluorescence correlation spectroscopy 57
 - membrane model system 3
 - raft domains 9
- glucose transport, stimulation 131
- glucose transporter 4 (GLUT4)
 - caveolin 199–200
 - translocation 131
- glutathione S-transferase (GST)-CSD fusion proteins 235
- glycoproteins, immunological synapse 151
- glycosphingolipid GM1 ganglioside, lipid microdomains 164
- glycosphingolipids 9
 - raft hypothesis 45
- glycosyl-phosphatidyl-inositol *see* GPI
- GM1 gangliosides, distribution 160
- GPI, membrane traffic 4, 6–8
- GPI-anchor
 - proximity measurements 60
 - PrP^c 207–208
 - raft hypothesis 48
 - transmembrane signaling 143
- GPI-anchored proteins 8, 48, 51, 54, 63, 92, 207, 214, 257
 - caveolae 175
 - raft immobilization 84
 - signal transduction 92
 - Thy-1 8

- green fluorescent protein *see* GFP
- growth conditions, caveolae structure 96
- growth factor, vascular endothelial 241
- growth factor-mediated signaling 104
- GST *see* glutathione S-transferase
- GTP-binding proteins, TC10 200
- GUV *see* giant unilamellar vesicle

h

- H-Ras, FRAP 56
- HA, single-molecule tracking 54
- hairy-aspect, caveolae 25
- HASM 53
- HDL *see* high-density lipoprotein
- HDL uptake, caveolin-1 182
- heart, role of nitric oxide 234
- heart rate regulation, muscarinic cholinergic 244–245
- HeLa cells, endocytosis 79
- hemagglutinin *see* HA
- hetero-FRET 6
 - proximity measurements 62–63
- heteroclusters, cell fusion 156
- heterodimerization, lipid rafts 157
- heterologous expression, caveolin-1 in cancer cells 252–254
- hexamethylglutaryl coenzyme A (HMGCoA) 240
- high-density lipoprotein (HDL) 239
 - estrogen 185
 - signal transduction 94
- HMGCoA reductase inhibitors (statins) 240–241
- homeoproteins, endocytosis 183
- homo-FRET 6
 - proximity measurements 60–62
- homo-oligomers, caveolins 33
- homoclusters
 - cell fusion 156
 - immunological synapse 152
- Hooke's law, physical modeling of lipid membranes 27
- hop diffusion, single-molecule tracking 54
- human cancer, role of caveolin-1 251
- human coronary artery smooth muscle *see* HCASM
- human epidermal carcinoma *see* KB
- human myoepithelial cells 70
- human T lymphoma cells, lipid rafts 157
- hydrophobic regions, membrane proteins 31
- hyperphosphorylation, caveolin phosphorylation 118

i

- ICAM-1, co-localization 153
- IGF-I *see* insulin-like growth factor-I
- IL
 - co-localization 159, 162
 - raft assisted signaling 159
- IL-2, lipid rafts 156–162
- IL-6 254–255
- immunolocalization, caveolae 179, 182
- immunological synapse (IS) 150
- inclusions
 - due to sorting signals 15
 - membrane 31–34
- incompatibility (chemical), influence on lipid domain shape 29–30
- independent pathways, endocytosis 84
- inducible NOS isoform (iNOS) 234
- inhibition, Fyn 125–127
- iNOS *see* inducible NOS isoform
- insulin absence 70
- insulin in adipocytes, signaling pathways 116–117
- insulin-induced actin remodeling 131
- insulin-induced caveolin phosphorylation 119
- insulin-like growth factor-I (IGF-I) 254–255
- insulin receptor, caveolins 117–118
- integrins, focal adhesion complex 198–199
- interleukin *see* IL
- intermixing, cell fusion 155
- internalization 75
 - caveolae 81–82
 - PrP^c 209–210
- intracellular caveolin-associated structures, caveosomes 82–83
- intracellular chaperone complexes 175–194
- intracellular compartments
 - amyloid β -peptide (Ab) 215–217
 - PrP^c conversion 208–210
- intracellular polarity 195–196
- invaginated caveolae, equilibrium 92
- invaginated lipid rafts, caveolae 28–31
- invaginated membrane domains, bending energy 30
- invaginations, caveolar 84–85
- IS *see* immunological synapse

k

- K-Ras, FRAP 56
- K⁺ channels, voltage-gated 154–155
- KB, signal transduction 94
- kinases 127
 - caveolin 120, 129
 - caveolin tyrosine 123

