

Index

Note: entries followed by a lower-case *f* or *t* represent information to be found in figures or tables respectively.

- ABIN-2, and Tie2, 254
 ABO blood group, and von Willebrand factor, 1602
 Aborigines (Australia), 132
 ABT-510, 332
 acanthocephalans, 34
 accessory hearts, 67, 71
 ACE. *See* angiotensin-converting enzyme
 acetaminophen, and liver toxicity, 1233
 acetylated low-density lipoprotein (acLDL), 1432
 acetylcholine (Ach), 988, 1663, 1665
 acetylcholinesterase inhibitors, 1147, 1149
 acid-base balance, in diet, 130
 acidosis, 1525, 1526*f*
 acinar pancreas, 901
 acquired immune deficiency syndrome (AIDS). *See also* human immunodeficiency virus (HIV)
 Kaposi's sarcoma, 1471, 1472, 1475, 1476
 peliosis hepatis, 1233
 thrombotic thrombocytopenic purpura, 1339
 acquired protein S deficiency, 986
 actin, 696, 697*f*, 700, 701, 702
 actin-binding proteins, and platelets, 594*t*, 597–8
 actinomycin D, 1230
 activated factor VII, 1528
 activated leukocyte cell adhesion molecule (ALCAM), 1165
 activated protein C (APC). *See also* protein C
 acute respiratory distress syndrome, 1185–6
 anti-inflammatory activity, 975–7
 antithrombin, 962, 963
 apoptosis, 1088
 barrier regulation, 1025–6
 disseminated intravascular coagulation, 1334
 protein S, 983–4
 resistance to, 977–8, 1484
 sepsis, 1147, 1298
 therapeutic considerations, 979
 thrombomodulin, 939, 941
 transformation of protein C to, 974–5
 activating thrombin-activatable fibrinolysis inhibitor (TAFI), 939–40
 activation, of endothelial cells. *See also* coactivators
 acute respiratory distress syndrome, 1181–2
 atherosclerosis, 1214, 1216–17
 endothelial microparticles, 1622
 Ets factors, 815
 magnetic resonance imaging, 1649–50
 placental trophoblast cells, 1481–3
 use of term, 1112
 active targeting, of magnetic resonance imaging, 1646–7
 active transport pathways, 882
 activin receptor-like kinase (ACVRL1), 1115–16
 acute allograft rejection, 438, 1421*t*
 acute coronary syndrome (ACS), 1215, 1628, 1632*t*. *See also* coronary heart disease
 acute hemorrhagic leukoencephalitis (AHLE), 1147
 acute lung injury (ALI), 489, 1178–9, 1535. *See also* acute respiratory distress syndrome (ARDS); transfusion-related acute lung injury (TRALI)
 acute mountain sickness (AMS), 516–18
 acute renal failure (ARF), 1275, 1280. *See also* renal failure
 acute respiratory distress syndrome (ARDS). *See also* acute lung injury (ALI); transfusion-related lung injury (TRALI)
 antithrombin, 967
 blood flow regulation, 1186–7
 blood transfusion, 1535
 burn injury, 1507
 clinical features and physiology, 1179
 endothelial barrier function, 1184
 endothelial cell activation and injury, 1181–2
 future directions in research, 1188
 hemostasis, 1184–6
 leukocyte and platelet interactions, 1183*f*, 1187–8
 leukocyte transmigration, 581
 malaria, 1303
 origin and use of term, 1178–9
 oxidative stress, 1188
 platelet-endothelial-leukocyte interaction, 1183*f*
 study of endothelium, 1180–1
 tidal volume ventilation, 489, 493
 trauma, 1527
 ADAMTS13 deficiency, 1338, 1339, 1340–1
 adaptation. *See also* evolution
 avian endothelium, 92–3
 definition, 74*n*2
 exercise, 509–10
 giraffe cardiovascular system and gravity, 99–105
 space travel and cardiovascular, 520–1
 teleost endocardium, 82
 use of term, 66*n*1
 adaptive immunity, 430–1
 AdCA5 (adenovirus), 251–2
 Ad-COX-1, 1009, 1010
 adeno-associated viruses (AAVs), 1726, 1727*t*, 1728*t*
 adenomatous polyposis coli (APC), 773
 adenosine deaminase (ADA), 390
 adenosine triphosphate (ATP), and diabetes, 1371
 adenoviruses
 fate mapping, 168, 169
 gene transfer, 1726, 1727–31

- adenoviruses (*Cont.*)
 hypoxia-inducible factor 1 and angiogenesis, 251–2
 tumor-like blood vessels, 1463
- adenyl cyclase associated protein I, 594*t*
- adherens junction. *See also* adhesion; cell junctions
 barrier regulation and restoration, 1019, 1024
 β -catenin, 774–6
 blood-brain barrier, 1127–8
 cytoskeleton, 696
 Ebola virus, 1312
 electron microscopy, 649
 leukocyte transendothelial migration, 1033
- adhesion, of endothelial cells. *See also* antiadhesive therapeutics; cell adhesion molecule complexes; focal adhesion; leukocyte adhesion deficiency; matrix adhesion
 atherosclerosis, 1218–20, 1221
 barrier regulation and role of junctional and matrix, 1019–20
 burn injury, 1509–10
 drug targeting, 1739
 Ebola virus, 1312–13
 endothelial microparticles, 1627–8
 Eph/ephrin system, 349
 fever-range thermal stress and lymphocyte-HEV, 472–7
 high endothelial venules, 1573–6
 inflammation, 1299*t*
 integrins, 709
 leukocyte transendothelial migration, 1031–3
 luminal glycocalyx and leukocyte, 692
 nuclear factor- κ B signaling, 790
 opioid receptors, 455
 platelets, 588–90, 593*t*
 protein kinase C, 750
 protein tyrosine phosphatases, 767–8
 P-selectin, 1052
 real-time imaging, 1655–6
 sickle cell anemia, 1352–3, 1355
 skin inflammation, 1439
 syndecans, 400
 von Willebrand factor, 918–19
- adhesive glycoproteins, 597
- adipocytokines, and diabetes, 1377
- adipogenesis, and peroxisome proliferator-activated receptors, 797
- adipose tissue blood flow (ATBF), 1265–7, 1268
- adipose tissue endothelium, 1265–9
- AdLacZ (adenovirus), 251
- Ad-PGIS, 1009, 1010
- adrenal vein thrombosis, 1345
- adrenomedullin, 564*t*
- adult respiratory distress syndrome. *See* acute respiratory distress syndrome (ARDS)
- adult vasculogenesis, 1444–5
- advanced glycation end-products (AGEs), 419–26, 1373, 1544
- Aequorea victoria*, 1657
- aerobic capacity, and endothelial function, 506–509, 511
- aestivation, 82*n*4
- afferent arteriole, 1273*t*
- affinity purification, and phage displays, 899
- Afghanistan, and opioids, 451
- Africa, and Kaposi's sarcoma in children, 1472
- age and aging. *See also* age-related macular degeneration; age-related vascular disease; children
 erectile dysfunction, 1544–5
 hepatic sinusoidal endothelial cells, 1229
 natural selection, 123
- agent-based models (ABMs), 217, 1752, 1754–8, 1793–7. *See also* models and modeling
- age-related macular degeneration (AMD), 432, 434*t*, 1399
- age-related vascular disease, 1397–1401
- aggressive autoimmune syndrome, 434*t*
- Agkistrodon blomhoffi brevicaudus*, 466
- Agkistrodon caliginosus*, 464
- agonistic angiotensin (AT)-1 receptor autoantibodies, 1495–6
- agriculture, and ancestral human biomedical environment, 129, 130, 131
- AIDS. *See* acquired immune deficiency syndrome; human immunodeficiency virus (HIV)
- air breathing, evolution of in fishes, 42
- Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS), 1671
- air pollution, 531
- Akt signaling
 cell migration, 732–3
 estrogen, 1674–5
 nitric oxide synthase regulation, 731–2, 991
 retinal vascular development, 1157
 statins, 733, 1669–70
 survival signals, 730–1
 tissue factor expression, 934
 upstream activators and downstream targets, 729–30
- Alagille disease, 373
- albumin, 596*t*, 1017
- albuminuria, 1290
- alcohol use, and avascular necrosis, 1550
- aldose reductase (AR), 420
- Alexander the Great, 451
- alicaforfen, and inflammatory bowel disease, 1251–2
- ALK1, 309, 310, 1117, 1119–20, 1121
- allergic contact dermatitis, 1421*t*
- allergic encephalomyelitis, 1065
- allograft rejection, and T cells, 1105. *See also* cardiac allografts; chronic allograft nephropathy
- allometry, 107, 111
- allotransplantation, 438
- alpha granules, 590–1, 658
- altitude, 93, 516–18. *See also* space travel
- ALT-711, 1544
- alveolar blood vessels, 1161, 1164
- Alzheimer disease, 781, 832, 922, 1131, 1147–9
- Ambler, C. A., 269
- AMD (inflammatory condition), 439
- American Meteorology Society, 216
- amines, and metabolism in fish endothelium, 62
- amino acids, 635–6, 637–8, 819*f*. *See also* protein(s)
- aminoguanidine, 1544
- aminolevulinic synthase (ALAS-2) gene, 151
- aminopeptidase A (APA), 902
- aminopeptidase P (APP), 901
- ammonium, in blood, 259–60
- AMP-activated protein kinase (AMPK), 1374
- amphibians, 42–3, 85–6, 1555. *See also* *Xenopus laevis*
- Amphioxus (Branchiostoma)*, 40
- amphoterin, 422
- anabolic steroids, 1229
- analogy, and organization of information, 199, 204–205
- anaphylotoxins, 435–7, 438
- anaplastic cancers, of thyroid, 1391
- anatomic imaging, of blood vessels, 1661–2
- anchoring villi, 1480
- androgens, 1518
- androstenediol, 1517–18
- aneural heart, 67*n*4
- aneurysms, and Kawasaki disease, 1405
- angina, and organic nitrates, 1682, 1683
- angina pectoris, 1605*t*
- angioblasts, and vascular development in zebrafish, 152–3
- angiogenesis. *See also* angiogenic switch; angiogenic tone; antiangiogenic therapy; development; vasculogenesis
 agent-based model of tumor growth, 1793–7
 age-related vascular disease, 1399, 1400–401
 Akt signaling, 729–33
 Alzheimer disease, 1148–9
 apoptosis, 1087, 1093
 aquaporin 1 and, 717, 718
 blood vessel growth, 1449–52
 bronchial circulation, 1174–5
 cardiac myocytes, 603

- cytoskeleton, 702
 definition of, 1444–5
 diabetes, 1378–9
 endothelial cell differentiation in
 mammals, 162, 163–4
 Eph/ephrin system, 346–8
 Ets factors, 814–15
 evolution of vascular development, 53–4
 fate mapping, 167
 fibroblast growth factors, 295–6, 299
 heparan sulfate, 956
 hepatocyte growth factor, 288
 hereditary hemorrhagic telangiectasia,
 1117–19
 history of research, 1445–9
 hyperbaric oxygen, 482–3
 hypoxia-inducible factor 1, 250–3
 Id proteins, 868–70
 ion channels, 727
 Kallikrein-kinin system, 447–8
 Kaposi's sarcoma, 1475
 Krüppel-like factor-2, 824
 magnetic resonance imaging, 1644*t*,
 1650–1
 microvessel building, 1718–19
 mitogen-activated protein kinases, 742
 neovasculature, 1451–2
 neuropilins, 337
 Notch genes, 371–3
 placental vasculature, 1489, 1490
 platelet-endothelial cell adhesion
 molecule-1, 1040
 pulmonary vascular development,
 184–5, 186*f*, 188–90
 reactive oxygen species, 379
 real-time imaging, 1656
 retina and hyaloid vasculature, 1154–8
 Rho GTP-binding proteins, 757–8
 skin, 1435–6
 sphingolipids, 406
 therapeutic strategies, 1452
 thrombospondins, 325
 thyroid gland, 1388–90
 transforming growth factor- β , 313–14
 tumors, 1461–3
 vascular targeting, 902–903
 Wnt signaling, 780
 angiogenic switch, 711, 898, 1387, 1451
 angiogenic tone, and sickle cell disease,
 1356
 angioplasty, 273, 330, 1328, 1603. *See also*
 cardiac bypass
 angiotensin(s)
 angiogenesis, 250–1, 1446
 discovery of, 352
 endothelial phenotypes, 355–6
 ligand-receptor interactions, 353–4
 lymphatic system, 1560
 pericyte investment, 537–8
 placental vascular development,
 1491–2
 retinal vascular development, 1156
 signaling, 355*t*
 therapeutic implications, 356–7
angiopoietin-like-3 gene, 352
 angioproliferation, and pulmonary
 hypertension, 1194–5
 angiotensin(s), as vasoconstrictors, 564*t*,
 1088, 1543. *See also*
 angiotensin-converting enzyme
 antibody, 138
 angiotensin-converting enzyme (ACE)
 bronchial circulation, 1174
 cardiac myocytes, 605
 drug targeting, 1740
 lung capillary ECs, 1164
 metabolism of fish, 62
 vascular targeting, 888
 angiotensin-converting enzyme inhibitor
 (ACEI), 554, 1604
 angiotensin receptor blockers (ARB), 554,
 1291
Anguilla anguilla, 82
 animal cap induction assay, and *Xenopus*,
 147–8
 animal models. *See also Xenopus laevis*;
 zebrafish; mouse
 acute respiratory distress syndrome,
 1188–9
 atherosclerosis, 1215–1216
 cell therapy, 1702
 heparin-induced thrombocytopenia,
 1349–50
 lymphedema, 1562, 1563*t*
 prosthetic vascular grafts, 1504
 real-time imaging, 1654–5
 skin inflammation, 1438–9, 1440*t*
 animal-most blastomeres, 143
 annelids, and evolution of cardiovascular
 system, 37, 38*f*
 Annexin A1 (AnnA1), 891
 Annexin A5 shield, 1363–4, 1365*f*
 Annexin V/prothrombinase assay, 1626
 ankle-brachial index (ABI), 1379, 1704
 anoikis, 730, 1091
Anopheles gambiae, 325
 anoxia, definition of, 1202
 anoxia-reoxygenation, of lung, 1209–10
 antagonistic pleiotropy, 124
 Antarctic icefish (*Chaenocephalus aceratus*),
 24, 59, 74–7
 antiadhesive therapeutics, 1251–2,
 1357
 anti- α 4 integrin, and inflammatory bowel
 disease, 1252
 antiangiogenic therapy
 drug targeting, 1740
 fibroblast growth factors, 299
 Kaposi's sarcoma, 1475–6
 pericytes, 541
 Sox genes, 866
 thyroid endothelium, 1393
 tumors, 1452
 antiapoptotic genes, and nuclear factor- κ B
 signaling, 791–2
 anti- β ₂-glycoprotein I (anti- β ₂GPI),
 1414–15
 antibodies. *See also* antiendothelial cell
 antibodies
 heparin-induced thrombocytopenia,
 1347–9
 Kawasaki disease, 1406–407
 proteomic mapping, 884, 885*t*
 transfusion-related acute lung injury,
 1536
 vascular targeting, 888
 VCAM-1, 1065
 anticoagulants. *See also* coagulation
 antithrombin, 960, 966–7
 apoptosis, 1088
 hemostasis, 910
 heparan sulfate, 956
 protein S, 983–4
 trauma, 1527
 antiendothelial cell antibodies (AECAs),
 1406–407, 1411–16
 antigen(s)
 antiendothelial cell antibodies, 1416
 antiphospholipid syndrome, 1361–2
 general and historical considerations,
 1100–102
 heparin-induced thrombocytopenia,
 1346–7
 homeostasis, 1104–105
 in vivo studies, 1103–104
 Kaposi's sarcoma, 1474*t*
 naïve or experienced T cells and
 costimulators, 1102–103
 pathological T-cell responses, 1105
 T-cell homing, 1098–100
 transfusion-related acute lung injury,
 1536
 antigen presenting cells (APCs), 1098
 antigranulocyte antibodies, 1536
 anti-ICAM-1 conjugates, 1065–6
 anti-interleukin (IL)-1, 1757
 antineutrophil cytoplasmic antibodies
 (ANCAs), 1412
 antioxidants. *See also* free radicals
 benefits of dietary, 127
 endothelial dysfunction from cigarette
 smoking, 1326
 endothelial phenotypes in disturbed
 flow, 236*t*
 leukocyte-endothelial interactions,
 582
 reactive oxygen species, 378
 antiparallel architectures, 722
 antiphospholipid antibody syndrome
 (APS)
 antiendothelial cell antibodies, 1414–15
 endothelial dysfunction, 1379
 endothelial microparticles, 1631, 1632*t*
 platelet aggregation, 587
 role of endothelial cells in, 1360–6

- antiphospholipid antibody syndrome (APS) (*Cont.*)
 trophoblast cells and complications of pregnancy, 1484
- anti-P-selectin therapy, 1054
- antiretroviral therapy, and Kaposi's sarcoma, 1472
- antithrombin (AT)
 coagulation, 960, 962
 development, 966
 diagnostic and therapeutic implications, 969–70
 disseminated intravascular coagulation, 1333
 evolution, 965–6
 genes and mutations, 964–5
 history of research, 960–1
 homeostasis, 910, 912*f*, 966–8
 protein structure, 961–3
- anti-tumor necrosis factor (TNF), 1757
- anti-VCAM-1 carriers, 1065
- A1 domain, and von Willebrand factor, 918
- $\alpha(1,3)$ -fucosylation, 1577–80
- aorta, 68, 69*t*, 70, 176, 235–6. *See also* aortic valve; aortic valve disease; dorsal aorta
- aorta-gonad-mesonephros (AGM) region, 163
- aortic valve, hemodynamics and endothelial phenotypes, 237–8
- aortic valve disease, 237–8
- APC. *See* activated protein C; antigen presenting cells
- APN/CD13, 902–904
- apoptosis, of endothelial cells. *See also* antiapoptotic genes
- angiopoietins, 355
- antiphospholipid antibody syndrome, 1366
- cellular and molecular basis, 1081–4
- cigarette smoking, 1321
- definition, 1081
- endothelial microparticles, 1622
- hepatocyte growth factor, 288
- history of research, 1081, 1084, 1085*t*
- importance of, 1084–5
- lipopolysaccharide, 415–16
- magnetic resonance imaging, 1644*t*
- myocyte enhancer factor 2, 851–2
- nuclear factor- κ B signaling, 791–2, 793
- pathology, 1090–3
- platelet-endothelial cell adhesion molecule-1, 1042–3
- protein S, 985
- pulmonary hypertension, 1195–6
- regulators and regulation, 1084
- retinal vascular development, 1157
- signaling, 1086–90
- thrombospondins, 330
- transforming growth factor- β , 313
- apoptosis-inducing factor (AIF), 1083
- apoptotic protein translocation, 1085*t*
- Apo2 ligand (Apo2L), 1083
- ApoL, 1082
- aquaglyceroporins, 714, 715
- aquaporins (AQPs)
 angiogenesis and cell migration, 717, 718–19
 corneal function, 717
 definition of, 714
 diverse physiological roles, 717–19
 lacteal endothelium in small intestine, 717
 lung microvessels, 716
 nonendothelial roles, 714–16
 pleural space and peritoneal cavity, 716–17
 renal vasa recta, 716
- arachidonic acid (AA), 1004, 1509
- Arachnids, 38
- archaeology, and ancestral biomedical environment of humans, 129–33
- Arctogadus glacialis*, 80*f*
- Arenaviridae, 1533
- Arg306 and Arg506, 983–4
- arginase, 1544, 1545
- arginine, 638
- Aristotle, 203
- armadillo* (ARM) gene, 773
- Arp2/3 complex, 1032
- arrest, of leukocytes, 578–9
- arsenic, 527, 530, 531
- arterial arches, in crocodiles, 44–5
- arterial circuits, 155, 360
- arterial thromboembolism, 96, 97
- arterial thrombosis, 965
- arterial tree, and composition of endothelial cells, 256–7
- arterial-venous (A-V) identity, 25
- arterial-venous specification, and Notch genes, 370–1
- arteries. *See also* arterial circuits; blood vessels; coronary arteries; limb arteries; vertebral arteries; vessel wall
- brain blood supply, 1140
- decapod crustaceans, 39
- endovascular trophoblast and remodeling of maternal, 1480–1
- hagfish, 68, 70
- hepatic blood flow, 1240–1
- Notch genes and development, 369–70
- pulmonary vasculature, 181, 184, 1161–3
- renal vasculature, 1271
- thyroid gland, 1387
- arteriogenesis, 296, 1444, 1446*t*, 1719
- arterioles, 61, 1457. *See also* efferent arterioles; terminal arterioles
- arteriovenous malformation (AVMs), and hereditary hemorrhagic telangiectasia, 1114–15, 1120, 1121
- arthritis, kininogens and angiogenesis in, 448. *See also* osteoarthritis; rheumatoid arthritis
- arthropods, and evolution of cardiovascular system, 38–40
- ascending vasa recta (AVR), 1271, 1273, 1274*f*
- ascidians, 40
- ascites tumors, 1458
- Asellius, Gasper, 1554
- aseptic bone necrosis, 501
- asparagine 803 (Asn-803), 249
- aspartic acid, and VCAM-1, 1060
- asthma, 786*t*, 1065, 1200, 1421*t*, 1693
- astrocytes, 1125–6, 1157–8
- astronauts, 520
- asymmetric dimethylarginine (ADMA), 1278, 1281–4
- asymmetry, and cell membrane transport, 632, 634–5, 637
- atheroma(s), and atherosclerosis, 1215
- atheroma-plaque microvessels, 1060
- atheromata, 439
- atherosclerosis
 adhesion molecules and chemokines, 1218–20
 animal models, 1215–216
 apoptosis, 1087*f*, 1090–2
 circulating soluble markers, 1603, 1605, 1606*t*
 clinical and pathological features, 1214–15
 complement, 439
 disturbed flow as risk factor, 236
 in dogs and cats, 95*n*3
 endothelial cell activation, 1216–17
 evolutionary analysis of, 124–7
 gene expression in endothelial cells, 1220
 human ancestral biomedical environment, 132
 ICAM-1 and VCAM-1, 1065
 leukocytes, 1217–18
 luminal glycocalyx, 692
 magnetic resonance imaging, 1649
 nuclear factor- κ B signaling, 786*t*
 platelet(s), 587, 589–90, 597
 platelet-endothelial cell adhesion molecule-1, 1041
 receptor for AGE and diabetic, 423–4
 risk factors, 1214, 1220
 sphingolipids, 407–408
 statins, 1670
 tissue factor expression, 935–6
 toxins, 529
 transforming growth factor- β , 315–16
 vascular smooth muscle cells, 545, 550–1
 VEGF and VEGF receptors, 273
- atorvastatin, 1670
- ATP-sensitive K⁺ channels, 726
- atrial fibrillation, and aging, 1400
- attractors, and modeling of complex systems, 1752, 1771–7

- atypical hemolytic uremic syndrome (ATTUS), 432
- Auerbach, Robert, 16
- Augustin, Hellmut, 360
- autocrine survival strategy, 1194
- autocrine system, 990, 1051–3, 1077–8
- autoagglutination, and malaria, 1306–307
- autoimmune diseases. *See also* acquired immune deficiency syndrome; aggressive autoimmune syndrome; autoimmune thyroid disease; heparin-induced thrombocytopenia; severe combined immunodeficiency
- antigen presentation, 1105
- emphysema as, 1199–1200
- leukocyte-endothelial interactions, 582
- protein S deficiency as, 986
- autoimmune thrombosis syndrome, 1360
- autoimmune thyroid disease, 1390–1, 1421*t*, 1423
- autologous conduit vessels, 1714
- autophosphorylation, and c-MET signal transduction, 286–7
- autoregulation, of liver blood flow, 1242
- autoseeding, and vascular stents, 1699, 1701, 1706. *See also* cell seeding
- avascular necrosis (AVN), 1550–2
- avascular tumor growth state, 1797
- Avastin, 268
- avian endothelium, and comparative biology, 92–3
- avidin staining, 887
- azathioprine, 1229, 1231
- azidodeoxythymidine (AZT), 1132
- bacteria, 1533, 1534*t*. *See also* *Escherichia coli*; infection; *Leptospira interrogans*; *Salmonella* spp.
- Bak protein, 1083, 1084
- balloon angioplasty, 330
- Barker's hypothesis, 127
- baroreflex, and space travel, 522, 523*f*
- barotrauma, 489–94
- barrier, endothelial. *See also* blood-brain barrier; blood-CSF barrier; blood-retinal barrier; glomerular filtration barrier
- activated protein C and regulation, 1025–6
- contractile apparatus and regulation, 1017–19
- integrity of and toxic insult, 529
- junctional and matrix adhesion in regulation, 1019–20
- mechanical stress and signal transduction in regulation, 1021
- mitogen-activated protein kinases, 742–3
- modified tensegrity model and regulation, 1017, 1018*f*, 1020, 1026
- platelet-endothelial cell adhesion molecule-1, 1043–4
- Rho GTP-binding proteins, 759
- sphingosine 1-phosphate, 1021–5
- vascular targeting, 887
- Bartonella* spp., 1233
- Barx2 gene, 190
- basal expression, of E-selectin, 1074
- basement membrane, 102, 178–9, 1125, 1148
- bats, 107, 109
- battlefield hemostasis, 1523–9
- BAY-43-9006, 1394
- β -catenin, 773–81
- B-cell leukemia/lymphoma 2 (BCL2) family, 253, 1083, 1084
- Behçet disease, 1416
- benfotiamine, 1373, 1382
- benzo(a)pyrene, 1326
- Bernard, C., 680
- betaglycan, 309
- bevacizumab, 866, 888, 1452, 1476
- Bichat, Xavier, 10
- Bid-dependent mitochondrial dysfunction, 1082
- bifurcation, and nonlinear dynamics, 1751
- bile pigments, and heme oxygenase, 999
- bilirubin, 999
- Billroth, Theodor, 9, 1255
- bimodal distribution, and cell fate dynamics, 1768
- bioconjugation, and drug targeting, 1735
- biocontainment, of filoviruses, 1317
- biodistribution analyses, and vascular targeting, 891
- bioengineering, of vascular prosthetics, 1501–503. *See also* genetic engineering
- biohybrid conduit vessels, 1714–15
- biomarkers. *See also* cellular markers; circulating soluble markers
- chronic valvular disease in dogs, 95
- drug targeting, 1737–8
- endothelial cell dysfunction, 1622–3
- Kawasaki disease, 1407
- tumors and angiogenesis, 1451–2
- biomedicine. *See* comparative biology; endothelial cells; endothelium; health and health care; therapeutic implications
- biomessengers, endothelial microparticles as, 1628
- biopanning, and phage displays, 899–900
- Biopanning and Rapid Analysis of Selective Interacting Ligands (BRASIL), 900
- biosensors, and platelet-endothelial cell adhesion molecule-1, 1040–2
- biosynthesis. *See also* genetic engineering
- of eicosanoids, 1005–1006
- of heparan sulfate, 949–51, 965
- biotinylation, and proteomic mapping, 887
- biotoxins, 528*t*
- biotransformation, and organic nitrates, 1682–3
- birds
- comparative biology and endothelium of, 92–3, 108, 109
- testosterone and neuronal development, 176
- vascular development, 25
- birth weight, and hypertension in pregnancy, 137, 139
- blastocyst, 1488
- blastomeres, 143, 145, 146*f*
- blood. *See also* ABO blood group; blood endothelial cells; blood flow; blood pressure; blood transfusion; blood vessels; coagulation; hemodynamics; hemoglobin; myoglobin; red blood cells
- angiopoietins, 356
- composition of arterial, 256–7
- composition of venous, 257–60
- ion channels and coagulation of, 727
- platelets and coagulation of, 594–5*t*
- supply to brain, 1140
- blood-brain barrier (BBB)
- barrier properties of ECs, 1141–2
- continuous endothelia, 882
- development of concept, 1124
- diabetes, 1376
- disease, 1129–33
- drug targeting, 1741
- evolution of endothelial heterogeneity, 55–6
- functions, 1126–9
- hagfish, 69*t*, 71
- morphology and microenvironment, 1124–6
- selective vectorial transport, 638
- blood-CSF barrier, 1129
- blood endothelial cells, 1612–16. *See also* blood outgrowth endothelial cells; blood vascular endothelial cells
- blood flow. *See also* adipose tissue blood flow; hemodynamics; shear stress and shear forces
- acute respiratory distress syndrome and regulation, 1186–7
- apoptosis, 1086
- autoregulation in liver, 1242
- avian endothelium, 92
- cerebrovascular innervation, 1142
- hemostasis, 910
- hepatic macrocirculation, 1239
- kidney, 1271
- lung ischemia, 1208
- maternal-fetal conflict over uteroplacental, 135–9
- measurement, 1659–60, 1662–6
- tumor blood vessels, 1459–60
- blood islands, 162–3
- blood outgrowth endothelial cells (BOECs), 1613–14, 1616–18

- blood pressure. *See also* hemostasis and hemostatic balance; hypertension giraffe and adaptations to gravity, 101–102, 103*f*, 104 hemodynamics, 231 hunter-gatherer populations, 129–30 blood-retinal barrier (BRB), 1129, 1154 blood transfusion, 1533–7 blood vascular endothelial cells (BECs), 1553 blood-vascular system, of annelids, 37 blood vessels. *See also* aorta; arteries; arterioles; capillaries; malformations; microvessels; veins; vessel walls anatomic imaging, 1661–2 angiogenesis and growth of, 1449–51 building of, 1714–19 E-selectin, 1077 pericytes, 1157 Sox genes, 863 structure and function, 1712–14 tumors, 1457–67 BMP activin membrane-bound inhibitor (BAMBI), 309 BMP receptor II gene (BMPRII), 316 body acceleration applied synchronously with the heartbeat (BASH), 1691 body mass index (BMI), 130, 131 body size hypertension in humans, 130 of mammals, 24–5, 107 Böhm, A. A., 13 *Bombyx mori*, 325 bone marrow, and hemostasis, 912, 913 bone marrow-derived cells, in pulmonary arterial hypertension, 1704–705 Bone Marrow Transfer to Enhance ST-elevation Infarct Regeneration (BOOST) trial, 1702 bone marrow transplantation, 871–2, 576, 936, 1230, 1550 bone morphogenetic protein (BMP), 162, 164–5, 174*t*, 176 bony fishes, 42, 59, 61. *See also* fish book lung, 38 bootstrap analysis, 115 bortezomib (Velcade), 253, 1394 *Bothrops jararaca*, 465, 466 botrocetin, 919 bovine pulmonary artery endothelial cell (BPAEC), 410, 415–16 brachial artery vascular reactivity, 1660 bradykinin(s), 447, 448, 499–500, 564*t*, 1007–1008 bradykinin potentiating peptides (BPPs), 463*t*, 467 brain. *See also* blood-brain barrier; brain disease cerebral malaria, 1303 comparison of brain ECs and peripheral ECs, 1143–4 composition of arterial and venous blood, 258 decompression sickness, 501 immune mediators in disease, 1144–9 opioid receptors, 457 structural properties of endothelium, 1141–3 supply of blood to, 1140 transport of drugs and xenobiotics, 638 vascular targeting, 888 venous drainage from, 1140 brain-derived neurotrophic factor (BDNF), 1132 brain disease, treatment of, 1131–3 brain multidrug resistance protein (BMDP), 1129 brain tumors, 1131 branching morphogenesis, 288 breast cancer cellular phenotype, 1795 forkhead signaling, 839 hypoxia-inducible factor 1, 250, 252 neuropilins, 342 secondary lymphedema, 1562 thrombospondins, 331 tissue factor expression, 935 vascular endothelial growth factor receptors, 272 breast cancer resistance protein (BCRP), 1129 bridged mother vessels, 1463*t*, 1464–5 bright field microscopy, 1656 Broglie, Louis de, 15 bromodomain, and PHD finger-containing protein 3, 595*t* bronchial vasculature, 1171–6 bronchiectasis, 1421*t* bronchoalveolar fluid (BALF), and acute respiratory distress syndrome, 1180, 1182 bronchopulmonary dysplasia (BPD), 191–2 brown adipose tissue (BAT), 110–11 Bruch membrane, 439 B7 family, 1099, 1102, 1104 β 2GPI glycoprotein, 1361–2, 1366 β 2-integrins, 1434 Budd-Chiari syndrome, 1246 Bunyaviridae, 1533 bupropion, 1329 burn injury, 1506–11, 1523 burn shock, 1507 butterfly effect, 1751 cadherins, 774–6, 1019, 1127 cadmium, 527, 528*t*, 530–1 *Caenorhabditis elegans* Akt genes, 729 β -catenin, 773, 774 fibroblast growth factors, 291 forkhead signaling, 834, 838, 841 heparan sulfate, 952 integrin genes, 707 phylogenetic analysis, 119, 120 protein-protein interaction networks, 1774 calcification, of blood vessels, 541. *See also* atherosclerosis calcific sclerosis, 237, 238 calcineurin, 828 calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia (CREST), 1113, 1193 calcium. *See also* calcium channel blockers composition of blood, 259 ion channels, 723 lung ischemia, 1207 muscle contraction, 548–9 vascular smooth muscle cells, 551–2 calcium channel blockers (CCB), 554 calcium ion-sensitive potassium ion channels, 725–6 caldesmon, 740–1, 1020 calibration, of agent-based models, 1757, 1758 calmodulin, 595*t* calreticulin (CRT), 327, 435 calumenin, 595*t* CAM-mediated endocytosis, 1065, 1066 camptothecin, 253 cancer. *See also* breast cancer; chemotherapy; prostate cancer; tumor(s) antiangiogenic therapy, 541 β -catenin, 781 Ets factors, 812 fibroblast growth factors, 294, 299 forkhead signaling, 834–5, 839 hemolytic uremic syndrome, 1337, 1338*t* high endothelial venule-like vessels, 1427 hypoxia-inducible factor 1, 252–3 neuropilins and semaphorins, 341–2 nuclear factor- κ B signaling, 786*t*, 792 opioid receptors, 458 pericytes, 1157 platelets, 597 Rho GTP-binding proteins, 759 thrombospondins, 330–2 thyroid, 331, 1391–2 vascular endothelial growth factor, 267, 268 canonical pathway, and Wnt signaling, 776, 779 capacitance veins, 104 capillarization, and hepatic sinusoidal endothelial cells, 1227, 1229 capillaroscopy, 1653 capillary. *See also* blood vessels; glomerular capillary; respiratory capillaries; vessel wall artificial systems, 1204

- barotrauma and leakage of in lung, 489–91
- bronchial circulation, 1173
- capillary-genesis, 1719
- caveolae, 670–2
- hagfish, 70–1
- normal microvasculature, 1457–8
- Notch genes and development, 369–70
- pancreatic islets, 177
- permeability of, 13, 61–2, 670–2, 882
- placental villi, 1492–3
- pulmonary endothelium and lung, 181, 1161–3
- renal vasculature, 1271
- skin, 1431, 1432
- specialized tissue-blood interface, 1719
- structure and function, 1712–14
- tumors, 1463*t*, 1464–5
- capillary basement membrane, of giraffe, 102
- carbohydrate metabolism, and ancestral human diet, 130–1
- carbon dioxide, 258–60, 484–5
- carbon monoxide
- cellular effects of, 994–5
 - cigarette smoking, 1325
 - endogenous production, 996
 - therapeutic applications, 999–1000
 - vascular remodeling, 998
 - vasomotor control, 997–8
- Carcinoscorpius rotundicauda*, 430
- cardiac allografts, 316, 936. *See also* allograft rejection
- cardiac bypass, and blood transfusions, 1537. *See also* angioplasty; coronary artery bypass
- cardiac cushion development, and transforming growth factor- β , 314–15
- cardiac endothelial cells, and fate mapping, 168–9
- cardiac malformations, and HIP-1 deficiency, 247, 248*t*
- cardiac myocytes, 547–8, 602–606
- cardiac neural crest, 169
- cardiac vasculopathy, and tissue factor expression, 936
- cardinal hearts, 67, 69*t*
- cardinal vein, 153–4
- cardioblasts, 120
- cardioglycoside, 528
- cardiomyopathy, in cats, 96
- cardiopulmonary bypass surgery, 591
- cardiopulmonary resuscitation (CPR), 1693
- cardiovascular depression, following trauma-hemorrhage, 1518
- cardiovascular diseases. *See also* coronary artery disease; ischemia; myocardial infarction; stroke
- age-related, 1400
 - in cats and dogs, 94–7
 - cigarette smoking, 1320–9
 - circulating endothelial cells, 1623
 - dietary salt intake, 1289–91
 - early growth response (Egr)-1, 818
 - exercise, 1693–4
 - hemodynamics and endothelial phenotype, 243
 - mortality rates, 1599, 1808
 - nitric oxide, 506, 991
 - opioid receptors, 456–7
 - organic nitrates, 1683
 - platelet-endothelial cell adhesion molecule-1, 1041
 - staging of, 1600*f*
 - toxins, 529–30, 531
 - uremia, 1278, 1281, 1282–3
 - vascular smooth muscle cells, 550–4
 - von Willebrand factor levels, 1603
- cardiovascular system. *See also* cardiovascular diseases; heart
- Antarctic icefish and evolution of hemoglobinless, 74–7
 - developmental evolution, 50–2
 - evolution of invertebrate, 30–40, 45–6
 - evolution of vertebrate, 40–6
 - giraffe and adaptations to gravity, 99–105
 - hagfish and structure or function, 67–72
 - key features, 29–30
 - maternal during pregnancy, 137
 - metabolism of shrew, 109–10
 - space travel and adaptation, 520–1
- cargo loading, and Weibel-Palade bodies, 658–9
- carotid artery, 1140, 1661–2
- carrier-mediated transport, and blood-brain barrier, 1128, 1132
- cartilaginous fishes, and evolution of cardiovascular system, 42. *See also* fish
- caspase cascades, and apoptosis, 1082, 1083–4, 1085*t*, 1091, 1093
- caspase-3, and endothelial microparticles, 1628
- cat(s), and cardiovascular disease, 96–7
- catalytic domain
- of protein kinase C, 747
 - of protein tyrosine phosphatases, 764
- cataract surgery, 1421*t*
- catch bonds, and P-selectin, 1052
- cathepsin S, 1175
- Catholic Church, and history of medicine, 6
- caudal hearts, 67, 69*t*
- causality, and cell fate dynamics, 1768–9
- causal network, 219–20
- caveolae
- continuous endothelia, 882
 - definition, 664–8
 - drug targeting, 1737
 - exercise, 513
 - functions, 668–72
 - heme oxygenase, 998, 999*f*
 - history of research, 664
 - therapeutic implications, 672–4
 - vascular permeability, 680–1, 682, 684–5
- caveolin gene family, 664, 669, 671–2, 674
- caveolin-1, and heme oxygenase, 998, 999*f*
- cavernosal smooth muscle, 1546
- cavernous transformation, 1245
- CC chemokine ligand 21 (CCL21), 1424–5, 1426, 1561, 1578*t*
- cell(s). *See also* angiogenesis; apoptosis; dendritic cells; endothelial cell(s); epithelial cell(s); high proliferative potential-colony forming cells; low proliferative potential-colony forming cells; perivascular cells; skeletal muscle cells; smooth muscle cells; T cell(s)
- autonomous effects of hypoxia-inducible factor 1, 252
 - differentiation of and vascular development in mammals, 161–5
 - fibroblast growth factors, 292*t*, 293–4
 - history of medicine, 9
 - proteomic mapping, 884, 885*t*
 - tensegrity, 1787–90
- cell adhesion molecule (CAM) complexes, and drug targeting, 1739. *See also* CAM-mediated endocytosis
- cell-cell interactions
- Eph/ephrin system, 348
 - E-selectin, 1076
 - hepatic sinusoidal endothelial cells, 1227
 - syndecans, 398–9
 - thrombomodulin, 941
- cell culture. *See* culture
- cell cycle, 551–2, 839
- cell differentiation, 839, 858–9
- cell-extracellular matrix interactions, and apoptosis, 1087
- cell fate, 368, 1768–70
- cell-free screening, and phage displays, 899
- cell growth, 727, 749–50, 792. *See also* cell proliferation; growth factors
- cell junctions, and blood-brain barrier, 1127–8. *See also* adherens junctions
- cell migration
- Akt signaling, 732–3
 - aquaporin 1, 717
 - Krüppel-like factor-2, 824
 - mitogen-activated protein kinases, 740–1
 - Rho GTP-binding proteins, 756–7
- cell motility, 288, 750, 870–3
- cell proliferation. *See also* tumor(s)
- endothelial progenitor cells, 1591–3
 - hepatocyte growth factor, 288
 - Krüppel-like factor-2, 824
 - lung ischemia, 1209, 1210*f*
 - pulmonary hypertension, 1194–5
 - tumor vascular endothelial cells, 1461
- cell scattering, and hepatocyte growth factor, 288