- focal adhesion 199, 256–257
 - non-receptor tyrosine 119
 - phosphoinositide 254–256
 - receptor 106
 - receptor tyrosine 163–166
 - Src-family *see* Src-family kinase
 - tyrosine 116, 119
- kiss-and-run, transendothelial transport 74

l

- labeled molecules, local concentration 148
- lactase-phlorizin hydrolase *see* LPH
- lag time, FCS 148
- large unilamellar vesicles *see* LUV
- latranaculin A, FRAP 56
- LAURDAN, amphiphilic dye 5
- LDL *see* low-density lipoprotein
- line tension 13
- linear pathway, caveolin phosphorylation 121
- lipid-anchored proteins 48
- lipid bilayer 1, 141
 - order 31–32
 - structure 28
- lipid components, cellular membranes 2, 143–144, 175
- lipid composition, caveolae 12
- lipid domain shape, influence of chemical incompatibility 29–30
- lipid membrane 141
 - artificial 50
 - bilayer structure 28
 - physical modeling 26–29
 - *see* membranes
- lipid microdomains 141–174
 - receptor tyrosine kinases 163–166
- lipid phosphate phosphohydrolase, signal transduction 94
- lipid rafts 1–17, 51–52, 141, 143, 156–162, 175
 - biophysical characterization 45–68
 - co-localization 153
 - invaginated 28–31
 - membrane traffic 12–17
 - planar 92
 - processing of prion protein 205–223
 - signal transduction 91
 - voltage-gated K⁺ channels 154–155
- lipid uptake, caveolin 188
- lipids, two-dimensional fluids 45
- lipoproteins, caveolin-eNOS interaction 239–241
- liquid crystalline state, lipids in membranes 49–50
- liquid-disordered phases 3–5

- liquid-ordered phases 3–5
 - lipid rafts 92
- loading, FC 102–104
- local motility, endocytosis 73–74
- local regulatory processes 154–155
- localization
 - caveolae 182–183
 - caveolin 178–182, 187
 - cholesterol 182–183
 - co- *see* co-localization
- locomotion, roles of caveolae and caveolin 195–202
- low-density lipoprotein (LDL) 103
 - cholesterol 239–241
- LPH, single-molecule tracking 54
- lung cancer, role of caveolin-1 251
- LUV 3
- lysotracker, caveosomes 82

- m**
- mAChR *see* muscarinic cholinergic
- macrodomains, lipid 143
- macrophage apoptosis, mouse 258
- Madin-Darby canine kidney (MDCK)
 - cells 16, 50
 - endocytosis 72
- mammary tumor cells, caveolin-1 expression 252
- mbCD 58
- MCF-7 cells, caveolin-1 expression 253–254
- MDCK *see* Madin-Darby canine kidney
- MDR human cancer cells 258
- mean barrier-free path, domain size 144
- mechano-regulation/-sensitivity, caveolae 38–42
- melting temperature, lipid mixtures 3
- membrane-associated proteins 49
- membrane cap, spherical 28
- membrane components 142–143
- membrane crossing, caveolin 183–184
- membrane domain shape, influence of
 - chemical incompatibility 29–30
- membrane domains 45
 - bending energy 30
 - caveolae 71
 - nonendocytic 71
 - scaffolded *see* scaffolded membrane domains
- membrane extension, actin remodeling 127
- membrane inclusions 31–34
- membrane interactions, caveolin 177–178
- membrane model, Singer-Nicolson 141
- membrane molecules, single-molecule tracking 53
- membrane phases, fluorescence correlation spectroscopy 57
- membrane protein clusters, cell fusion 156
- membrane proteins
 - aggregation 32
 - asymmetric 33–35
 - hydrophobic regions 31
 - lateral organization 144–149
 - reorganization 142
 - thermodynamic phase separation 35–38
- membrane raft hypothesis, development 48
- membrane systems, phase separation 3–5
- membrane temperature, effective 27
- membrane tension
 - caveolae 38–42
 - in relation to domain energy and shape 39
- membrane topology 48
- membrane traffic 1–17
 - cargo sorting and vesicle formation 15
 - caveolae and lipid rafts 12–17
 - cellular organelles 12
 - GPI 4, 6–8
- membrane transporter proteins 97
- membranes
 - cell *see* cell membrane
 - detergent-insoluble 50
 - detergent-resistant *see* detergent-resistant membranes (DRM)
 - diffusion process 58
 - lipid *see* lipid membrane
 - plasma *see* plasma membrane
 - *see* apical membrane
- metalloproteases 214
- methyl- β -cyclodextrin *see* mbCD
- MHC I
 - co-localization 153, 162
 - homoassociation 151
 - transendothelial transport 75
- MHC I glycoprotein, domain size 145
- microdomains
 - cholesterol/sphingolipid (FC/SPH)-rich 91
 - lipid 141–174
 - plasma membrane 175
- microscopy
 - atomic force 149
 - confocal laser scanning 144
 - electron 51
 - fluorescence 144–145
 - quantitative immunogold labeling electron 71
- migratory synapses, immunological synapse 150