- cell seeding, of vessel wall, 1699–1701, 1714–15. *See also* autoseeding
- cell sodding, 1715
- cell specialization, and evolution of vascular development, 51*f*
- cell tagging methods, in fate mapping, 167–8
- cell therapy, with vascular stents and prostheses, 1699–1706
- cellular automata (CA), 217–19
- cellular markers, and circulating endothelial cells, 1605, 1607. *See also* biomarkers
- cellular phase, of inflammation, 654
- cellular vascular linings, hypotheses for evolution of, 45–6
- cellulitis, 1437*t*
- central arterioles, 1256
- central memory T cells, 1100
- central nervous system
 β -catenin and tumors of, 781
 blood-brain barrier, 1124, 1131
 retinal microvasculature, 1154
- Cephalochordata (lancelets), 40–1, 71
- cephalopods, and evolution of cardiovascular system, 35–7
- ceramide, and apoptosis, 1089, 1091
- ceramide/S1P rheostat, 1043
- cerebral arteries, 1140
- cerebral arteriovenous malformations, 1115
- cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), 373
- cerebral cavernous malformation-1 (CCM1), 373
- cerebral hemorrhage, and renal disease, 1279
- cerebral malaria, 1130, 1632*t*
- cerebral vasculature, and drug targeting, 1741
- cerebrospinal fluid (CSF), and lymphatic system, 1554
- cerebrovascular innervation, and cerebral blood flow, 1142
- C5a signaling, 438
- C5b-9 signaling, 435–7, 438
- C4B-binding protein (C4BP), 984–5, 986
- Chaenocephalus aceratus*. *See* Antarctic icefish
- Chagas disease, 1533
- Charcot arthropathy, 1665
- chelicerates, 38
- Chelonians (turtles and tortoises), 43–4
- chemokine(s). *See also* platelet factor 4
 angiogenesis regulation, 1448*t*
 atherosclerosis, 1218–20
 high endothelial venule-like vessels, 1424–5, 1572–3
 leukocyte arrest, 578
- malaria, 1304
- nuclear factor- κ B signaling, 790–1
- peroxisome proliferator-activated receptors, 798
- P-selectin, 1054
- skin inflammation, 1434
- chemokine thymus and
 activation-regulated chemokine (CTACK), 1439
- chemotherapy, 299, 1230, 1246
- chetomin, 253
- chicken embryo, and comparative biology of endothelium, 92–3
- Chien, S., 242
- children. *See also* age and aging
 hemolytic uremic syndrome (HUS), 1337
 Kaposi's sarcoma, 1472
 Kawasaki disease, 1405
 lymphedema, 1562
- China, and opioids, 451
- Chionodraco hamatus*, 76, 81
- Chionodraco rastrispinosus*, 75
- Chlamydia pneumoniae*, 125, 126, 132
- chlorophyll, and photosynthesis, 122
- choanocytes, 32
- cholesterol. *See also* hypercholesterolemia;
 high-density lipoprotein; low-density lipoprotein
 ancestral human diet, 131
 atherosclerosis, 124, 125, 126, 127
- cholesterol-lowering drugs, 702. *See also* statins
- Cholesterol and Recurrent Events (CARE) trial, 1671
- choline acetyltransferase (ChAT), 1142
- cholinergic agonists, 1147
- cholinergic anti-inflammatory pathway, 1144–5
- cholinergic neurotransmitters
 acetylcholine (ACh), 1142
- Chondrichthians, 42
- chondroitin sulfate (CS), 948
- chordin, 238
- chorioallantoic membrane (CAM), 92–3
- chorioamnionitis, 1072
- choroidal vasculature, 1154
- Chomsky, Noam, 203
- chromatin characterization, of apoptosis, 1085*t*
- chronic allograft nephropathy (CAN), 1289–90
- chronic heart failure, exercise and health status, 507*t*, 508*t*, 510
- chronic inflammatory diseases, and high endothelial venule-like vessels, 1419–27
- chronic inflammatory liver disease, 614
- chronic intravascular hemolysis, 566
- chronic kidney disease (CKD), 1280, 1281, 1291. *See also* uremia
- chronic thromboembolism, 1174–5
- chronic valvular heart disease, 94–5
- chronic vasculopathy, and sickle cell disease, 1357
- Churg-Strauss syndrome (CSS), 1413, 1437*t*
- chylomicrons, 1227–8
- cigarette smoking
 atherosclerosis, 1606*t*
 cardiovascular disease, 1320–9
 emphysema, 1199
 endothelin-1, 1604
 thrombomodulin, 1603
 toxic agents, 531
- Ciona intestinalis*, 325
- Circle of Willis, 1140
- Circle of Willis disease, 1358
- circulating endothelial cells (CECs)
 biological significance, 1613
 cardiovascular diseases, 1623
 cellular markers, 1605, 1607
 clinical usefulness of, 1613
 enumeration of, 1613
 origin of, 1612–13
 phenotype, 1612
 sickle cell disease, 935, 1354–5, 1551
 soluble markers, 1602–605
 systemic vasculitis, 1416
 tissue factor, 1614*f*
- circulating marrow-derived EPCs, 1594
- circulatory system, and history of medicine, 7–10. *See also* vascular system
- circumventricular organs (CVOs), 1127, 1141–2, 1145–6
- cirrhosis, 1243, 1245
- cis*-acting elements, and forkhead signaling, 835–6
- citrate anions, in blood, 259
- city, as metaphor for biological system, 211–14
- c-jun N-terminal kinase (JNK) pathway, 837
- clade, and phylogenetic analysis, 116, 118
- classification system, for tumor blood vessels, 1459, 1463*t*. *See also* phylogenetic analysis
- claudins, 1127
- cloche* mutation, 152–3
- cloning, of thrombospondins, 325*t*
- Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events (CAPRIE) and Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) studies, 391
- clotting cascade, 910, 912*f*
- ClustalW program, 114, 115, 117*f*, 118*f*, 119*f*
- clusterin, 593*t*
- clustering coefficient, 1761
- c-MET, as receptor for HEPATOCYTE GROWTH FACTOR, 286–8

- C-natriuretic peptide (CNP), and regulation of vasoreactivity, 824
- Cnidaria*, 951
- cnidarians, and evolution of cardiovascular system, 32–3
- cnidocyte, 32n4
- coactivators, and peroxisome proliferator-activated receptors, 797
- coagulation. *See also* anticoagulants; coagulopathy; disseminated intravascular coagulation; hemostasis; hypercoagulability; hypercoagulation; LPS-induced coagulation; procoagulant effects
- acidosis, 1525
- aging, 1398
- antithrombin, 961
- burn injury, 1506, 1510–11
- definition, 909–10
- diabetes, 1378
- endothelial microparticles, 1626–7
- hemodilution, 1525
- hemostasis, 913
- heparan sulfate, 956
- hypothermia, 1525
- pathology, 1314, 1523–9
- pathway for, 912*f*
- protein C, 975
- real-time imaging, 1656
- sepsis, 1298
- sickle cell disease, 1356–7
- thrombomodulin, 939
- thrombophilia-associated pregnancy complications, 1483–5
- coagulopathy, 1314, 1523–9
- codon usage bias, 113
- coelomic cells, 34
- coenzyme Q, 257
- coevolution, 126
- cofactors, and GATA transcription factors, 809*t*
- cofilin, 594*t*
- Cohnheim, Julius, 16, 1030
- coiled-coil domains, and vascular permeability, 684
- cold exposure, and high altitude, 518
- colitis-associated cancer (CAC), 792
- collagen, and endocardial cells of teleosts, 81. *See also* collagen columns; collagen gels
- collagen α -chain receptor, 1228
- collagen columns, in fish gills, 60
- collagen gels, 1717
- colloidal carbon, and electron microscopy, 652–3
- colony-forming unit in culture (CFU-C), 1590
- combat wounds, 1523–4
- combrestatin A4 phosphate (CA4P), 1392, 1393
- common lymphatic endothelial and vascular endothelial receptor (CLEVER)-1, 1576
- COMP (thrombospondin), 326
- comparative biology
- avian endothelium, 92–3
- cardiovascular and endothelial disorders in dogs and cats, 94–7
- energy turnover and oxygen transport in shrew, 107–11
- evolution of vascular development, 50–7
- fish endothelium, 59–64
- giraffe cardiovascular system, 99–105
- reasons for study, 23–5, 66
- skin breathing in amphibians, 85–90
- teleost heart and endocardium, 79–83
- comparative embryology, of vascular development, 53–4
- compartmentalization
- of biological organisms, 632
- of skin inflammation, 1437, 1438
- complement
- burn injury, 1508
- inflammatory mediators, 437–9
- innate and adaptive immunity, 430–1
- regulators of activation, 432, 435
- sepsis and multiorgan dysfunction, 1298
- signaling pathways, 431–2, 435–7
- thrombomodulin and activation, 939–40
- complex adherens, 780
- complexity, and endothelium as system, 1751–2. *See also* educational tools; models and modeling
- compressed-air therapy, 480
- computed tomography, and vascular smooth muscle cells, 555
- computer(s), and metaphors for endothelium, 215–22
- computer-based interactive diagrams, 1802
- concept simulation, 1801–803
- conceptual metaphors, 203
- conduit vessels, 679, 1713, 1714–16
- CIq effects, 435–7, 438
- confocal microscopes, 1656
- congenital homozygous protein C deficiency, 912
- congenital hypercoagulable states, 909, 910, 911*t*
- congenital lymphedema, 1562
- congenital nephrosis, 620
- congestive heart failure (CHF), 94–5, 96, 510
- conjunctival inflammation, after cataract surgery, 1421*t*
- Connaught Laboratories, 960
- constraint, concept of in evolutionary biology, 26–7
- container metaphors, 203
- context principle, 203
- continuous endothelium, 680, 881–2
- contractile apparatus, and barrier regulation, 1017–19
- convergent evolution, 30, 113
- Copernicus, 208
- coreceptor(s), for transforming growth factor- β and endoglin, 310
- coreceptor model, of heparan sulfate proteoglycan action, 953–5
- CO-releasing molecules (CORMs), 999–1000
- corepressors, and peroxisome proliferator-activated receptors, 797
- core proteins, 396, 948–9, 950*t*
- cornea, vascularization of, 1158
- corneal endothelium, and aquaporin, 717, 718–19
- coronary angioplasty, 1328
- coronary arteries, and endothelial function assessment, 1660–1. *See also* coronary artery disease
- coronary artery bypass, 298–9, 1501–505. *See also* cardiac bypass
- coronary artery disease (CAD)
- aging, 1398*t*
- atherosclerosis, 1214, 1215
- cigarette smoking, 1320, 1326–7
- circulating endothelial cells, 1416, 1603, 1605
- endothelial microparticles, 1628–9
- exercise and health status, 507–508*t*, 510
- as leading cause of death, 847
- myocyte enhancer factor 2, 848–50
- opioid receptors, 457
- organic nitrates, 1683
- statins, 733
- coronary heart disease, 943, 944, 1808. *See also* acute coronary syndrome
- coronary reactive hyperemia, 690
- coronary vascular endothelial cells, and fate mapping, 169
- corpus cavernosum, 70
- corpus luteum, and apoptosis, 1093
- cortactin, 1023
- cortical medullary junctional region, 1275
- corticosteroids, 582, 1550, 1676–8. *See also* steroid hormones
- costimulators, and antigen presentation, 1099, 1100, 1102–103
- coupling, of endothelial cells
- Akt signaling, 729–33
- aquaporin water channels, 714–19
- β -catenin, 773–81
- caveolae, 664–74
- cell integrins, 707–12
- cytoskeleton, 696–703
- early growth response-1, 818–20
- Ets factors, 812–16
- forkhead signaling, 834–43
- GATA transcription factors, 806–10
- Id proteins, 868–74
- introduction to, 629–31

- coupling, of endothelial cells (*Cont.*)
 ion channels, 721–7
 Krüppel-like factor 2, 822–5
 luminal glycocalyx, 689–93
 MEF2 signaling pathway, 847–52
 mitogen-activated protein kinases, 737–44
 NFAT transcription factors, 828–33
 nuclear factor- κ B signaling, 784–93
 peroxisome proliferator-activated receptors, 796–803
 protein kinase C, 746–51
 protein tyrosine phosphatases, 764–70
 Rho GTP-binding proteins, 753–60
 selective vectorial transport, 632–4
 Sox genes, 861–6
 vascular permeability, 679–85
 Vezf1, 855–9
 Weibel-Palade bodies, 657–61
- Cowdry, Edmund, 14
- coxsackie-adenovirus receptor (CAR), 1727
- crabs, 39, 67n3. *See also* horseshoe crab crayfish, 39
- C reactive protein (CRP), 1378
- creatinine, 1280, 1291
- Cre-lox approach, to fate mapping, 168
- Creutzfeldt-Jakob disease (CJD), 1534*t*
- critical limb ischemia (CLI), 1704, 1705*t*
- Crk-associated substrate p130, 241–2
- Crk family, 287
- Crk-like (CRKL) proteins, 287
- Crocodylia, and evolution of cardiovascular system, 44–5
- Crohn disease (CD), 1248, 1249, 1251, 1252, 1421*t*, 1423
- cross-talk signaling pathway, and β -catenin, 779
- Crotalus atrox*, 466
- crustaceans, and evolution of cardiovascular system, 38, 39–40
- cryopreserved allograft veins (CAV), 1503
- Ctenophora*, 951
- C-terminus, and forkhead signaling, 837
- C3 (complement), 430–2, 433*f*, 434*t*, 435, 438
- C-type lectin like proteins, 463*t*, 466–7, 941–2
- culture
 of blood endothelial cells, 1613–16
 of high endothelial cells, 1569
 history of biomedicine, 15–16
 tissue factor expression, 932–3
- culture modified mononuclear cells (CMMC), 1615–16, 1617*f*, 1618
- cumulative population doubling levels (CPDLs), of endothelial progenitor cells, 1591
- cutaneous circulation and vasculature, in amphibians, 85–6
- cutaneous leukocyte-associated antigen (CLA), 1433
- cutaneous lupus erythematosus, 1421*t*
- cutaneous lymphomas, 1421*t*
- cutaneous respiration. *See* skin breathing
- CXCL13, and high endothelial venule-like vessels, 1424, 1425, 1426
- cyanide, 568
- cyclic adenosine monophosphate (cAMP), 1022, 1126
- cyclic guanosine monophosphate (cGMP), 1682
- cyclic nucleotide-gated channels (CNG), 725
- cyclic strain, 699, 1021, 1086
- cyclooxygenase (COX), 1004, 1005*f*, 1006, 1008–1009
- cyclooxygenase inhibitors, 1173
- cyclophilins, 593*t*, 597
- cyclophosphamide, 332, 1230, 1231
- cyclosporine A (CsA), 793
- Cyclostomes, and evolution of cardiovascular system, 41
- cysteine-rich domain (CRD), and β -catenin, 776
- cystine-knot super family, of growth factors, 115–20, 308
- cytochrome-*c*, 1083
- cytochrome P450 (CYP450), 63, 82, 377–8, 1004
- cytokeratin, 698
- cytokines
 acute respiratory distress syndrome, 1181–2
 apoptosis, 1088–9
 brain endothelial cells, 1144–5
 burn injury, 1509
 diabetes, 1377
 high endothelial venule-like vessels, 1425
 Kaposi's sarcoma, 1473
 Krüppel-like factor-2, 825
 malaria, 1304, 1305
 nuclear factor- κ B signaling, 791
 peroxisome proliferator-activated receptors, 798
 prostacyclin production, 1008
 tissue factor expression, 933
 trauma, 1527
- cytolytic T lymphocytes (CTL), 1098, 1105
- cytomegalovirus (CMV), 1415, 1533, 1534*t*, 1729
- cytopathic effect, of Ebola virus, 1314–17
- cytoplasmic domain, of E-selectin, 1075
- cytoskeletal prestress, and tensegrity architecture, 1787–9
- cytoskeleton
 angiogenesis, 702
 as effector of morphology and heterogeneity, 698–700
 flow signaling, 240–1
 overview of, 696–8
 Rho GTP-binding proteins, 755–6
 syndecans, 400
- therapeutic implications, 702–703
- vascular permeability, 700–702
- cytosolic PGES (cPGES), 1006
- cytosolic protein tyrosine phosphatases, 765, 767*t*
- cytotoxic action, of drugs and chemicals, 528
- cytotrophoblasts, 272
- dacarbazine, 1230
- Danio rerio*. *See* zebrafish
- DARC, 1573, 1578*t*
- Darwinian medicine, 23n1, 122–7
- daughter vessels, of tumors, 1463
- Da Vinci, Leonardo, 230, 231
- dead metaphor, 202
- death, causes of. *See also* mortality rates
 cardiovascular diseases, 550, 1808
 chronic noncommunicable diseases, 1807–808
 cigarette smoking and premature, 1320
 combat wounds, 1523
 coronary artery disease, 847
 sepsis, 1294
 snake toxins, 461
 trauma, 1513
 vascular thrombotic disorders, 909
- death effector domain (DED), 1082
- death-inducing signaling complex (DISC), 1082
- decapods, 39–40
- decentralized endothelial mechanotransduction, 239–40
- decompression sickness (DCS), 497, 499, 500–502
- decorin, 314
- dedifferentiation, of vascular smooth muscle cells, 550
- dedifferentiation-differentiation, and endothelial development, 147
- deep vascular plexus (DVP), 1431–2
- deep venous thrombosis, 927, 1054
- De Fabrica* (Vesalius 1543), 7
- defenses, and trade-offs in natural selection, 124
- deficiency
 of ADAMTS13, 1338, 1339, 1340–1
 adhesion molecules and inflammation, 1299*t*
 of antithrombin, 965, 967
 of E-selectin, 1076, 1077
 of platelet-endothelial cell adhesion molecule-1, 1041, 1044
 of protein C, 977
 of protein S, 985–6
 of P-selectin, 1054, 1077, 1219
- degree distribution, and complex systems as networks, 1760, 1761*f*
- degrees of freedom, and cell fate dynamics, 1776
- dehydroepiandrosterone (DHEA), 1517, 1518

- Delbrück, Max, 1774
 Deleted in Colorectal Cancer (DCC)
 receptor, 363–4
 Delta-Notch signaling, 155–7
De motu cordis (Harvey 1628), 7
 dendritic cells, 1099, 1474*t*
Dendroaspis angusticeps, 465
 dense granules, 591
 dermal angiogenesis, and
 thrombospondins, 331
 dermal microvascular endothelium, in
 hagfish, 72*f*
 dermis, 85–6, 1431, 1439–40, 1507
 De Saussure, Ferdinand, 203
 Descartes, René, 8
 descending vasa recta (DVR), 1271, 1273,
 1274*f*
 desmosomes, 79, 634
 Desmosponges, and β -catenin, 774
 detergent resistance, of cellular
 components, 668
 deterministic models, 1752
 development. *See also* angiogenesis;
 embryogenesis; vascular development;
 vasculogenesis
 antithrombin, 966
 β -catenin, 780, 781
 bronchial circulation, 1171–2
 constraints on, 26–7
 Eph/ephrin system, 346–8
 E-selectin, 1072
 fate mapping, 167–71
 heparan sulfate, 952–3
 history of medicine, 9
 integrins, 707
 lymphatic system, 1554–61
 maternal-fetal conflict over
 uteroplacental blood flow, 135–9
 myocyte enhancer factor 2, 851
 Notch genes, 369–70
 of pancreas and liver, 173–9
 podocyte-endothelial interactions, 621–2
 protein C, 978
 reasons for study of, 25
 Sox genes, 863
 sphingolipids, 406
 splenic endothelium, 1259–60
 syndecans, 397, 399
 thrombomodulin, 942
 thrombospondins, 326
 Tie1 and Tie2 signaling system, 352–3
 tissue factor pathway inhibitor (TFPI),
 923
 toxicology, 531–2
 vascular endothelial growth factor
 receptors, 268–70
 vascular smooth muscle cells, 546–7
 Vezf1, 857–8
 view of endothelium from perspective
 of, 26–8
 Xenopus and study of endothelial, 142–8
 developmentally regulated endothelial
 locus-1 (Del-1), 890
 Dextran 40, 693
 D-glucose transport, 637
 diabetes. *See also* diabetic retinopathy
 adipocytokines, 1377
 adipose tissue endothelium, 1268
 advanced glycation end-products, 1373
 AGE-RAGE interactions, 419–20, 421,
 423–4, 425
 aging, 1400
 angiogenesis and vascular repair, 1378–9
 circulating soluble markers, 1604, 1605*t*,
 1606*t*
 coagulation, 1378
 dietary salt intake, 1291
 endothelial microparticles, 1630, 1632*t*
 endothelin-1, 1373–4, 1604
 erectile dysfunction, 1544
 exercise and health status, 508*t*, 510
 flow-mediated dilatation in insulin
 resistance, 1374–5
 forkhead signaling, 838–9
 glucose levels, 1370
 hexosamine pathway, 1372
 inflammation, 1377–8
 insulin action, 1375–6
 low-density lipoprotein, 1376–7
 microangiopathy, 1379
 microvascular blood flow, 1665
 nephropathy, 1379–80
 neuropathy, 1380–1
 nitric oxide, 1374
 permeability, 1376
 poly(ADP-ribose)-polymerase activity,
 1373, 1666
 polyol pathway, 1371–2
 protein kinase C, 751, 1372–3
 superoxide overproduction, 1370–1
 thermoregulatory response of skin, 1435
 transketolase activity, 1373, 1382
 vascular complications, 1382
 Diabetes Control and Complications Trial
 Research Group (DCCT), 420
 diabetic retinopathy
 complement signaling, 439
 endothelial dysfunction, 1381–2
 hypoxia-inducible factor-1, 251
 pericyte-endothelial cell interactions,
 541
 protein C expression, 978
 VEGF, 272–3, 1376, 1378–9
 diacylglycerol (DAG), 722, 723–4
 diagnosis. *See also* disease; health and
 health care; therapeutic implications;
 specific conditions
 antithrombin, 969
 blood endothelial cells, 1612–18
 circulating markers of endothelial
 function, 1602–607
 endothelial cell dysfunction, 1659–66
 endothelial microparticles, 1621–33
 E-selectin, 1078
 heparan sulfate, 956
 hereditary hemorrhagic telangiectasia,
 1113–14
 introduction to, 1599–1601
 magnetic resonance imaging, 1637–51
 P-selectin, 1054
 real-time imaging, 1654–7
 steroid hormones, 1674–8
 thrombomodulin, 943
 tissue factor pathway inhibitor, 927–8
 vascular smooth muscle cells, 554–5
 diagrams, and visual metaphor, 206–208
 diapedesis, 576. *See also* leukocyte
 transendothelial migration
 diet, human. *See also* health and health
 care; obesity
 ancestral biomedical environment, 130,
 131, 132
 atherosclerosis, 125, 126, 127
 chronic disease and modern, 123
 salt intake, 1287–92
 differential equations, 1780–3
 differentiation, of endothelial cells, 161–5,
 360. *See also* transdifferentiation
 diffuse alveolar damage, 1179
 diffusion. *See also* diffusion trapping
 blood vessel structure, 1712
 Fick's law of, 24, 70
 skin as gas exchanger in frog, 86–8
 diffusion-boundary layer, in amphipods,
 87–8
 diffusion trapping, and platelet-endothelial
 cell adhesion molecule-1, 1038
 dihydroxy eicosatetraenoic acid
 (di-HETE), 1004
 DiI-acetylated-low-density lipoprotein
 (DiI-Ac-LDL), 1591
 dilatation, and tumor blood vessels, 1459
 dilated cardiomyopathy, 95–6
 dimerization, of ICAM-1, 1064
 dimethylarginine dimethylaminohydrolase
 (DDAH), 1282
 dinosaurs, 44, 99
 dioxins, 532
 dipeptidase, 901
 diphenyleneidonium (DPI), 1205
 discontinuous endothelium, 680, 881
 disease. *See also* autoimmune diseases;
 brain disease; cardiovascular disease;
 deficiency; diagnosis; epidemics;
 genetic diseases; infection; pathology;
 prevention; risk factors; therapeutic
 implications; tumor(s); *specific*
 diseases
 adipose tissue endothelium, 1268
 age-related vascular disease, 1397–1401
 blood-brain barrier, 1129–33
 brain endothelium and immune
 mediators, 1144–9

- disease (*Cont.*)
 bronchial endothelium, 1172–5
 cell motility, 288
 disseminated intravascular coagulation, 1332–5
 endothelial function and dysfunction in chronic, 1111–112, 1809
 endothelial mimicry of placental trophoblast cells, 1479–85
 endothelial progenitor cells, 1594
 endothelial reactivity and susceptibility to, 1305–306
 genetic mutations in zebrafish and identification of human, 151
 hepatic microcirculation, 1239–46
 heterogeneity of ECs in pulmonary vascular, 1168–9
 high endothelial venule-like vessels, 1419–27
 history of medicine and understanding of, 9, 16–17
 homeostatic mechanisms, 246
 human ancestral biomedical environment, 132
 Notch genes, 373
 phage display, 903
 renal endothelium, 1275–6
 screening and early detection of, 1810
 skin endothelium, 1436–40
 Sox genes, 866
 splenic endothelium, 1260–2
 study of development, 25
 systemic vasculitis, 1411–17
 thrombomodulin, 943–4
 thrombotic microangiopathy, 1337–41
 thyroid endothelium, 1390–2
 vascular development defects and lung, 191–2
 vascular endothelial growth factor, 268
Diseases of the Arteries (Osler), 9
 disintegrins, 463*t*, 466
 disseminate intravascular coagulation (DIC), 1526–7
 disseminated intravascular coagulation (DIC), 977, 978, 1312, 1332–5, 1345
 dissipative systems, and cell fate dynamics, 1775
 distal angiogenesis model, 186*f*
 distant/vertical analogies, 202
 “distributed information processing,” 1769–70
 distributed reasoning, 202
 disturbed flow, 233, 234, 235–6
 divergent evolution, 113
 diving, and decompression sickness, 44, 45, 93, 497–502
 DNA-binding domains, 797, 813*f*, 828, 837
 DNA laddering, and apoptosis, 1085*t*
 DNAszymes, and early growth response (Egr)-1, 819–20
 docking structures, 701, 759, 1032
 dog(s), and cardiovascular disease, 94–6
 Dok-R molecule, 354
 domain mapping, 200*f*, 201
 domain organization, of protein tyrosine phosphatases, 764–5
 dorsal aorta (DA), 145, 147, 153–4
 dorsal longitudinal anastomotic vessels (DLAV), 154
 dorsal root ganglia (DRG), 337
doublebubble gene, 151
 doxorubicin, 884
 Down syndrome critical region 1 (DSCR-1) gene, 832–3
 downstream signaling, 240, 327–9, 354–5, 956
 drinking water, and arsenic, 530
Drosophila melanogaster
 Akt genes, 729
 β -catenin, 773, 774
 fibroblast growth factors, 291
 heparan sulfate, 952–3, 966
 homeotic transformation, 188
 integrin genes, 707
 phylogenetic analysis, 119–20
 protein-protein interaction networks, 1774
 Prox1 gene, 1556
 selectin genes, 1071
 Slit genes, 364
 thrombospondins, 325–6
 transient receptor potential channels, 722
 vascular smooth muscle cells, 546
 drug(s). *See also* chemotherapy; drug-induced toxicity; pharmacology; therapeutic implications; *specific drugs*
 blood-brain barrier, 1131–3
 caveolae, 672–4
 endothelial toxicity and overdoses of, 527, 528*t*
 ICAM-1 and VCAM-1, 1065
 selective vectorial transport, 638
 targeted delivery, 673–4, 887–91, 1734–42
 vasoactive delivery, 1662–3
 drug-eluting stent (DES), 552–3
 drug-induced toxicity, and hepatic sinusoidal endothelial cells, 1229
 drusen, 439
 Dürck nodules, 1303
 dynamic heterogeneity, of cell population, 1776
 dynamic instability, of microtubules, 697
 dynamin, 671
 early growth response (Egr)-1, 818–20
 Ebola virus (EBOV), 671, 1311–17
 ECs. *See* endothelial cells
 E-cadherin, 294
 EC activation, 1112
 EC dysfunction, 1112
 EC junction, 649
 eclampsia, 1494, 1495. *See also* preeclampsia
 ECM. *See* extracellular matrix
 EC markers, 883
 economics, and opportunity cost, 135
 EC-SOD gene therapy, 1545–6
 ectonucleotidases, 384, 389–90, 391*t*
 eczema, 1437
 Eddington, Sir Arthur, 1752
 edema, and burn injury, 1507
 EDRFs. *See* endothelium-derived relaxing factors
 educational tools, for understanding complexity, 1801–806
 eel. *See* lampreys
 effector caspases, 1083–4
 effector T cells, 1100
 efferent arteriole, 1273*t*
 EGFR. *See* endothelial growth factor receptor
 EGFR gene-protein interaction network, 1794–5
 Egypt, and history of medicine, 1030, 1240*t*
 eicosanoids, 1004–111
 elasmobranchs (sharks, skates, and rays), 59, 79
 elastase, 581, 1528
 Electron Microscope Society of America, 15
 electron microscopy
 endothelial microparticle heterogeneity, 1624–5
 history of endothelial biomedicine, 15, 643
 luminal glycocalyx, 689
 ultrastructural description of endothelium, 643–4
 vascular permeability, 679–81
 elephant, basal metabolic rate and oxygen consumption, 25
 Eli Lilly & Co., 751
 embryo. *See also* embryogenesis
 comparative biology and avian endothelium, 92–3
 endothelial development studies and *Xenopus*, 142–5
 E-selectin, 1072
 vasculature in zebrafish, 151–2
 embryogenesis, 352–3, 370, 779. *See also* development; embryo
 EM-800, 1676
 emergent properties, 629–30, 1751
 emilin, 313
 emperipoleis theory, 1296
 emphysema, 1092, 1199–1200
 enabling constraint, 26*n*4
 encoding endoglin (*ENG*), and hereditary hemorrhagic telangiectasia, 1115–16
 endemic disease, 132, 1472
 endocapillary layer, 689

- endocardial endothelial cells, and fate mapping, 168–9
 endocardial-mesenchymal transformation (EMT), 830
 endocardiosis, 94
 endocardium, of teleost heart, 79–83
 endocrine pancreas, 178
 endocrine system, 63, 1265, 1266–7. *See also* estrogen; hormones; steroid hormones; testosterone
 endocytosis, 294, 1064, 1065f, 1128, 1228
 endodermal organogenesis, 163
 endoderm differentiation, and GATA transcription factors, 807
 endogenous metabolites, and apoptosis, 1089
 endoglin
 hereditary hemorrhagic telangiectasia, 1116–17, 1119, 1121
 transforming growth factor- β , 309–10, 312, 314, 315, 316
 vascular targeting, 888
 endoplasmic reticulum (ER), and caveolae, 665
 endorepellin, 711
 endosialin, 890, 942
 endostatin, 711, 1077, 1495. *See also* statins
 endothelial barrier. *See* barrier
 endothelial cell(s) (ECs). *See also*
 activation; adhesion; cell(s); blood endothelial cells; cardiac endothelial cells; circulating endothelial cells; coupling; endocardial endothelial cells; endothelial progenitor cells; endothelium; gene expression; heterogeneity; high endothelial venules; human intestinal microvascular ECs; human umbilical venous ECs; liver sinusoidal endothelial cells; lymphatic endothelial cells; microvascular endothelial cells; phenotypes; signaling; tumor-associated ECs
 cigarette smoking, 1320–6
 comparison of brain and peripheral, 1143–4
 dietary salt intake, 1287–92
 distribution of transport systems, 635–6
 general anatomy, 646–7
 inflammation and functions, 1295–8
 specification, 1167–8
 endothelial cell-derived signals, 176
 endothelial cell-predominant proteins, 309–10
 endothelial-derived microparticles (EDMPs), 1377. *See also* endothelial microparticles
 endothelial dysfunction
 in chronic disease, 1809
 macrocirculation, 1659–62
 microcirculation, 1662–6
 use of term, 16–17, 1541
 endothelial growth factor receptor (EGFR), 766–7. *See also* EGFR gene-protein interaction network
 endothelial leukocyte adhesion molecule (ELAM)-1, 1049
 endothelial-mesenchymal transdifferentiation (EMT), and cardiac cushion development, 314–15
 endothelial microparticles (EMPs). *See also* endothelial-derived microparticles; microparticles
 clinical applications, 1628–33
 composition, 1625
 definition, 1621–2
 heterogeneity, 1624–5
 history of research, 1622
 measurement, 1626
 mechanisms of generation, 1623–4
 perturbation, 1622–3
 potential functions, 1607, 1626–8
 vascular activation, 1416
 endothelial mimicry, of placental trophoblast cells, 1479–85
 endothelial nitric oxide synthase (eNOS). *See also* nitric oxide synthase
 Akt signaling, 731–2
 cardiac myocytes, 605
 cigarette smoking, 1322
 diabetes, 1374
 exercise, 511
 gene regulation, 990
 glucocorticoids, 1677–8
 hemodynamics, 234
 hereditary hemorrhagic telangiectasia, 1116–17, 1121
 hyperbaric oxygen, 483
 Krüppel-like factor-2 and vasoreactivity, 824
 paracrine function, 991
 reactive oxygen species, 377
 regulation of NO production, 563t
 statins, 1668–71
 endothelial pockets, and vascular permeability, 683
 endothelial progenitor cells (EPCs)
 assays to quantitate proliferative potential, 1591–3
 asymmetric dimethylarginine and renal lesion repair, 1283
 as biomarkers of angiogenesis, 1452
 culture of blood samples, 1615–16
 definition, 1589
 disease and diagnostic implications, 1594
 identification from adult peripheral and umbilical cord blood, 1590–1
 liver regeneration, 610
 new blood vessel formation, 1379
 paradigms for other cell lineages, 1590
 reendothelization of prosthetic grafts, 1701
 vessel-derived endothelial cells, 1593–4
 endothelial protein C receptor (EPCR), 910, 911, 942–3, 975–6, 1334. *See also* protein C
 endothelin-converting enzyme (ECE)-1, 1374
 endothelin-1
 cardiac contractility, 603, 605
 cigarette smoking, 1323
 circulating soluble markers, 1603–604
 diabetes, 1373–4
 erectile dysfunction, 1542–3
 leukocyte-platelet interactions, 1187
 portal hypertension, 1243
 trauma-hemorrhage, 1516
 as vasoconstrictor, 564t
 endothelium. *See also* angiogenesis; avian endothelium; barrier; comparative biology; continuous endothelium; coupling; development; discontinuous endothelium; disease; endothelial cell(s); endothelial dysfunction; evolution; fenestrated endothelium; genetics; glomerular endothelium; gut-specific endothelium; hemogenic endothelium; history; input systems; lymphatic endothelium; lymphoid endothelium; metaphor; models and modeling; output systems; phenotypes; pulmonary endothelium; renal endothelium; special conditions; vascular endothelium
 adipose tissue as distinct from other types, 1267
 as complex system, 1751–2
 definition, 213
 as emergent system, 630
 exercise and protection of, 511–13
 high endothelial venules and plasticity of, 1581
 history of medicine, 5–17
 homeostatic balance, 914
 importance of apoptosis, 1084–5
 as integrated system, 1112, 1815
 introduction of term, 10–12
 microheterogeneity of in lung, 1161–9
 outputs as core property, 879
 reactivity of and susceptibility to disease, 1305–1306
 reconceptualization of biomedicine, 1815–816
 response to reactive oxygen species, 378–93
 responsiveness to local hemodynamics, 230
 role in disease, 1111–12
 sphingolipids and injury to, 407
 structural properties in brain, 1141–3

- endothelium (*Cont.*)
 surface of and tissue factor pathway inhibitor, 925
 as target for therapy, 1599
 use of term, 29
 “endothelium as barrier” hypothesis, on
 evolution of cellular vascular linings, 45
 endothelium-dependent relaxation, and reactive oxygen species, 379
 endothelium-dependent vasodilation (EDV), 1321
 endothelium-derived hyperpolarizing factor (EDHF), 511–12, 1542
 endothelium-derived relaxing factors (EDRFs), 63, 562, 988, 989
 endotoxemia, 415, 934–5
 endotoxins, 410, 1041. *See also* lipopolysaccharide
 endovascular fetal trophoblast cells, 1479
 end-stage renal disease (ESRD), 1280, 1283
 endurance training, 509–10, 511
 energy supply, and cardiac myocytes, 605–606
 enhanced external counterpulsation (EECP), 1692
 Entrez database, 115
 environment. *See also* altitude; microenvironment; temperature; tissue environment; weather
 atherosclerosis, 125
 cigarette smoking, 1326–7
 cutaneous breathing, 89
 disease and natural selection, 123
 hereditary hemorrhagic telangiectasia and stresses, 1121
 humans and ancestral biomedical, 129–33
 lung endothelial ECs, 1165, 1167
 teleost endocardium, 82–3
 enzyme-linked immunosorbent assay (ELISA), 1054
 enzymes and enzymatic systems. *See also* angiotensin-converting enzyme
 angiogenesis regulation, 1448*t*
 coenzymes, 257, 999, 1669
 endothelin-converting, 1374
 histone-modifying, 1769
 metabolism in fish endothelium, 63
 mitochondrial, 595*t*
 reactive oxygen species, 378
 EphB4
 arterial and venous EC differentiation, 346, 360
 pulmonary circulation, 184
 tumor angiogenesis, 348
 vascular development, 155, 345
 Eph/ephrin system
 cellular functions, 348
 characteristics, 345
 developmental angiogenesis, 346–8
 regulation of gene expression, 346
 shared neural and vascular guidance mechanisms, 361–2
 tumor angiogenesis, 348
 vascular development, 345–6
 Eph receptors. *See* Eph/ephrin system
 ephrinB2 (*efnb2*), 155, 345, 346–8, 360
 epidemics. *See also* disease
 chronic kidney disease, 1281
 definition of, 132
 hemolytic uremic syndrome, 1337, 1338*t*
 epidermal growth factor (EGF), and thrombomodulin, 940–1
 epidermis, 86, 1431, 1439–40, 1507
 epigenetic landscape, 1768, 1769, 1772–3, 1777
 epigenome, 129*n*2
 epistemic ladder, 205
 epithelial cell(s), and transport systems, 636–7
 epoxy eicosatetraenoic acid (EET), 1004, 1007
 equation-based models, 1780–4
 Erdos-Renyi (ER) model, of random networks, 1761, 1762*f*
 erectile dysfunction (ED), 1397, 1398*t*, 1401, 1541–7
 erysipelas, 1437*t*
 erythema nodosum leprosum, 1437*t*
 erythrocytes, and evolution of cardiovascular system in icefish, 74–7
 erythroid Krüppel-like factor (EKLF/KLF1), 822
 erythromelalgia, 1435
 erythropoietin (EPO), 247, 258
Escherichia coli
 complex networks, 1764, 1765, 1774
 heme oxygenase, 996
 hemolytic uremic syndrome, 1275
 recombinant tissue factor pathway inhibitor, 925, 927–8
 sepsis, 934, 975
 tissue factor pathway inhibitor and disseminated intravascular coagulation, 1333
 E-selectin
 atherosclerosis, 1217
 autocrine and paracrine effects, 1077–8
 circulating soluble markers, 1604
 development, 1072
 diagnostic and therapeutic implications, 1078
 evolution, 1071
 genetics and gene regulation, 1050, 1072–6
 high altitude, 517
 history of research, 1071
 homeostasis, 1076–7
 inflammation, 1059*t*
 leukocyte transendothelial migration, 1032, 1033
 nuclear factor- κ B signaling, 790
 protein structure, 1074–5
 protein tyrosine phosphatases, 768
 P-selectin interaction, 1053–4
 skin inflammation, 1439
 ESE-1. *See* Ets factors
 estrogen
 factor XII, 444
 forkhead signaling, 839
 menopause and thermoregulation, 1435
 selective receptor modulators, 1675–8
 trauma-hemorrhage, 1516–17, 1518
 Etanercept, 1426
 ET-1. *See* endothelin-1
 Ets binding sequences, 353
 Ets factors, 812–16, 851
 euglycemic inflammatory responses, and AGE, 422–3
 Eumetazoans, and heparan sulfate, 951–2
 evacuation time, and combat trauma, 1523–4
 evo devo (evolutionary developmental biology), 26, 46
 evolution. *See also* adaptation
 adaptive and innate immunity, 430
 ancestral biomedical environment of humans, 129–33
 antithrombin, 965–6
 β -catenin, 773–4
 cardiovascular system, 29–47, 74–7
 c-MET homologues, 286
 comparative biology of vascular development, 50–7
 Darwinian medicine, 122–7
 energy turnover and oxygen transport in shrew, 107–11
 E-selectin, 1071
 extracellular nucleosides and nucleotides, 385–6
 fibroblast growth factors, 291
 hagfish as model for early endothelium, 66–73
 heme oxygenase, 996
 heparan sulfate, 951–2
 heterogeneity of ECs, 1111
 immune adherence-mediated clearance, 437
 integrins, 707
 ion channels, 721–2
 metaphor, 209*f*
 mitogen-activated protein kinases, 737
 molecular phylogeny, 113–20
 nitric oxide, 989–90
 peroxisome proliferator-activated receptors, 796
 protein C, 974
 reasons for study, 23, 66
 Sox genes, 862
 thrombomodulin, 941–2
 thrombospondins, 325–6
 Tie1 and Tie2 signaling systems, 352