- mitosis, signal transduction 96
 - MLV 3
 - model membrane systems, phase separation 3–5
 - modeling, lipid membranes 26–29
 - modulation of polarity, caveolin 195–196
 - molecular specificity, SNOM 149
 - molecules
 - adhesion 151
 - dipole moment 5
 - labeled 148
 - motion 52
 - signaling 133
 - single, tracking 53–54
 - motility, caveolae 73–74
 - multi-protein complexes, signal transduction 95
 - multifunctional adaptor proteins 249
 - multilamellar vesicles *see* MLV
 - multiphoton excitation, domain size 144
 - multi-protein complexes, functional 103
 - multistage caveolin lipidation cycle 105
 - muscarinic cholinergic (mAChR), heart rate regulation 244–245
 - mutant caveolin 180, 252
 - caveolae formation 37–38
 - mYFP-GPI, proximity measurements 60
 - myocytes, cardiac 234, 244–245
 - myoepithelial cells, human 70
- n**
- N-terminal
 - caveolins 25, 177
 - endocytosis 70
 - N-WASP, actin polymerization 130
 - NCAM 53
 - negative data evaluation, caveolae determination 179
 - neural cell adhesion molecule *see* NCAM
 - nitric oxide synthase (NOS), endothelial 233–246
 - NMR *see* nuclear magnetic resonance
 - NO-mediated vascular relaxation 242–243
 - non-receptor tyrosine kinases 119
 - noncaveolar rafts, endocytosis 69
 - nonendocytic membrane domains, caveolae 71
 - nongenomic actions, caveola 185–186
 - NOS *see* nitric oxide synthase
 - NOSIP *see* eNOS interacting protein
 - NOSTRIN *see* eNOS traffic inducer
 - NPC-1 fibroblasts, cholesterol transport 188
 - nuclear magnetic resonance (NMR)
 - lipid microdomains 163
 - lipid rafts 50
- o**
- organelles, membrane traffic 12
 - ovarian cancer cells, pro-apoptotic activity of caveolin-1 253
 - overexpression techniques, caveolin-1 253
 - oxidative stress, signaling pathways 125
- p**
- P132L, mutant caveolin-1 252
 - partitioned fluid, single-molecule tracking 53
 - pathways
 - APP cleaving 218
 - caveolin trafficking 188
 - compensatory activation, caveolae 176
 - endocytic 84, 176
 - PI3K/Akt 254–256
 - signaling 116–123
 - paxillin, signaling pathways 124
 - pbFRET 146
 - pbFRET microscopy, lipid microdomains 164
 - PC 2–5, 9
 - DRM 50
 - PDGF 117
 - signal transduction 96
 - PDGFR, signal transduction 105
 - PDK1 *see* phosphoinositide-dependent protein kinase-1
 - PE 2–3
 - peptide contributions, free-cholesterol-binding sites 100
 - percolating raft membrane 9–10
 - peripheral SMAC *see* pSMAC
 - PHA 160
 - phalloidin, phosphorylation 129
 - phase diagram (ternary), SM/PC/cholesterol 4
 - phase separation
 - cargo sorting and vesicle formation 15
 - caveolin oligomers 38
 - cell membranes 5–7
 - fibroblasts 10
 - model membrane systems 3–5
 - phases
 - liquid-disordered 3–5
 - liquid-ordered 3–5
 - phosphatidic acid, signal transduction 94
 - phosphatidylcholine *see* PC
 - phosphatidylethanolamine *see* PE
 - phosphatidylinositol-3'-phosphate *see* PI(3)P
 - phosphatidylserine *see* PS