- tissue factor pathway inhibitor (TFPI), 922
 view of endothelium from perspective of, 25–8
 “evolutionary feasibility study,” 44
 exchange vessels, 679, 1713
 exercise
 adaptation and endurance training, 509–10
 aerobic capacity, 506–509, 511
 cardiovascular diseases, 1593–4
 health status and intensity of, 510–11
 hemodynamic alterations, 1691–2, 1693–4
 high altitude, 518
 protection of endothelium, 511–13
 vascular bubble formation, 498–9
 von Willebrand factor levels, 1602
 exocrine pancreas, 177
 exocytosis, 595*t*, 659–61
 exosomes, 591, 1621–2
 exotoxins, 1533
 expanded polytetrafluoroethylene (ePTFE), 1501–503
 experimental autoimmune
 encephalomyelitis (EAE), 1044, 1103, 1130–1
 experimentally induced allergic rhinitis, 1421*t*
 expert systems, 219
 exportins, and forkhead signaling, 836
 expressed sequence tags (ESTs), 147
 expression. *See* gene expression
 exTek, 357
 extra-alveolar vessels, 1161
 extracellular fluid volume (ECF), 259
 extracellular matrix (ECM), 288, 1086–8, 1125, 1215
 extracellular nucleotides and nucleosides
 ectonucleotidases and triphosphate diphosphohydrolase, 389–90
 evolution and primordial signaling molecules and mediators, 385–6
 history of research, 384–5
 homeostasis, 390–1
 pathobiology, 391
 purinergic receptors, 387–9, 391*t*
 role of in vasculature, 386–7
 therapeutic implications, 391
 extracellular-signal-regulated kinase (ERK), 1020
 extraembryonic vasculogenesis, 162–3
 extrinsic pathway, of apoptosis, 1081–3, 1085
 eye. *See* cataract surgery; cornea; retina; retinopathy
 facilitated variation, 27
 factor inhibiting HIP-1 (FIH-1), 248
 factor V mutations, 909, 910, 927, 978
 factor XII, 444, 445*t*, 909
 fallout endothelialization, 1699, 1716
 familial adenomatous polyposis (FAP), 773
 familial exudative retinopathy (FEVR), 780*t*, 781
 familial thrombophilia, 943
 farnesylpyrophosphate (FPP), 1669
 Fas-associated DD (FADD), 1081–2, 1084, 1088
 fascinae fenestrae, 683
 Fas ligand (FasL), 580–1, 1081, 1091
 fate mapping, 27, 82, 167–71
 fatty acids, and peroxisome proliferator-activated receptors, 799–800
 Fc- γ receptor, 1228
 femoral head, and avascular necrosis, 1550
 fenestrae
 electron microscopy, 647, 648, 681
 microfilaments, 700–701
 morphological heterogeneity, 881
 sphingolipids, 405
 vascular permeability, 682–3
 fenestral diaphragms, and vascular permeability, 684
 fenestrated endothelium, and vascular permeability, 680, 685
 Fenofibrate Intervention and Event Lowering in Diabetes (FIELD), 800
 fentanyl, 457
 ferritin, 81, 650, 654
 fetal circulation, and placental villous angiogenesis, 1489, 1490
 fetal liver kinase 1 (FLK 1), 268, 269–70
 fetal lung mesenchyme, 191
 fetal-maternal conflict, 125, 135–9
 fetal pneumonia, 1072
 fever-range thermal stress, and lymphocyte-HEV adhesion, 472–8
 FGF family, 953, 955
Fgfr1 knockout studies, 296
 fiber, in human diet, 131
 fiber matrix concept, and vascular permeability, 691–2
 fibrillin-1, 307, 315
 fibrin, 910, 1462. *See also* fibrinolysis
 fibrinogen γ -chain, 595*t*
 fibrinolysis
 acute respiratory distress syndrome, 1186
 aging, 1398
 anticoagulant mechanisms, 910, 912*f*
 burn injury, 1510–11
 diabetes, 1378
 disseminated intravascular coagulation, 1333–4
 Kallikrein-kinin system, 447
 statins, 1671
 thrombomodulin, 939–40
 trauma, 1527
 fibritin-CD40L virus, 1728
 fibroblast(s), and Kaposi’s sarcoma, 1474*t*.
 See also fibroblastic reticular cells
 fibroblast growth factors (FGFs)
 evolution, 291
 gastrulation and postgastrulation events, 162, 164–5
 heparin sulfate proteoglycan, 295
 history of research, 291
 knockout studies, 297–8
 lymphatic system, 1561
 overview of functions, 291–4
 receptors and signaling, 294–5
 secretion and endocytosis, 294
 therapeutic applications, 298–9
 vascular development, 295–6
 vasomotor regulation, 296–7
 fibroblastic reticular cells (FRC), 1571–2
 fibronectin, 890
 fibrous cap, and atherosclerotic plaque, 1215
 Fick’s law of diffusion, 24, 70
 filamin, 594*t*
 filariasis, 1562
 filipin, 671
 filoviruses, 1311, 1314, 1317
 fish. *See also* Antarctic icefish; bony fishes; hagfishes; zebrafish
 comparative biology of endothelium, 59–64
 gill vessels, 59–60
 oxygen diffusion, 24
 teleost heart and endocardium, 79–83
 vascular development, 25, 150–7
 flatworms, and evolution of cardiovascular system, 33
 flavonoids, and nuclear factor- κ B signaling, 793
Flk 1 gene, 152, 164
floating head (flh) mutation, 153–4
 floppy mitral valve syndrome, 94
 flow cytometry, 1054, 1626
 flow-mediated dilatation (FMD), in insulin resistance and diabetes, 1374–5
 flow-mediated endothelial cell orientation, 233*f*
 flow-mediated endothelial mechanotransduction, 238–43
 flow-mediated induction, of Krüppel-like factor-2 expression, 824–5
 flow-mediated vasodilation (FMD), 1660
 flow velocity, and shear stress, 233–4
 fluorescence microscopy, 1656
 fluorescence resonance energy quenching (FREQ), 1657
 fluorescent tags, for real-time imaging, 1656–7
 fluvostatin, 873
 fms-like tyrosine kinase (*FLT*), 268
 flutamide, 1518
 flux-balance approaches (FBA), 1764
 flux utilization, of networks, 1764–5

- focal adhesion, 696, 1019–20, 1021, 1024
 focal adhesion kinase (FAK), 191, 241–2, 1020, 1021
 focal contacts, 696
 focal segmental glomerulosclerosis (FSGS), 620
 follicular carcinomas, 1391
 Food and Drug Administration (FDA), 268, 568, 1784
 foramen of Panizza, 44
 forearm blood flow (FBF), 1659, 1660
 forecasting, computer models for weather, 216
 force conversion or transmission, and
 flow-mediated mechanotransduction, 239–40
 forkhead signaling, 834–41
 formyl-Met-Leu-Phe (fMLP), 1033
 FOXC2 gene, 1562
 FoxO proteins, and forkhead signaling, 837–8, 839, 840–1
 fractal(s), concept of, 1751–2
 fractalkine, 577, 1220
 FRC conduit, 1571
 free radicals, 1322, 1326, 1515, 1685, 1686.
See also antioxidants; oxygen-free radicals
 fresh frozen plasma (FFP), 1536, 1537
 Friend of GATA (FOG), 809
 frogs, 25, 85–90, 142–8. *See also Xenopus laevis*
 fructose, and platelets, 595*t*
 fruit fly. *See Drosophila melanogaster*
 frustrated phagocytosis, 581
 FTY720, 408, 702–703
 fucosyltransferases-IV and FucT-VII, 1577–80
 full-body simulation, 1805
 fumagillin, 1476
 functional/pathological approach, to
 understanding of endothelium, 13–14
 funisitis, 1072
 furin inhibitor, 313
 FYVE domains, 308
 Galen, 5–7, 8, 230, 1240*t*, 1255
 Galileo, 207
 ganglion cell layer (GCL), 1154
 gap formation, and electron microscopy, 652
 gas bladder, 42, 59
 gas exchange, and pulmonary circulation, 1163
 Gas6 (antiapoptotic protein), 985
 gastritis. *See Helicobacter pylori*
 gastrointestinal injury, radiation-induced, 1092
 gastrointestinal tract, and intestinal
 microcirculation, 1248–9. *See also Helicobacter pylori* gastritis; intestinal tract
 gastrovascular cavity, 32, 952
 gastrulation, 52, 161–2
 GATA transcription factors, 806–10
 Gax gene, 190
 Gblocks analysis, 114
 Gd complexes, and magnetic resonance, 1642–6
 GDP-fucose transporter gene, 1075
 GDP/GTP exchange factors, 754–5
 gelsolin, 593*t*
 gender dimorphism, and
 trauma-hemorrhage, 1516–18
 gene clustering, by hemodynamic location, 236
 gene deletions, in transforming growth
 factor- β superfamily, 306*t*
 gene expression
 atherosclerosis, 1220–1
 cell fate dynamics, 1770
 disturbed and undisturbed flow in aorta, 235–6
 early growth response (Egr)-1, 818
 Eph/ephrin system, 346
 Ets factors, 813
 histones, 1168
 ICAM-1, 1059–60, 1063–5
 integrins, 707–708
 Krüppel-like factor-2, 824–5
 neuropilins, 339
 nitric oxide, 990
 peroxisome proliferator-activated
 receptors, 797
 platelet-endothelial cell adhesion
 molecule-1, 1037–9
 protein C, 978
 Rho GTP-binding proteins, 757
 syndecans, 397
 thrombomodulin, 943
 Tie1/Tie2 signaling system, 353
 tissue factor pathway inhibitor, 923
 Toll-like receptors, 412
 vascular bed-specific, 813–14
 vascular endothelial growth factor, 266–8
 vascular endothelial growth factor
 receptors, 269
 VCAM-1, 1059–60, 1063–5
 gene mapping, 150. *See also* human
 genome project; proteomic mapping
 gene profiling, 183–4, 252
 gene regulation. *See* gene expression;
 regulation
 gene therapy, 299, 672–4. *See also* genetic
 diseases
 gene transfer, 1009–11, 1725–31. *See also*
 genetic engineering
 genetic(s). *See also* DNA binding domains;
 gene expression; genetic diseases;
 genetic mutations; gene transfer;
 phenotypes; Sox genes; target genes;
 transcription and transcriptional
 activity
 antithrombin, 964
 biological networks, 1765
 hereditary hemorrhagic telangiectasia,
 1115–16
 protein C, 974
 protein kinase C, 746–8
 protein tyrosine phosphatases, 764–6
 P-selectin, 1049–50
 pulmonary vascular development,
 185–91
 Rho GTP-binding proteins, 753–4
 sickle cell disease, 1358
 thrombomodulin, 940–1
 von Willebrand factor, 915–16
 genetically modified cells, and cell seeding,
 1701
 genetic cell labeling methods, in fate
 mapping, 167–8
 genetic diseases, 780*t*, 781. *See also* gene
 therapy; *specific diseases*
 genetic engineering, 127, 936, 1009–11. *See
 also* bioengineering; gene transfer;
 recombinant technology
 genetic mutations. *See also* factor V
 mutations
 antithrombin, 964–5, 966
 E-selectin, 1075–6
 hereditary hemorrhagic telangiectasia,
 1115–16
 Sox genes, 863–4, 865
 thrombomodulin, 943–4
 vascular development in zebrafish, 150–7
 genitourinary system, and opioids, 457
 genomic analysis, and proteomic mapping,
 885*t*, 887
 Genstruct, Inc., 219
 geranylgeranylpyrophosphate (GGPP),
 1669
 geranylgeranyl transferase inhibitors, 760
 germ layers, and development, 9
 Gestalt principles, and visual perception,
 208
 giant capillaries, 1463
 giant-cell arteritis, 1414
 Gillespie algorithm, 1782
 gills, and fish, 42, 59–60, 62
 giraffe, and adaptations of cardiovascular
 system to gravity, 24, 99–105
 glabrous skin, 1434
 Gla domain, 973, 982–3
 Gleevec, 252
 glial cell(s), and retinal angiogenesis,
 1157–8
 glial cell line-derived neurotrophic factor
 (GDNF), 1126
 glial fibrillary acidic protein (GFAP),
 1125–6, 1158
 gliomas, 1131
 glomerular capillary, 1273*t*
 glomerular endothelium, 56
 glomerular filtration barrier (GFB), 620–4

- glomerular filtration rate (GFR), 1271, 1280–1
- glomeruloid microvascular proliferations (GMP), 1463*t*, 1465–6
- glomeruloid vessels, 1156
- glomerulonephritis, 307, 944, 1421*t*
- Gloydius halys*, 465
- glucocorticoids, 793, 1551, 1676–8
- glucose, and diabetes, 1370
- glucose-regulated protein 78 (GRP78), 902
- glutamate, and transport systems, 638
- glutamic acid, and ICAM-1, 1060
- gluteal artery biopsy, and vascular smooth muscle cells, 555
- glycanation, 419, 955
- glyceraldehyde 3-phosphate dehydrogenase (GAPDH), 595*t*, 1371
- Glycine max*, 1164, 1166*f*
- glycocalyx, 882
- glycoproteins
- antiphospholipid antibody syndrome, 1361–2, 1366
 - Ebola virus, 1315
 - platelet-endothelial interactions, 589, 593*t*, 597
 - von Willebrand factor, 918, 919
- glycosylaminoglycans (GAGs), 327, 690, 947, 1572
- glyoxalase pathway, and AGE detoxification and removal, 420
- Gnathostomes, 42, 66–7
- Gobionotothen gibberifrons*, 75
- Golgi apparatus, and caveolae, 665
- GPI-anchored proteins, 925
- G-protein-coupled receptors (GPCRs), 452, 455, 668
- graft-versus-host disease, 582
- Gram-negative bacterial sepsis, 413
- granule(s), and platelets, 590–2
- granule membrane protein of 140 kDa (GMP-140), 1049
- granulocyte-specific antigens, and transfusion-related acute lung injury, 1536
- graphs, and organization of information, 205, 208
- Grave disease, 1389, 1421*t*
- gravity, and adaptation, 99–105, 520, 521, 522
- gray platelet syndrome, 591
- Grb2-associated binding protein-1 (Gab1), 287
- Grb2 protein, 287
- green fluorescent protein (GFP), 1657
- gridlock* gene, 150, 151
- Griffonia simplicifolia*, 1164–5, 1166*f*, 1167*f*, 1169, 1194
- grl/hey2* gene, 156
- Growth of biological Thought, The* (Mayr), 122
- growth factors. *See also* epidermal growth factor; fibroblast growth factors; hedgehog growth factors; hematopoietic growth factors; heparin-binding growth factors; hepatocyte growth factor; insulin-like growth factor; peptide growth factors; placental growth factor; platelet-derived growth factors; transforming growth factor- β ; vascular endothelial growth factor
- angiogenesis, 250–2
- apoptosis, 1088–9
- liver regeneration, 612*t*, 614
- platelet-endothelial interactions, 597
- prostacyclin production, 1008
- retinopathy, 1156
- growth hormone receptor (GHR), 796
- GTPase activating proteins, 755
- guanine nucleotide exchange factors (GEFs), 1022–3
- gut-derived mesenteric lymph, 1516
- gut-specific endothelium, 1248–9
- hagfishes, 41, 59, 66–73, 79. *See also* fish
- hair follicles, 1435
- Hairy/Enhancer of Split (HES) genes, 368
- half-life, of HIF-1 subunits, 247
- Hansen disease, 1361
- Hanta virus, 1533
- haplosufficiency model, for hereditary hemorrhagic telangiectasia, 1119
- Harvey, William, 5, 7–8, 203–204, 230, 1240*t*, 1255, 1554
- Hashimoto thyroiditis, 1390, 1421*t*
- Hawking, Stephen, 1751
- health and health care. *See also* deficiency; diagnosis; diet; disease; inflammation and inflammatory response; malformations; mortality rates; organ transplantation; pathology; pharmacology; prevention; public health; therapeutic implications; treatment; wound healing
- placental vasculature development, 1488–93
- steps for improving, 1810–811
- vascular bed of spleen, 1255–60
- vascular pathology in older persons, 1397
- heart. *See also* aorta; cardiovascular disease; cardiovascular system; chronic heart failure; chronic valvular heart disease; congestive heart failure; coronary artery disease; heart valves
- arthropods, 38–9
- β -catenin, 780
- blood composition, 258
- crocodiles, 44–5
- crustaceans, 39–40
- Cyclostomes, 41
- hagfish, 67, 69*t*
- molluscs, 34–5, 36
- Oligochaeta, 37
- reptiles, 43–4
- teleosts, 79–83
- transforming growth factor- β and development, 315
- heart muscles and heart rate, of shrew, 109–10
- heartstring* mutant, 150
- heart valves, and endothelial gene expression, 237–8. *See also* chronic valvular heart disease
- heat shock proteins (HSPs), 501–502
- heavy metals, as toxins, 528*t*, 530–1
- HECA-452, 1420, 1423–4
- hedgehog growth factors, and Wnt signaling, 779
- hedgehog* (*Hh*) signaling pathway, 157
- Helicobacter pylori* gastritis, 1421*t*, 1423, 1424, 1764
- Helix pomatia*, 1164, 1165, 1166*f*
- HELLP syndrome, 1494
- hemangioblast, 52–3, 145–7, 152, 162
- hemangiosarcoma, in dog, 96
- hematopoietic cells and hematopoiesis. *See also* hematopoietic stem cells
- endothelial progenitor cells, 1590–1
 - E-selectin, 1074, 1076–7
 - GATA transcription factors, 806, 807
 - identification of, 1590
 - Xenopus* embryos, 145–7
- hematopoietic growth factors, and regulation of angiogenesis, 1448*t*
- hematopoietic stem cells (HSCs), 1702
- heme oxygenase (HO)
- bile pigments, 999
 - isozymes, 995
 - regulation of, 996
 - role in vascular function, 994
 - therapeutic applications, 999
 - vascular remodeling, 998
 - vascular response to injury, 996–7
 - vasomotor control, 997–8
- Hemichordata (acorn worms), 40
- hemochorial type, of placentation, 1479
- hemodilution, and combat trauma, 1525–6
- hemodynamics
- alterations of, 1691–4
 - endothelial phenotypes, 234–8
 - factors involved in endothelial output, 1690–1
 - forces in, 231–4
 - history of research, 230–1
 - organic nitrates, 1682
 - of pregnancy, 135–6
 - responsiveness of endothelium to local, 230
 - therapeutic applications, 1691–4
- hemogenic endothelium, 145–7

- hemoglobin, 74–7, 419–20, 563–6, 568–70, 1537
- hemoglobin/oxygen dissociation curve, 258*f*
- hemolymph, 30, 35, 67*n*3
- hemolytic disease, and nitric oxide-dependent vascular homeostasis, 565–6
- hemolytic uremic syndrome (HUS)
 antiendothelial cell antibodies, 1415
 apoptosis, 1093
 complement activation and signaling, 434*t*, 439
Escherichia coli infection, 1275
 nitric oxide-dependent vascular homeostasis, 566
 thrombotic microangiopathy, 1337
- hemopexin, 595*t*
- hemophilia, 915, 978, 1528
- hemorrhages, 1303, 1513–19, 1523
- hemorrhagic fevers, 1311–17
- hemorrhagic shock, 1513–14, 1518
- hemostasis and hemostatic balance.
See also battlefield hemostasis
 acute respiratory distress syndrome, 1184–6
 cardiac myocytes, 602
 definition, 909
 integrated model, 912–14
 luminal glycocalyx, 692
 placental trophoblast cells, 1481, 1482*t*
 primary versus secondary, 909–10
 regulators of angiogenesis, 1448*t*
 spatial and temporal dynamics of, 911–12
 toxins, 529
 Virchow's triad, 910–11
 von Willebrand factor, 916
- hemostatic resuscitation, and trauma, 1528–9
- heparan sulfate (HS)
 antithrombin, 960
 biosynthesis, 949–51, 963
 chain structure, 949
 core proteins, 948–9
 development, 952–3
 diagnostic and therapeutic implications, 956
 downstream signaling and cell phenotype, 956
 evolution, 951–2
 heparin-induced thrombocytopenia, 1346
 history of research, 947–8
 ligand-receptor interactions, 953–6
- heparan sulfate proteoglycans (HSPGs)
 antithrombin anti-inflammatory activity, 968
 biological processes regulated by, 947
 coreceptor model of signaling, 953–5
- fibroblast growth factor interaction, 294, 295
- heparin, 961
 structure, synthesis, and postsynthetic modification, 948–51
- heparin, 960–1, 963, 968, 969
- heparin-binding growth factors, 947, 948*t*
- heparin-induced thrombocytopenia (HIT), 587, 969, 1112, 1344–50, 1415
- hepatic arterial blood flow, 1240–1
- hepatic arterial buffer response, 1242
- hepatic arteriovenous malformations, 1115
- hepatic macrocirculation, 1239–46
- hepatic sinusoidal endothelial cells (HSECs), 1226–34
- hepatic venous pressure gradient (HVPG) monitoring, 1245
- hepatic venous wedge pressure (HVWP), 1245
- hepatitis C, and blood transfusion, 1534*t*
- hepatocellular carcinoma, 614
- hepatocyte(s), 609–14, 913
- hepatocyte growth factor (HGF)
 c-MET as receptor, 286
 c-MET signal transduction, 286–7
 effects of signaling on ECs, 287–8
 history of research, 285
 liver regeneration, 610–11, 614
 lymphatic system, 1561
 structural and functional characteristics, 285–6
 therapeutic implications, 288–9
- hepatocyte nuclear factors (HNFs), 1769
- hepatopulmonary syndrome, 1244
- Herceptin, 252
- hereditary hemorrhagic telangiectasia (HHT)
 functional proteins, 1116–17
 genetics, 1115–16
 historical perspectives, 1113
 mechanisms of pathogenesis, 1120–1
 murine models, 1119–20
 transforming growth factor- β , 304, 316, 1117–19
 vascular lesions, 1113–15
- hereditary pseudothrombophilia, 915
- hereditary pulmonary arterial hypertension, 316
- hereditary stomatocytosis
 postsplenectomy, 1537
- heregulin, 250
- Hermansky-Pudlak syndrome, 591
- herpes simplex, 1437*t*
- herpesvirus, 1471. *See also* KS-associated herpesvirus
- Herting, Arthur, 1445
- HES-related (*Hey*) genes, 368
- Hesse, Mary B., 202
- hetastarch, 1525
- heterogeneity, of endothelial cells
 cell fate dynamics, 1776–7
- cytoskeleton, 700
- endothelial microparticles, 1624–5
- E-selectin, 1073
- evolution, 51*f*, 54–6, 1111
- heparin-induced thrombocytopenia, 1350
- history of concept of endothelium, 16
 metaphor and description of, 206
 morphological, 881–2
 pulmonary vasculature, 1161–9
 teleost endocardium, 82
 thrombosis, 977
- hey* gene family, 156
- Hex* genes, 188*t*, 189
- hexosamine pathway, and diabetes, 1372
- Hewson, William, 1255
- Hibbs, R. G., 15
- hierarchical network model, 1762–3
- Hieronymous Fabricius of Aquapendente, 7
- high-altitude cerebral edema (HACE), 516–18
- high-altitude pulmonary edema (HAPE), 516–18
- high-density lipoprotein (HDL), and atherosclerosis, 124, 125, 126. *See also* cholesterol
- high-density lipoprotein (HDL)-like nanoparticle, 1649
- high-dimensional attractors, 1775–6, 1777
- high endothelial cells. *See* high endothelial venules
- high endothelial venules (HEVs)
 developmental evolution, 56
 fever-range thermal stress, 471–8
 historical and comparative perspectives, 1568–9
 in vitro and in vivo models, 1569–70
 lymphocyte traffic molecules, 1576–81
 morphology and anatomy, 1570–6
 plasticity of endothelium, 1581
 rheumatoid arthritis, 1419–27
- high-fidelity patient simulation, 1801, 1802*t*, 1805–806
- high flux backbone (HFB), 1765
- highly active antiretroviral therapy (HAART), 1472, 1476
- high-mobility group box-1 (HMGB1), 422
- high mobility group (HMG) domain, and Sox genes, 861, 862
- high pressure circulations, evolution of, 45–6
- high pressure edema, 1179
- high proliferative potential-colony forming cells (HPP-CFCs), 1590, 1593, 1594–5
- high-sensitivity C-reactive protein (hs-CRP), 1670–1
- high tidal volume ventilation, and barotrauma, 489–94
- hindlimb-unloading rodent model, for space travel, 520, 521, 522, 523–4

- Hippocrates, 6–7, 451, 1081, 1240*t*, 1278, 1554, 1563
- hip surgery, 910, 1550
- His, Wilhelm, 10–12, 26, 161, 204
- histamine, 1007–1008, 1508
- histone(s), 789, 1168
- histone deacetylase inhibitors, 253
- histone-modifying enzymes, 1769
- history, of medicine
- ancestral human environment and diet, 129–33
 - angiogenesis, 1445–9
 - antigens, 1100–102
 - antithrombins, 960–1
 - apoptosis, 1081, 1084, 1085*t*
 - caveolae, 664
 - Darwinism and impact of evolution on, 122–7
 - diving, 497
 - early concepts of endothelium, 5–17
 - Egypt, 1030, 1240*t*
 - eicosanoids, 1004
 - electron microscopy, 643
 - endothelial microparticles, 1602
 - extracellular nucleotides and nucleosides, 384–5
 - hemodynamics, 230–1
 - heparan sulfate, 947–8
 - heparin, 960–1
 - hereditary hemorrhagic telangiectasia, 1113
 - high endothelial venules, 1568–9
 - ICAM-1 and VCAM-1, 1058–9
 - intercellular adhesion molecule-1, 1058–9
 - leukocyte transendothelial migration, 1030–1
 - mitogen-activated protein kinases, 737
 - neuropilins, 337
 - nitric oxide, 988–9
 - nuclear factor- κ B, 784
 - opioids, 451
 - peroxisome proliferator-activated receptors, 796
 - platelet-endothelial cell adhesion molecule-1, 1037
 - P-selectin, 1049
 - reactive oxygen species, 375
 - Rho GTP-binding proteins, 753
 - snake toxins, 461
 - thrombospondins, 324–5
 - thyroid gland, 1386–7
 - uremia, 1278–9
 - vascular cell adhesion molecule-1, 1058–9
 - vascular endothelial growth factor, 1445–6
 - von Willebrand factor, 915
- Hka, and angiogenesis, 447, 448
- HMG-CoA reductase inhibitors, 554, 759.
See also statins
- homeobox (Hox) genes, and pulmonary vascular development, 186–90, 192
- homeodomain, 188
- homeostasis
- antigen presentation, 1104–105
 - antithrombin, 966–8
 - E-selectin, 1076–7
 - evolution of hagfish endothelium, 71–2
 - extracellular nucleosides and nucleotides, 390–1
 - hypoxia-inducible factor 1, 246–8
 - ICAM-1 and VCAM-1, 1065
 - nitric oxide, 990–1
 - P-selectin, 1051–4
 - vascular endothelial growth factor and lung, 1195, 1199–1200
- homologous characters, 114
- homozygous protein C deficiency, 977
- Hooke, Robert, 204
- horizontal metaphor, 201
- hormone(s), and regulation of
- angiogenesis, 1448*t*. *See also* endocrine system
 - hormone-sensitive lipase (HSL), 1266
- horseshoe crab (*Limulus*), 38, 113
- horticulture and horticulturalists, 130, 131
- hot links, in biological networks, 1765
- Hox genes, 187*t*, 188–9
- HSP27, 741
- HSP90, 252
- HS 6-O-sulfotransferase (HS6ST), 950
- HS 3-O-sulfotransferase (HS3ST), 950, 965, 967
- Hughes syndrome, 1360
- human(s)
- adaptations to gravity, 99, 101
 - ancestral biomedical environment of, 129–33
 - energy turnover compared to shrew, 108–109, 109–10
 - fibroblast growth factors, 291
 - genome project, 887
 - human bone-derived ECs (HBDECs), 1551*f*, 1552
 - human CAR (hCAR), 1729–31
 - human dermal microvascular ECs (HDMECs), 328
 - human immunodeficiency virus (HIV). *See also* acquired immune deficiency syndrome (AIDS)
 - avascular necrosis, 1550
 - blood-brain barrier, 1129–30
 - blood transfusions, 1533, 1534*t*
 - Kaposi's sarcoma, 1471, 1472, 1475
 - protein transduction domains, 1132
 - Prox1 gene, 1556
 - thrombotic thrombocytopenic purpura, 1339
 - human intestinal microvascular ECs (HIMECs), 1250
 - human leukocyte antigen (HLA), 1536
- human motion platform, 1693
- human umbilical venous ECs (HUVECs), 156, 274, 328, 1143, 1348–9
- humoral phase, of inflammation, 652–4
- hunter-gatherer groups, in Paleolithic, 129–33
- hyaloid vasculature, 1154, 1157, 1158
- hyaluronan, 81, 690, 692. *See also* intracellular hyaluronan-binding protein p57
- hyaluronan receptor for endocytosis (HARE), 1228, 1229
- hybridoma-based technology, for proteomic mapping, 884
- hydraulic conductivity, and wall permeability, 691
- hydromorphone, 457
- hydrophobic and hydrophilic molecules, and transcellular transport, 634
- hydrophobic site, and protein kinase C, 747
- hydroxymethylglutaryl coenzyme A (HMG-CoA), 999, 1669
- hyperbaric oxygen therapy, 480–6
- hyperbilirubinemia, 999
- hypercholesterolemia
- atherosclerosis, 125, 127, 1215, 1217, 1606*t*
 - endothelin-1, 1604
 - erectile dysfunction, 1545, 1546
 - plasma markers, 1605*t*
- hypercoagulability, 910–11, 1525. *See also* congenital hypercoagulable states
- hypercoagulation, and burn injury, 1511
- hyperdynamic circulation, and portal hypertension, 1243–5
- hyperemia. *See* zone of hyperemia
- hyperglycemia, 1370, 1372, 1375
- hyperlipidemia, 126, 127
- hyperpermeability, 423, 1460
- hyperplastic goiter, 1390
- hypertension. *See also* blood pressure; portal hypertension; pulmonary hypertension
- age-related vascular disease, 1400
 - atherosclerosis, 1606*t*
 - blood-brain barrier, 1131
 - endothelial microparticles, 1630, 1632*t*
 - hemolytic disease, 566
 - in hunter-gatherer populations, 130
 - nitric oxide, 570
 - pericytes, 541
 - plasma markers, 1605*t*
 - preeclampsia and pregnancy-induced, 137–9
 - problems in treatment, 1600–601
 - prostacyclin, 1009
 - vascular smooth muscle cells, 553–4
- hypertrophic cardiomyopathy, 96
- hypoadrenergic responses, to microgravity, 521
- hypotension. *See* orthostatic hypotension

- hypothermia, and combat trauma, 1525, 1526*f*
- hypotrichosis-lymphedema-telangiectasia (HLT), 864, 866, 1562
- hypovolemia, in astronauts, 521
- hypoxemia, and hyperbaric oxygen therapy, 482
- hypoxia
 bronchial vasculature, 1175
 high altitude, 516, 518
 hyperbaric oxygen therapy, 482
 opioid receptors, 457
 protein tyrosine phosphatases, 768
 Tie1/Tie2 signaling system, 353
- hypoxia-induced expression, of VEGF receptors, 271–2
- hypoxia-inducible factor 1 (HIF-1), 246–53
- iatrogenic Kaposi's sarcoma, 1472
- ICAM-1. *See* intercellular adhesion molecule-1
- icefishes, 81–3. *See also* Antarctic icefish
- idiopathic arterial PH (IAPH), 1193, 1194
- Id proteins, 868–73
- I κ B kinase (IKK) complex, 784–8, 837, 1221
- IL-1 receptor-associated kinase (IRAK), 411
- iloprost, 1009
- imaging scanners, for magnetic resonance, 1640–1
- imaging technologies, and site-directed therapies, 891. *See also* computed tomography; magnetic resonance imaging; positron emission tomography; single photon emission computed tomography (SPECT)
- IM862, 1476
- immune adherence-mediated clearance, 437, 439
- immune cells, and vascular permeability, 701–702
- immune mediators, and brain endothelium, 1144–9
- immune modulators, and released platelet chemokines, 592, 596–7
- immune system and immunity. *See also* antibodies; antigens; autoimmune diseases
 developmental evolution, 56
 hepatic sinusoidal endothelial cells, 1228–9
 innate and adaptive immunity, 430–1
 proteasomal system, 1098
 reactive oxygen species, 376
- immune thrombocytopenic purpura (ITP), 1622
- immunoglobulins, and inflammation, 1299*t*
- immunohistochemistry, 1569
- immunoliposome, 1133
- immunomodulation, and opioid receptors, 455
- immunoreceptor tyrosine-based inhibitory motifs (ITIMs), 1037, 1043
- immunosuppressive agents, and nuclear factor- κ B signaling, 793
- Imo2* gene, 153
- impedance spectroscopy, 1315–16, 1317
- importins, and forkhead signaling, 836
- increased-permeability pulmonary edema, 1179, 1180, 1186
- India, and opioids, 451, 457
- individual dynamic, of agent-based model, 1757
- inducible nitric oxide synthase (iNOS), 483, 524–5, 968. *See also* nitric oxide synthase
- induction principle, and developmental evolution of endothelial heterogeneity, 55
- industrial toxicants, 528*t*
- infection. *See also* bacteria; diseases; virus(es)
 blood-brain barrier, 1131
 blood transfusions, 1533, 1534*t*, 1535
 E-selectin, 1075
 lipopolysaccharide, 412–13
 neurological dysfunction, 1146–7
 platelet-endothelial cell adhesion molecule-1, 1041
 sepsis, 1295
 tissue factor expression, 932
- inferior mesenteric artery (IMA), 1248
- inflammation and inflammatory response. *See also* chronic inflammatory diseases; inflammatory cell agents; inflammatory mediators; inflammatory myopathies; proinflammatory activation; proinflammatory mediators; systemic inflammatory response syndrome (SIRS)
 activated protein C, 975–7
 agent-based modeling, 1755–6
 AGE receptors, 422–3, 425
 antithrombin, 967–8
 barotrauma and high tidal volume ventilation-induced, 491–4
 blood transfusion, 1535–7
 brain ECs and, 1144–6
 bronchial circulation, 1175
 cardiac myocytes, 603
 cell adhesion molecules, 1059*t*
 cellular phase of, 654
 diabetes, 1377–8
 disseminated intravascular coagulation, 1332–3, 1334–5
 drug targeting, 1740–1
 electron microscopy, 644–5, 652–4
 endothelial cell functions during, 1295–8
 E-selectin, 1071, 1072, 1076
- hepatocyte growth factor, 288, 289
 high altitude, 517
 humoral phase, 652–4
 ICAM-1, 1059*f*, 1060, 1063
 immune adherence clearance, 437
 inflammatory bowel disease, 1249–51
 leukocytes, 580–2
 magnetic resonance imaging, 1644*t*
 mitogen-activated protein kinases, 743
 nuclear factor- κ B signaling, 792
 platelet(s), 593*t*
 platelet-endothelial cell adhesion molecule-1, 1041, 1059*t*
 P-selectin, 1053–4, 1059*t*
 reactive oxygen species, 379
 Rho GTP-binding proteins, 759
 sickle cell anemia, 1355
 skin, 1434, 1437, 1438–9
 statins, 1670–1
 thrombomodulin, 939, 941
 toxicity, 529
 transforming growth factor- β , 315
 trauma and trauma-hemorrhage, 1513–14, 1526–7, 1528–9
 VCAM-1, 1059*f*, 1060, 1063
- inflammation-induced permeability edema, 1163
- inflammatory bowel disease, 786*t*, 935*t*, 936, 1248–53, 1421*t*
- inflammatory cell agents (ICAs), 1755–6
- inflammatory mediators, and brain ECs, 1142–3
- inflammatory myopathies, 1421*t*
- inhaled nitric oxide (iNO), 1186. *See also* nitric oxide
- inhibitor of caspase-activated DNase (ICAD), 1084
- inhibitors of apoptosis protein (IAP), 1083, 1084
- inhibitory PAS domain protein (IPAS), 247
- initiator caspases, 1083–4
- innate immunity, 430–1
- inner plexiform layer (IPL), 1154
- innervation, of giraffe vascular system, 104–105
- inositol triphosphate (IP₃), 241
- input-output device. *See* input systems; output systems
- input systems. *See also* receptors; signaling; special conditions
 cardiomyocyte-endothelial cell interactions, 602–606
 complement, 430–40
 definition, 879
 Eph receptors and ephrin ligands, 345–9
 extracellular nucleotides and nucleosides, 384–92
 fibroblast growth factors, 291–9
 hemodynamics of phenotype and flow mechanotransduction, 230–43
 hepatocyte growth factor, 285–9