- phosphocaveolin 126–129
- Csk 124–125
- phosphocholine *see* PC
- phosphoinositide 3-kinase (PI3K), cell survival 254–256
- phosphoinositide-dependent protein kinase-1 (PDK1) 255
- phospholipase D2, signal transduction 94
- phosphoprotein, signaling pathways 124
- phosphorylation 115
- actin/plasma membrane attachment sites 128
 - caveolin *see* caveolin phosphorylation
 - cell migration 130
 - eNOS activity 238
 - signaling pathways 116–123
 - stable 129
 - tyr14 256–257
 - tyrosine 116–123
- photobleaching
- fluorescence recovery *see* fluorescence recovery after photobleaching
 - FRET 146
- phytohemagglutinin *see* PHA
- PI(3)P 2
- PI3K *see* phosphoinositide 3-kinase
- PI3K/Akt pathway, cell survival 254–256
- picket-fence model 54, 56
- placental alkaline phosphatase *see* PLAP
- planar lipid rafts, equilibrium 92
- PLAP 4, 8, 50
- plasma membrane 127–129
- fluid-mosaic model 46
 - microdomains 175
 - protein complexes 141
 - *see also* membranes
- plasmalemmal vesicles *see* caveolae
- plasmalogens, caveolae 94
- platelet-derived growth factor *see* PDGF
- polarity, modulation by caveolin 195–196
- polyacrylamide gel electrophoresis *see* PAGE
- polyethylene glycol, artificial frustration 32
- potassium channels *see* K⁺ channels
- preadipocytes, caveolin phosphorylation 117
- preassembly, IL-chains 157
- prebeta-HDL, signal transduction 94
- preferred bulb radius, caveolae 36–37
- primary cells, differentiated 91
- prion conversion, raft action 211–214
- prion diseases 205–223
- prion proteins
- internalization 81
 - processing 205–223
 - *see also* PrP^c
- pro-apoptotic activity, caveolin-1 253
- prostate cancer cells, survival-promoting activity of caveolin-1 253–254
- proteases, metallo- 214
- protein acylation, caveolae 186
- protein anchor, raft hypothesis 48
- protein clusters, cell fusion 155–156
- protein co-mobility 147
- protein coats, recyclable 13
- protein complexes, supramolecular 141–174
- protein organization, caveolae 187
- protein patterns, plasma membrane 142
- protein-protein interactions, tyrosine phosphorylation 123
- protein structure, caveolin 177–178
- protein transport, raft hypothesis 49
- proteins
- basolateral 14
 - caveolae 95–98
 - contact site 99
 - FC binding 101–102
 - GPI-anchored 51
 - lipid-anchored 48
 - membrane-associated 49
 - prion *see* prion proteins
- proteolytic attack on PrP^c, role of rafts 214
- proximity measurements 59–63
- PrP^c
- lipid rafts 205, 207–214
 - *see also* prion protein
- PrP^c conversion, role of rafts 208–210
- PrP^c-PrP^{Sc} transconformation 208, 210–214
- PrP^{Sc} 207
- formation 210–211
- PS 2–3
- pSMAC, immunological synapse 150
- PTEN, tumor suppressor protein 255
- q**
- quantitative immunogold labeling electron microscopy, endocytosis 71
- r**
- radiolabeled tracers, caveola 184
- raft action, prion conversion 211–214
- raft-aspect, caveolae 25
- raft concept, phase separation in cell membranes 5–7
- raft domains, clustered 8–9
- raft hypothesis, origin 45–48
- raft immobilization, caveolin 84–85
- raft integrity 159
- raft membrane, percolating 9–10
- raft models, current 47

- raft signaling, protein acylation 186
- rafts
 - lipid *see* lipid rafts
 - noncaveolar 69, 75
 - role in PrP^c conversion 208–210
- rapamycin, chaperone complexes 184
- rat basophilic leukemia *see* RBL
- receptor, insulin binding 117
- receptor autophosphorylation, signal transduction 104
- receptor families, lipid microdomains 163
- receptor kinase, signal transduction 106
- receptor tyrosine kinases, function 163–166
- recyclable protein coats 13
- regulation, caveolin-1 182
- regulatory cycle, caveolin-eNOS 236–238
- regulatory processes, local 154–155
- reorganization, membrane proteins 142
- reserve rafts, diffusion-based measurements 55
- resolution, SNOM 149
- resonance energy transfer process, fluorescence 59
- Rho GTPase activity, modulation by caveolin 195, 197–198
- rigidity, bending 27–28
- s**
- Saffman-Delbruck model, single-molecule tracking 54
- saturated acyl chains, transmembrane signaling 143
- scaffold hypothesis, caveolin 98–101
- scaffold motifs, signal transduction 99
- scaffold sequence, endothelin receptor-A 99
- scaffolded membrane domains
 - caveolae 10–12
 - caveolin *see* caveolin scaffolded domain
- scanning near-field optical microscopy 149
- scavenger receptor BI *see* SRBI
- scavenger receptors, caveolae 187
- SCLC *see* small-cell lung cancer
- scrapie PrP *see* PrP^{Sc}
- SDS-PAGE
 - caveolae 177
 - lipid rafts 51
- SDS-resistant complexes 117
- secondary structure, caveolin 177
- secretase 215–223
- α -secretase, role of caveolae and lipid rafts 220–221
- β -secretase, role of caveolae and lipid rafts 206, 214–218
- γ -secretase, role of caveolae and lipid rafts 221–222
- secretory synapse, immunological synapse 150
- Semliki Forest virus, raft hypothesis 49
- Ser1177 phosphorylation, eNOS activity 238
- sex hormone action, caveola 185
- SFK *see* Src-family kinase
- SH2 120
- SH2-mediated binding, phosphocaveolin 126
- shaping forces, caveolae 25–42
- Shiga toxin, endocytosis 77
- sialidase, signal transduction 95
- signal transduction
 - caveolae 91–114
 - FC changes 104–106
- signaling
 - caveolae 115–140
 - time course 105
 - transmembrane 141–174
- signaling cascades
 - activation 124
 - caveolin 115
- signaling complexes, caveolin 132
- signaling molecules, caveolin phosphorylation 133
- signaling pathways 116–133
 - caveolin phosphorylation 121
 - phosphorylation 256–257
- signaling platforms, lipid rafts 156–162
- signaling proteins
 - classes 96
 - scaffold motif 99
- Simian virus 40 (SV40) 200
 - raft and caveolar endocytosis 14
 - transendothelial transport 74
- Singer-Nicolson fluid mosaic membrane model, validity 141
- single kinase knockout mice 119
- single-molecule studies, diffusion-based measurements 52–55
- single-particle tracking 52
 - immunological synapse 151
 - membrane molecules 53
- SM 2–4, 9
 - DRM 50
- small-cell lung cancer (SCLC), role of caveolin-1 251
- SNARE, fluorescence correlation spectroscopy 58
- SNOM 149, 165
- sodium dodecyl sulfate *see* SDS
- sodium dodecyl sulfate-polyacrylamide gel electrophoresis *see* SDS-PAGE