- hepatocyte interaction with liver sinusoidal endothelial cells, 609–14
- hypoxia-inducible factor 1, 246–53
- integrative physiology of ECs, 256–60
- introduction to concept, 227–8
- Kallikrein-kinin system, 444–8
- leukocyte-endothelial cell interactions, 576–82
- lipopolysaccharide, 410–16
- nitric oxide as paracrine and endocrine regulator, 562–71
- Notch genes, 368–73
- opioid receptors, 451–8
- pericyte-endothelial interactions, 536–42
- platelet-endothelial interactions, 587–98
- podocyte-endothelial interactions, 620–4
- reactive oxygen species (ROS), 375–80
- receptor for advanced glycation end-products (RAGE), 419–26
- slits and netrins in vascular patterning, 360–5
- sphingolipids, 403–408
- syndecans, 396–401
- thrombospondins, 324–33
- Tie1 and Tie2 signaling pathways, 352–7
- transforming growth factor- β , 204–18
- vascular endothelial growth factors, 266–76
- vascular smooth muscle cells, 545–55
- insects, 38–40, 527
- inside-out signaling, of leukocytes, 578
- In silico* modeling, of vascular development, 183
- in-stent restenosis, 553
- Institute of Medicine, 1807
- insulin, 130–1, 797, 1128–9, 1374–5, 1604.
See also diabetes
- insulin-like growth factor (IGF), 1496, 1561
- integrated model, of hemostasis, 912–14
- integrated system, view of endothelium as, 1112
- integrative physiology, of endothelial cells, 256–60
- integrin(s)
- angiostatic proteins, 711
 - apoptosis, 1086–8
 - endothelial cell functions, 709–11
 - evolution and development, 707
 - gene regulation, 707–708
 - history of research, 707
 - inflammation, 1299*t*
 - leukocyte arrest, 578
 - protein structure, 708–709
 - receptor tyrosine kinases, 709
 - skin inflammation, 1434
 - therapeutic implications, 711
 - vascular targeting, 888
- integrin-mediated mechanotransduction, 242
- interbundle plexus, 1272
- intercellular adhesion molecule-1 (ICAM-1)
- atherosclerosis, 1217
 - burn injury, 1509–10
 - cerebral malaria, 1306
 - drug targeting, 1739
 - E-selectin interactions, 1078
 - expression pattern, structure, and domains, 1059–60
 - high endothelial venules, 1578*t*
 - history of research, 1058–9
 - leukocyte transendothelial migration, 1032–3, 1034
 - platelet-endothelial cell adhesion molecule-1, 1041
 - regulation, 1063–5
 - as signal transducer, 1060–3
 - as therapeutic target, 1065–6
 - vascular targeting, 890
- intercellular cement, 644
- intercellular clefts, and cell junctions, 649
- intercellular junctions, and polymorphonuclear cells, 654
- interleukin(s) (ILs), 902, 903, 1527
- interleukin-1 receptor associated kinase (IRAK)-1, 1088
- intermediate filaments, and cytoskeleton, 698, 701
- intermittent breathing, in reptiles, 44
- International Brachial Artery Reactivity Task Force, 1660
- International Society of Thrombosis and Haemostasis, 1626
- intersectin, 671
- intersegmental vessels, and vascular development in zebrafish, 154–5
- intersomitic vessels, 144*f*, 145
- intestinal microcirculation, 1248–9
- intestinal perfusion, and chronic inflammation, 1250–1
- intestinal tract, and composition of blood, 259–60. *See also* gastrointestinal tract; small intestine
- intimal hyperplasia, 330
- intima media thickness (IMT), of carotid artery, 1283, 1661
- intraaortic balloon pump counterpulsation (IABP), 1692
- intracellular hyaluronan-binding protein p57, 595*t*
- intraembryonic vasculogenesis, 163
- intrahepatic resistance, 1243, 1245–6
- intravascular catheters, and heparin-induced thrombocytopenia, 1345
- intravascular stents, and cell seeding, 1699–1700
- intravital microscopy (IVM), 690, 691*f*, 1570
- intrinsic pathway, for apoptosis, 1083, 1085
- intussusceptive angiogenesis, 164
- intussusceptive microvascular growth (IMG), 1444, 1489
- invadopodia, 702
- invasive strategies, for treatment of brain disease, 1131–2
- invertebrates, evolution of cardiovascular system, 30–40
- inversion recovery sequences, and magnetic resonance imaging, 1639
- investment, of pericytes, 536–8
- in vivo* and *in vitro* studies
- antigen presentation, 1103–104
 - differences in EC morphology and protein expression, 883
 - panning strategy for phage or viral libraries, 884–6
 - phage display, 900–1
- involuntary muscle, 548
- inward eutrophic remodeling, 549
- inward hypertrophic remodeling, 549
- ion channels, 721–7
- ionophoresis, 1662
- iron, 528*t*, 531, 1129
- ischemia. *See also* ischemia-reperfusion injury; limb ischemia; normoxic lung ischemia
- angiogenesis and treatment of, 956
 - fibroblast growth factors, 296, 298
 - heparan sulfate, 956
 - hypoxia-inducible factor 1, 246, 252
 - pulmonary vasculature and mechanotransduction, 1202–211
 - thrombomodulin, 944
 - vascular endothelial growth factor, 268
- ischemia-reperfusion injury
- apoptosis, 1092
 - bronchial artery, 1174
 - eicosanoids, 1009
 - hyperbaric oxygen therapy, 480–6
 - leukocytes, 581
 - lung injury, 1209
 - nitric oxide, 570
 - nuclear factor- κ B signaling, 786*t*
 - opioid receptors, 456–7
 - protein C, 979
 - P-selectin, 1054
 - tissue factor expression, 936
- ischemic preconditioning, and organic nitrates, 1684
- isoforms
- of fibroblast growth factors, 294
 - of VCAM-1 and ICAM-1, 1064
- isotope-coded affinity tags (ICAT), 886
- isozymes, of heme oxygenase, 995
- jararhagin, 462, 464
- jellyfish, and phylogenetic analysis, 33*f*, 119, 120
- jet propulsion system, of cephalopods, 36
- Jewish tests, and von Willebrand factor, 915

- jugular vein, and innervation in giraffe, 104–105
- junctional adhesion molecules (JAMs), 1019–20, 1575–6. *See also* adherens junction; cell junctions
- junctional mechanosensors, 242–3
- junctional transport, and electron microscopy, 651–2
- junctionology, and electron microscopy, 648–9
- Jun N-terminal kinase (JNK), 287
- juvenile polyposis (JP), 1115, 1116
- Kallikrein-kinin system (KKS), 444–8
- Kaposi's sarcoma, 1471–6, 1558, 1615
- Kawasaki disease (KD), 438, 1405–408, 1413–14, 1416
- Kepler, Johannes, 207
- keratinocyte(s), 1431, 1435–6, 1439–40
- keratinocyte precursors, 353
- kidney(s). *See also* kidney disease
- aquaporin, 716
 - composition of blood, 258
 - hagfish, 69*t*
 - podocyte-endothelial interactions, 620–4
 - renal endothelium, 1271–7
 - renal function measurement, 1280–1
 - thromboembolism, 97*n*4
- kidney disease, and hepatocyte growth factor, 289. *See also* chronic kidney disease; hemolytic uremic syndrome; renal disease; uremia
- kinin(s), 1508
- kininogens (LK), 445–8
- knockout studies, and fibroblast growth factors, 297–8
- Knowledge Assembly model, 219–20
- Komodo dragon, 44
- Krüppel-like factor-2, 822–5
- KS-associated herpesvirus (KSHV), 1471, 1558
- Kunitz domain, 922, 923
- Kupffer cells, 609, 1228, 1734
- Ku proteins, 815
- lacteal endothelium, and aquaporin, 717
- La Mettrie, Julian Offray de, 8
- Lam G domain, and protein S, 983
- lamina, and caspase cleavage, 1084
- laminar flow, in cephalopods, 37
- laminar shear stress (LSS), 236–7, 799, 933, 1690. *See also* shear stress and shear forces
- lampreys (eel), 41, 66, 79
- language, and metaphor, 203. *See also* terminology
- large amino acid transporter type (LAT)-1, 1128
- large-vessel vasculitis, 1411, 1413–14
- L-arginine, 989, 1544, 1545
- L-arginine methyl ester (L-NAME), 313
- Laser Doppler flowmetry, 1665
- Lassa virus, 1317
- latency-associated peptide (LAP), 304, 306
- latent AT (L-AT), 963, 964
- latent TGF- β binding protein (LTBP), 304, 306, 307, 593*t*
- lateral borders, and cell junctions, 649
- L-dopa, 1132
- lead, as toxic agent, 528*t*, 530
- lectins and lectin binding, 942, 1074, 1164–5, 1166*f*, 1266
- left ventricular ejection fraction (LVEF), 1702
- Leiden mutation. *See* factor V mutations
- leishmaniasis, 1361
- lentiviruses, 1726
- Leonardo da Vinci, 1171, 1172*f*, 1240*t*
- leptin, 138
- Leptospira interrogans*, 412
- leptospirosis, 1361
- leucine-rich region (LRR) family, 918
- leukemia, and forkhead signaling, 839. *See also* B-cell leukemia/lymphoma 2
- leukocyte(s). *See also* leukocyte transendothelial migration;
- polymorphonuclear leukocytes
 - acute respiratory distress syndrome, 1183*f*, 1187–8
 - adhesion and transmigration of endothelial microparticles, 1627–8
 - arrest, 578–9
 - atherosclerosis, 1217–18, 1221
 - bronchial circulation and recruitment, 1174
 - burn injury, 1509–10
 - cerebral malaria, 1306
 - high endothelial venules, 1573–5
 - inflammatory bowel disease, 1249–50
 - lifespan, 580–1
 - lipopolysaccharide, 414–15
 - luminal glycocalyx, 692
 - normal microvasculature, 1458
 - nuclear factor- κ B signaling, 790
 - rolling, 576–8, 790, 1053–4
 - signaling, 581
 - therapeutic implications, 581–2
 - toxicity, 529
 - transmigration, 579–80, 701
 - trauma, 1527
- leukocyte adhesion deficiency (LAD)-2, 1075, 1076
- leukocyte function-associated antigen (LFA)-1, 1058
- leukocyte microparticles (LMPs). *See* endothelial microparticles
- leukocyte transendothelial migration (TEM). *See also* diapedesis
- adhesion and signaling, 701, 1031–3
 - diapedesis at junctions, 1033
 - E-selectin, 1077
 - historical perspective on, 1030–1
 - nonjunctional diapedesis, 1033–4
 - platelet-endothelial cell adhesion molecule-1, 1033, 1039–40
- leukocytoclastic vasculitis, 1437*t*, 1438
- leukocytosis, and sickle cell anemia, 1355
- Lewis Lung carcinoma, 332, 869
- lichen ruber planus, 1437*t*
- lifespan (LS). *See also* death; mortality rates
- of metaphors, 202
 - of shrew, 111
- ligand(s). *See also* Eph/ephrin system; ligand traps
- angiopoietins and interactions with receptors, 353–4
 - drug targeting, 1735–6
 - heparan sulfate and receptor interactions, 953–6
 - magnetic resonance imaging, 1647
 - neuropilin structure and function, 338–9
 - phage displays, 899
 - proteomic mapping, 884, 885*t*
 - thrombospondins and receptor interactions, 327–9
 - vascular endothelial growth factor receptors, 269
- ligand-based cell surface signaling, 668–9
- ligand-binding domain (LBD), of peroxisome proliferator-activated receptors, 797
- ligand traps, and transforming growth factor- β , 308, 309
- likelihood methods, 114
- limb arteries, and innervation in giraffe, 105
- limb ischemia, 1705*t*
- limiting constraint, 26*n*4
- LIM kinase (LIMK), 701
- lipid(s), 131, 498, 499, 528, 799. *See also* lipid rafts; sphingolipids
- lipid rafts
- caveolae, 665, 666*t*, 667–8
 - fibroblast growth factors, 294
 - sphingosine 1-phosphate signaling, 1023–4
 - sphingolipids, 403, 405
 - tissue factor pathway inhibitor, 925–6
- lipooxygenase (LOX), 1004, 1005*f*, 1006, 1007
- lipopolysaccharide (LPS)
- acute respiratory distress syndrome, 1182
 - apoptosis, 1088, 1092
 - CD14 and LPS-binding protein, 413
 - cell injury and apoptosis, 415–16
 - endothelial permeability, 413–14
 - endothelium infection, 412–13
 - endotoxemia, 415
 - inflammation and toll-like receptors, 1297
 - leukocyte interactions, 414–15
 - nitric oxide synthase, 416

- preconditioning with, 415
 procoagulant activity, 415
 structure, 410, 411*f*
 teleost endocardium, 82
 toll-like receptors, 410–12
- lipoprotein, and atherosclerosis, 125, 126
- lipoprotein lipase (LPL), 1266
- liposomes, 1132–3, 1727*t*, 1734–5
- liver. *See also* hepatic sinusoidal endothelial cells; liver disease
 acetaminophen toxicity, 1233
 apoptosis and transplantation, 1092
 autoregulation of blood flow, 1242
 hemostasis, 912, 913
 hepatic macrocirculation, 1239–46
 hereditary hemorrhagic telangiectasia, 1115
 injury during transplantation of, 1233–4
 leukocyte recruitment and endotoxemia, 415
 mutual signaling during development of, 173–9
 regeneration after partial hepatectomy, 609–14
 sinusoidal endothelial cells and cell-cell interactions, 1227
 liver disease, 271, 1229. *See also* chronic inflammatory liver disease
 liver sinusoidal ECs (LSECs), 178–9, 609–14, 1105
 liver-transcription activating protein (LAP), 1009
 liver-transcriptional inhibitory protein (LIP), 1009
- lizards, and evolution of cardiovascular system, 43–4
- local epigenetic plasticity, 1776
- local flux structures, 1764
- local heat, and vasodilatory response, 1664
- local/horizontal analogies, 202
- local metaphor, 201
- locomotion, of cephalopods, 36
- lovastatin, 1357
- low-density lipoprotein (LDL), 124–7, 1090, 1217, 1376–7. *See also* cholesterol; very-low-density lipoproteins
- low-molecular-weight heparin (LMWH), 969, 1344, 1347
- low proliferative potential-endothelial colony forming cells (LPP-ECFCs), 1593
- LPS-binding protein (LBP), 413
- LPS-induced coagulation, 936
- L-selectin
 domain organization, 1050*f*
 high endothelial venules, 1574–5, 1578*t*
 P-selectin and interaction, 1053
 skin inflammation, 1439
 therapeutic implications, 1078
 thermal stress, 474
- Lumbricus*, 37, 38*f*
- luminal glycoalkalylx, 689–93
- lung. *See also* acute respiratory distress syndrome (ARDS); emphysema; lung cancer; respiratory system; pulmonary hypertension
 apoptosis and transplantation of, 1092
 aquaporin in microvessels, 716
 capillary leak and barotrauma, 489–91
 EC markers, 883
 endothelium of avian, 92
 endotoxemia and lipopolysaccharide, 415
 evolution of in fish, 42
 mechanotransduction and ischemia, 1202–211
 microheterogeneity of endothelium, 1161–9
 microvascular endothelial cells, 1193–4
 postnatal pulmonary endothelium, 181–4
 tissue factor expression in adenocarcinoma, 935
 vascular developmental defects and disease, 191–2
 vascular endothelial growth factor and homeostasis, 1195, 1199–1200
 lung cancer, 342
 lungfishes, 42, 59, 82–3. *See also* fish
 lung perfusion, 1202–203
 lung-targeting antibody, 888
 lupus erythematosus, 439, 1437*t*, 1550. *See also* systemic lupus erythematosus
 lupus nephritis, 978
 Lyme disease, 1360
 lymphadenectomy, 1562
 lymphangiogenesis, 1559, 1562
 lymphatic endothelial cells (LECs), 1553
 lymphatic endothelium, 56
 lymphatic heart, 145
 lymphatic system, 1553–61. *See also* lymphedema; lymph flow; lymph nodes; lymphocytes
 lymphatic vessel(s), and angiopoietins, 356
 lymphatic vessel endothelial receptor (LYVE)-1, 1229, 1559–60
 lymphedema, 540, 1553, 1562–3. *See also* hypotrichosis-lymphedema-telangiectasia
 lymph flow, 1571–2
 lymph nodes, 1100, 1257, 1553, 1562–3, 1571*f*. *See also* lymphatic system; mesenteric lymph nodes; peripheral lymph nodes
 lymphocytes, 471–8, 1218, 1424–5, 1576–81. *See also* lymphatic system
 lymphoid chemokines, 1424
 lymphoid endothelium, 55
 lymphoid neogenesis, 1425, 1427, 1581
 lymphotoxin (LT), 1304, 1425, 1427
- LyP-1 peptide, 903
- lysosomes, and platelets, 591, 595*t*
- LY294002, 1678
- LY333531, 751
- Macacus cynomolgus*, 1419
- Mac-1 (leukocyte integrin), 422
- macroalbuminuria, 1291
- macrocirculation, and endothelial cell dysfunction, 1659–62
- macromolecules, 1312, 1464
- macrophage(s)
 atherosclerosis, 125–6, 1217–18, 1220, 1221
 heart of teleosts, 82
 Kaposi's sarcoma, 1474*t*
 retinal vascular development, 1157
- macrophage inflammatory protein (MIP)-2, 1175, 1304
- macrovessels, and building of blood vessels, 1712–16
- MADH4* mutations, 1115
- Magnesium in Cardiac Arrest (MAGIC) trial, 1703
- magnetic resonance imaging (MRI), 555, 1637–51
- Maillard reaction, 419
- mainstream smoke, 1325
- major histocompatibility complex, and antigen presentation, 1098–9
- malaria, 562, 1303–307, 1533
- malformations, of blood vessels, 373, 1114–115, 1120, 1121, 1466–7
- malondialdehyde, 1546
- Malpighi, Marcello, 8, 1255
- mammal(s). *See also* animal models; bats; cat(s); dog(s); giraffe; manatee; mouse; shrew
 cell differentiation and vascular development in, 161–5
 size range of, 24–5, 107
- mammalian target of rapamycin (mTOR), 250, 253, 792
- manatee, and cornea, 1158
- manganese superoxide dismutase (MnSOD), 840
- mannose receptor, 1228
- manumycin, 1393
- MAPK. *See* mitogen-activated protein kinases
- MAPK cascade, 738, 739–43
- mapping. *See* fate mapping; proteomic mapping
- Marburg virus (MARV), 1311, 1317
- Marfan syndrome, 307, 315
- Massachusetts Male Aging Study (MMAS), 1541
- mass exponents, 107*n*1
- massive transfusion, 1535–6
- mass spectrometry (MS), and proteomic mapping, 884, 885*t*, 886–7