- sorting signals, cargo sorting and vesicle formation 15
 - spectroscopic ruler 145
 - spectroscopy, fluorescence *see* fluorescence correlation spectroscopy
 - spherical membrane cap 28
 - sphingolipid-rich microdomains 91
 - sphingolipids
 - APP processing 222
 - raft hypothesis 45
 - sphingomyelin *see* SM
 - sphingomyelinase, signal transduction 95
 - spontaneous curvature 27
 - SPT *see* single-particle tracking
 - SR-BI, scavenger receptors 187
 - SRBI 185
 - Src-family kinase (SFK) 118–119, 127, 256–257
 - inhibitors 119
 - phosphorylation 130
 - regulation 125
 - signal transduction 106
 - Src-homology 2 *see* SH2
 - SSR, diffusion-based measurements 55
 - statins
 - reduction of caveolin abundance 240–242
 - stimulation of endothelial tube formation 241
 - statistical confidence, FRAP 56
 - steady-state anisotropy, proximity measurements 61
 - sterol uptake, caveolin 188
 - stress fiber formation, roles of caveolae and caveolin 195–202
 - stress-induced changes, caveolin-1 expression 257–258
 - stress-induced pathways, opposing 130
 - strong cholesterol depletion 216
 - subcellular locations, caveolin-1 presence 181
 - superstructures, ErbB2-containing 164
 - suppression, caveolin-1 in cancer cells 252–254
 - supramolecular organization, immunological synapse 150
 - supramolecular protein complexes
 - formation 141–174
 - lipid rafts 162
 - surface scanning resistance *see* SSR
 - surface tension, lipid membrane 27
 - survival-promoting activity, caveolin-1 253–254
 - SV40 *see* Simian virus 40
 - syntaxin 3, apical t-SNARE 16
 - synthases, endothelial nitric oxide 233–246
 - synthetic lipid bilayers, signal transduction 92
- t**
- T-cell homeostasis, lipid rafts 156
 - T-cell receptor *see* TCR
 - T cells
 - activation 154
 - raft clustering 8
 - T lymphocytes 154
 - T lymphoma cells, human 157
 - t-SNARE, syntaxin 3 16
 - TAMRA-4D5-labeled ErbB2 receptors 165
 - TC10, GTP-binding protein 200
 - TCR complex, immunological synapse 150
 - TCZ 52
 - temperature
 - melting, lipid mixtures 3
 - membrane 27
 - ternary phase diagram, SM/PC/cholesterol 4
 - TfR 156, 160–162
 - TGFβ 82
 - TGN *see* trans-Golgi network
 - thermodynamic phase separation, membrane proteins 35–38
 - Thr495 phosphorylation, eNOS activity 238
 - Thy-1, GPI-anchored protein 8
 - TNFα 124
 - traffic, membrane *see* membrane traffic
 - trafficking
 - caveolin 183–184
 - prion protein 205–223
 - trafficking cycle, caveola 184–185
 - trafficking pathways, caveolin 188
 - TRAMP mouse model 253, 256
 - trans-Golgi network (TGN) 50, 215
 - APP cleaving pathways 218
 - endocytosis 72
 - transconformation, PrP^c-PrP^{Sc} 210–214
 - transendothelial transport, endocytosis 73–74
 - transferrin receptor *see* TfR
 - transforming growth factor beta *see* TGFβ
 - transient confinement zone *see* TCZ
 - transmembrane proteins 48
 - transmembrane receptor tyrosine kinases, lipid microdomains 163
 - transmembrane receptors, signal transduction 96
 - transmembrane signaling 141–174
 - complex 105
 - transport, transendothelial 73–74
 - trastuzumab, cancer therapy 165
 - Trojan peptide 102

- tube formation, endothelial 241
- tumor cell survival, role of caveolin-1 249–259
- tumor necrosis factor- α *see* TNF α
- tumors, angiogenesis 241–242
- tyr14 phosphorylation 256–257
- tyrosine, caveolin phosphorylation 116–123
- tyrosine kinases 119
 - signaling pathways 116
- u**
- unidentified intracellular compartment (UIC) 218
- v**
- vascular endothelial growth factor (VEGF) 241–242
 - signal transduction 97
- vascular functions, heart 234
- vascular permeability, transendothelial transport 74
- vascular relaxation, endothelium-dependent and NO-mediated 242–243
- vasodilation, caveolin-eNOS interaction 242–244
- VEGF *see* vascular endothelial growth factor
- venular endothelial cells, caveolin determination 180
- vesicle formation, membrane traffic 15
- vesicle trafficking, caveolin 183
- vesicular vacuolar organelle *see* VVO
- virus, caveolae wave 74
- voltage-gated K⁺ channels, lipid rafts 154–155
- VVO, caveolin 180
- w**
- water permeability, caveolae 94
- y**
- yellow fluorescent protein (YFP), single-molecule tracking 54