- maternal-fetal conflict. *See* fetal-maternal conflict
- maternal vascular remodeling, 1480–1, 1489, 1490*f*
- mathematical modeling, 1752
- matricellular protein, 327
- matrix adhesion, 1019–20
- matrix metalloproteinase (MMP), 288
- maximum parsimony methods, 114
- Mayr, Ernst, 122
- MCM1 agamous deficiens serum response factor (MADS), 847, 848
- measurement
 of blood flow by thermodilution technique, 1659–60
 of endothelial microparticles, 1626
- meat curing, and nitrite, 568
- MECA-79, 1420, 1421–3, 1576–7
- mechanical forces and mechanical stress.
See also shear stress and shear forces
 barrier regulation, 1021
 cardiac myocytes, 603
 cytoskeleton, 699
 Rho GTP-binding proteins, 758
- mechanical stretch, and barotrauma, 490–1, 492–3
- mechanistic conception, of organism, 8
- mechanosensing, and ion channels, 727
- mechanotransduction, 238–43, 669–70, 1202–211
- mediator-induced vascular leaking, and electron microscopy, 654
- Medicare, and chronic kidney disease, 1281
- medicine and medical care. *See* Darwinian medicine; diseases; drugs; gene therapy; health and health care; history; infection; inflammation and inflammatory responses; ischemia; nanotechnology; prevention; sepsis; therapeutic implications; thrombosis; treatment; wound healing
- medium-sized vessel vasculitis, 1411
- medullary cords, 1570
- medullary thyroid carcinoma, 1391
- megakaryocytes, 909, 1050, 1051
- megakaryocytic acute leukemia (MAL), 757
- Meige disease, 1562
- melanomas, 331, 332, 1467
- membrane-associated guanylate kinases (MAGUKs), 1127
- membrane-bound PGES (mPGES), 1006
- membrane depolarization, and reactive oxygen species generation, 1206
- membrane estrogen receptors, 1675
- membrane potential, and ion channels, 725
- membrane type-1 matrix metalloproteinase (MMP) (MT1-MMP), 314
- Mendel, Gregor, 66
- meningitis, 1065
- meningococcal infection, 434*f*
- meningococemia, 1332
- meningococemia-induced acquired protein C deficiency, 912
- menopause, and thermoregulation, 1435
- menstruation, and vascular endothelial growth factor receptors, 271
- mercury, as toxic agent, 528*t*, 530
- Merck Pharmaceuticals, 702
- Merostomata, 38
- mesangiolytic, 623
- mesenteric circulation, 1239, 1245
- mesenteric lymph nodes (MLNs), 1575
- mesoderm, and history of medicine, 10
- Mesopotamia, and opioids, 451
- metabolic syndrome, 511, 1629, 1632*t*
- metabolism
 blood-brain barrier, 1128, 1129
 bronchial endothelium, 1173–4
 comparative biology of shrew, 107–11
 cutaneous breathing, 89
 fish endothelium, 62–3
 forkhead signaling, 838–9
 peroxisome proliferator-activated receptors and fatty acids, 799–800
 sphingolipids, 403–405
- metal(s), as toxins, 528*t*, 530–1
- metalloids, as toxins, 528*t*
- metalloproteinases (MMPs), 461–6, 1231–3, 1391–2. *See also* tissue inhibitors of metalloproteinase 2
- metaphors, for endothelium
 computers, 215–22
 definition of and use of concept, 199–203, 1815
 organization of information, 204–205
 role of in endothelial biomedicine, 203–204
 urban design, 211–14
 visual, 206–209
- methemoglobin, 568
- MG132 (proteasome inhibitor), 253
- microalbuminuria, 1291
- microangiopathic hemolytic anemia, 566, 909
- microangiopathy, and diabetes, 1379
- microassays, 147–8, 183–4
- microcirculation, and adaptation to gravity, 100–101
- microdialysis, 1662–3
- micro-electricomechanical system (MEMS), 1718
- microenvironment, and blood-brain barrier, 1124–6
- microfilaments, and cytoskeleton, 696, 700–701
- microglia, 1158
- microgravity-induced cardiovascular changes, and space travel, 520–5
- microheterogeneity, of lung endothelium, 1161–9
- micronutrient intake, in ancestral human diet, 132
- microparticles (MPs), 591–2, 1305, 1621. *See also* endothelial microparticles
- microscopic angiogenesis grading system (MAGS), 1451
- microscopic polyangiitis (MPA), 1412–13
- microscopy. *See* bright-field microscopy; confocal microscopes; electron microscopy; fluorescence microscopy; intravital microscopy
- microtubule(s), and cytoskeleton, 697–8, 699, 701
- microtubule-organizing center (MTOC), 697
- microvascular endothelial cells, 1193–4, 1433–4
- microvascular permeability, 679
- microvascular remodeling, of retina, 1155
- microvasculature, 1431, 1457–8
- microvessel(s), 1433, 1716–19
- microvessel density (MVD), in tumors, 314, 1451
- military, and hemorrhagic combat deaths, 1523
- Miller's triangle, 1803
- Milroy disease, 1562
- mind bomb (mib)* mutation, 155–6
- missense point mutations, in VEGFR3 allele, 274
- mitochondria, 75, 377
- mitochondrial electron transport chain, and diabetes, 1370–1
- mitochondrial enzymes, and platelets, 595*t*
- mitochondrial outer membrane permeabilization (MOMP), 1083, 1085*t*
- mitogen(s), and vascular smooth muscle cells, 551–2
- mitogen-activated protein kinases (MAPKs). *See also* MAPK cascade
 carbon monoxide and p38 pathway, 994
 dietary salt, 1288–9
 estrogenic signaling, 1675
 history of research and evolution, 737
 reactive oxygen species, 380
 smad-independent signals, 310
 structure and function of, 737–9
- MLC kinase (MLCK), 1018–19, 1023
- MM-LDL, and tissue factor expression, 933
- modeling and model systems. *See also*
 agent-based models; animal models
 equation-based models, 1780–4
 retina and vessel formation, 1156–7
 scale-free networks, 1760–5
 transportation networks, 212–13
 types of, 1752
- moderately dense bodies (MDBs), of teleost endocardium, 79–81
- molecular markers, in chick embryo, 92
- molecular phylogeny, 113–20

- molluscs, and evolution of cardiovascular system, 34–7
- monocarboxylate transporter (MCT)-1, 1128
- monoclonal antibodies, to P-selectin, 1054
- monoclonal antibody-based approaches, to proteomic mapping, 884, 885*t*
- monocrotaline, 1230, 1231–3
- monocytes, 914, 1217–18, 1219–20, 1221, 1474*t*
- monomer, of ICAM-1, 1064
- mononuclear phagocytic cells, 1314
- monoplacophorans, 35
- Moore neighborhood, and agent-based model, 1755
- Morgan, Thomas Hunt, 66, 368
- morphine, 451, 454, 455, 456*f*, 457, 458
- morpholinos, 147
- morphological heterogeneity, 881–2
- morphological/histological view, of endothelium, 13–14
- mortality rates. *See also* death, causes of cardiovascular disease, 1599
 chronic kidney disease, 1281, 1282–3
 Ebola virus, 1311
 sepsis, 928, 1092, 1294
 sinusoidal obstruction syndrome, 1230
 snake envenomation, 461
- mosaic vessels, of tumors, 1467
- mother vessels, of tumors, 1463–5, 1466–7
- motion compensation, in magnetic resonance imaging, 1638
- mouse, 25, 291, 294, 340*t*. *See also* animal models; knockout studies
- mouse mammary tumor virus (MMTV), 294
- MRS 2500, 391
- mucosal addressin cell adhesion molecule (MAdCAM)-1, 1249, 1424, 1426, 1580–1
- multidrug resistance, of blood-brain barrier, 1127, 1129
- multifocal intramural myocardial infarction, 95
- multifunctional cytokine/immune mediators, and angiogenesis, 1448*t*
- multiphoton microscopy (MPM), 1570, 1656
- multiple organ dysfunction syndrome (MODS), 1507, 1513, 1527
- multiple organ failure (MOF), 1294, 1513, 1535
- multiscale models, 1783
- multiple sclerosis
 anti- α 4 integrin trials, 1252
 blood-brain barrier, 1130–1
 cytoskeleton as biomedical target, 702
 endothelial microparticles, 1631, 1632*t*
 FTY720, 408
 ICAM-1 and VCAM-1, 1065
- multipotent adult progenitor cells (MAPCs), 1615
- multistability, and modeling of complex systems, 1752, 1771–3, 1774
- multivesicular bodies, 1099
- mural cells, and cytoskeleton, 698–9. *See also* pericytes
- muscle(s), physiology of contraction, 548–9. *See also* skeletal muscle(s); skeletal muscle cells; smooth muscle cells; vascular smooth muscle cells
- muscle tissue, and heart or skeletal muscles of shrew, 110
- mutagenesis screens, 150
- mutual signaling, during development of pancreas and liver, 173–9
- MVEC injury, 1337, 1339–40, 1341, 1348–9
- Mycoplasma pneumoniae*, 1175
- Mycoplasma pulmonis*, 1175
- myeloablative conditioning, and bone marrow transplantation, 1230
- myeloid metaplasia (MMM), 1261
- myeloperoxidase (MPO), 1413
- myocardial contractibility, 603, 605
- myocardial hypertrophy, 96
- myocardial infarction
 age-related vascular disease, 1400
 β -catenin, 781
 cell therapy, 1701–703, 1705*t*
 cigarette smoking, 1328
 fibroblast growth factor, 296
 myocyte enhancer factor 2, 848–50
 thrombomodulin, 1603
 tissue factor pathway inhibitor, 927
 vascular targeting, 902
 Virchow's triad, 911
- myocardial ischemia, 316, 944
- myocyte(s), 32
- myocyte enhancer factor 2 (MEF2) proteins, 824, 847–52
- myoglobin, 75, 568–70
- myosin light chains (MLC), 1017–19
- Myxine*. *See* hagfish
- N*-acetylglucosamine, 950
- NADPH oxidases (NOXs), 376–7
- naïve T cells, 1100, 1102–103
- naloxone, 457, 458
- NANC-mediated cavernosal smooth muscle relaxation, 1546
- nanomedicine. *See* nanotechnology
- nanoparticles (NPs), 665, 1132–3
- nanotechnology, and caveolae, 665–7, 673
- NAP-2, 596
- natalizumab, 1252
- National Aeronautics and Space Administration (NASA), 520, 521, 1691
- National Cancer Institute, 253, 1452
- National Institutes of Health (NIH), 1726, 1784
- National Kidney Foundation, 1280
- Native Americans, and tobacco-linked disorders, 132
- natriuretic hormones, 82
- natriuretic peptides, 463*t*, 464–5
- natural selection, environment and modern chronic disease, 123–4
- nautilus, 36
- N*-deacetylase/*N*-sulfotransferase (NDST), 950, 951
- near-IR fluorescent probes, 1657
- neotrotizing and crescentic glomerulonephritis (NCGN), 1413
- Neisseria meningitidis*, 432, 434*t*, 702
- nematocysts, 32*n*4
- nematode. *See Caenorhabditis elegans*
- Nematostella vectensis*, 773
- nemertans, and evolution of cardiovascular system, 33–4, 35*f*
- neointimal anastomotic hyperplasia (NIH), 1501
- neointimal formation, and restenosis, 273
- neoplasia, 96, 839, 1644*t*
- neovascularization, 251, 882, 1451–2, 1703–704
- nephrin, 620
- nephropathy, and diabetes, 424, 1379–80
- nephrotic syndrome, 986
- nervous system, 337–8, 361–4. *See also* central nervous system; neurological dysfunctions; neurons; neuropathy
- N*-ethylmaleimide (NEM), 671
- netrin signaling pathways, 363
- networks, and modeling of complex systems, 1760–5, 1790–1
- neural-immune interface, and brain ECs, 1142–3
- neural stem cell(s) (NSC), 1126
- neurological dysfunction, during infection and sepsis, 1146–7
- neurons, and blood-brain barrier, 1125
- neuropathy, and diabetes, 1380–1
- neuropilins (NRPs)
 cancer, 341–2
 expression in endothelial cells, 339
 historical context, 337
 ligand-binding specificities and function, 338–9
 lymphatic system, 1561
 shared neural and vascular guidance systems, 361–2
 vascular development, 339
 VEGF receptors, 274
- neurosurgery, 1131–2
- neurovascular unit, and blood-brain barrier, 1124
- neurulation, 143*n*4
- neutral sphingomyelinase (N-SMase), 669–70
- neutrophils, 653*f*, 1031–2, 1528. *See also* polymorphonuclear leukocytes

- New England Journal of Medicine*, 1445
 NGR peptide, 902, 903–904
 nicotinamide adenine dinucleotide
 phosphate oxidase (NADPH), 1061,
 1204–206, 1370–1
 nicotinamide adenine dinucleotide
 phosphate-oxidase diaphorase
 (NADPH-d), 95
 nicotine, 1147, 1320–1, 1325–6, 1328–9
 nidogen, 593*t*
 Nipah virus, 349
 nitrate-induced endothelial dysfunction,
 1685–6. *See also* nitrite/nitrate
 nitrate tolerance, 1682, 1685–6. *See also*
 organic nitrates
 nitration, and trauma, 1528
 nitric oxide (NO). *See also* nitric oxide
 synthase; nitrite
 aorta of hagfish, 70
 apoptosis, 1090
 burn injury, 1510
 cardiovascular system of Antarctic
 icefish, 76–7
 cigarette smoking, 1321–3, 1327–9
 cirrhosis and portal hypertension, 1243
 diabetes, 1374
 dietary salt intake, 1287–8, 1289, 1290
 EDRF in fish, 63
 endocardial functions in teleosts, 82
 as endocrine mediator, 566–8
 erectile dysfunction, 1401
 evolution, 989–90
 exercise and endothelial function, 506,
 511
 fibroblast growth factors, 296–7
 gene regulation, 990
 historical perspective, 988–9
 homeostasis, 990–1
 hyperbaric oxygen therapy, 483, 485
 lung ischemia, 1206–1207, 1210*f*
 lung vascular development, 1168
 organic nitrates, 1684
 pericyte investment, 538
 red blood cells and hemoglobin in
 modulation of, 563–6
 space travel, 522, 524
 statins, 1668–70
 therapeutic implications, 570, 991
 uremia, 1281–2
 vasodilation and paracrine properties of,
 562–3
 vasoregulation, 1355–6
 nitric oxide synthase (NOS), 416, 731–2.
 See also endothelial nitric oxide
 synthase (eNOS); inducible nitric
 oxide synthase (iNOS)
 nitrite, 567–70
 nitrite/nitrate, and chronic heart failure in
 dogs, 95
 nitrogen. *See* reactive nitrogen species
 nitroglycerin (GTN), 553, 1682
 nitroprusside, and vasoconstriction in
 hagfish, 70
 nodular regenerative hyperplasia (NRH),
 1229, 1233
 noncanonical Wnt signaling, 776, 778
 nongenomic pathways, and steroid
 hormones, 1674–5
 nonglabrous skin, 1434–5
 “nonhemodynamic” hypothesis, for
 evolution of endothelium, 45–6
 noninvasive delivery, and treatment of
 brain disease, 1132
 nonlinear differentiation equations, 1771
 nonlinear dynamics, 1751, 1752
 nonnuclear steroid actions, 1674
 nonproliferative diabetic retinopathy, 1381
 nonreceptor protein tyrosine phosphatases
 (NRPTs), 764, 766
 nonstationary dynamics, 1751
 nonsteroidal anti-inflammatory agents
 (NSAIDs), 582, 793, 1149
 “no-reflow phenomenon,” in
 ischemia-reperfusion injury, 484
 normalization effect, and tumor
 angiogenesis, 1452
 normoxic lung ischemia, 1203–204, 1210
 Norrie syndrome, 780*t*, 781
 nosebleeds, and hereditary hemorrhagic
 telangiectasia, 1113, 1121
 Notch genes, 368–73
 Notch receptors, and *delta-notch* signaling
 in zebrafish, 155, 156
Notothenia coriiceps, 80*f*
 notothenioid fishes, 74–7
 Novo Nordisk, 769
NRPI and *NRP2* genes, 338, 339–40
 N-terminal domain of thrombospondin
 (NTSP-1), 327–8
 NTPDases, 391
 nuclear export signal (NES), and I κ B
 complex, 786
 nuclear factor of activated T cells (NFAT)
 transcription factors, 828–33, 932–3
 nuclear factor (NF)- κ B
 apoptosis, 1084
 atherosclerosis, 1221
 classical and alternative pathways of
 activation, 784–7
 high endothelial venule-like vessels,
 1426–7
 history of research, 784
 I κ B kinase regulation, 787–8
 regulation of endothelial cell responses,
 790–2
 therapeutic implications, 792–3
 tissue factor expression, 932, 933–4
 transcriptional activity regulation,
 788–90
 nuclear localization signal (NLS), 291, 293,
 784
 nucleolin, and vascular targeting, 888
 nucleosome ELISA, 1085*t*
 nucleotides and nucleosides. *See*
 extracellular nucleotides and
 nucleosides
 nucleus, and fibroblast growth factors, 291,
 294
 nutrient circulation, in fish gills, 60
 obesity
 adipose tissue endothelium, 1268
 diabetes, 1375
 disease and health status, 123, 127, 509*t*
 endothelin-1, 1604
 exercise, 509*t*, 510
 vascular bubble formation, 498
 occludens junctions, 649
 occludin, 1127
 ocular microvascular proliferative
 disorders, 272–3
 Oligochaeta, 37
 oligosaccharides, and angiogenesis
 regulation, 1448*t*
 O-linked carbohydrates, 1580
 oncofetal mechanism, and angiogenesis,
 1450
 oncogenes, and fibroblast growth factors,
 294
 opioid(s), 451, 454–6, 458. *See also*
 morphine; opioid receptors; opium
 opioid receptors, 451–8
 opium, 451, 457
 opportunity cost, and evolutionary biology,
 135
 opsonins, 435–7
 oral contraceptives, 1229
 ordinary differential equations (ODEs),
 1780–1
 organic nitrates, 1682–6. *See also* nitration
 organogenesis, and liver regeneration, 613
 organ transplantation. *See also* bone
 marrow transplantation
 antiendothelial cell antibodies, 1415
 avascular necrosis, 1550
 apoptosis, 1092
 Kaposi’s sarcoma, 1472
 leukocytes and rejection of, 582
 liver regeneration after partial
 hepatectomy, 609
 sphingolipids, 408
 organum vasculosum laminae terminalis
 (OVLT), 1146
 orthogonal polarization spectral imaging
 (OPS), 1655
 orthologous genes (orthologues), 113
 orthostatic hypotension or intolerance, and
 adaptations to gravity in humans, 100,
 520, 524, 525
 Osler-Weber-Rendu syndrome, 316
 Osteichthyans, 42
 osteoarthritis, 902
 osteoprotegerin (OPG), 238

- out of bounds (Obd) gene*, 361
 outer medullary descending vasa recta (OMDVR), 716
 outer plexiform layer (OPL), 1154
 out-group sequence, in phylogenetic analysis, 118
 output systems. *See also* input systems; permeability; regulation; signaling
 antigen presentation, 1098–1105
 antithrombin, 960–70
 apoptosis, 1081–93
 carbon monoxide, 994–1000
 cardiac myocytes, 603–606
 eicosanoids, 1004–11
 E-selectin, 1071–8
 hemostasis, 909–14
 heparan sulfate, 947–57
 intracellular adhesion molecule-1, 1058–66
 introduction to, 879–80
 leukocyte transendothelial migration, 1030–4
 nitric oxide as autocrine and paracrine regulator, 988–91
 phage display, 898–904
 platelet-endothelial cell adhesion molecule-1, 1037–44
 protein C, 973–80
 protein S, 982–91
 proteomic mapping and vascular targeting, 881–92
 P-selectin, 1049–55
 regulation of barrier responses and permeability, 1015–27
 thrombomodulin, 939–44
 tissue factor expression, 932–6
 tissue factor pathway inhibitor (TFPI), 922–8
 vascular cell adhesion molecule-1, 1058–66
 von Willebrand factor, 915–20
 outward hypertrophic remodeling, 549
 oxidation, and trauma, 1528
 oxidative phosphorylation, 257*f*
 oxidative stress. *See also* reactive oxygen species
 acute respiratory distress syndrome, 1188
 apoptosis, 189–90
 erectile dysfunction, 1545–6
 lung ischemia, 1209–10
 reactive oxygen species, 375–6
 toxicant-induced, 527–8, 530
 oxidized 1-palmitoyl-2-arachidonoyl-sn-glycerol-3-phosphorylcholine (oxPAPC), 933
 oxygen. *See also* heme oxygenase; homeostasis; oxidative stress; reactive oxygen species
 composition of venous blood, 258–60
 delivery of in hagfish, 67–8, 69*t*
 hepatic sinusoidal endothelial cells and delivery of, 1227, 1229
 metabolism of shrew and transport, 107–11
 oxygen-free radicals, and tissue factor expression, 936
 oxygen-independent expression, of hypoxia-inducible factor 1, 249–50
 oxygen-induced retinopathy (OIR), 1155–6
 oxygen sensing, and hypoxia-inducible factor 1, 248–9
 packed red blood cells (PRBCs), 1535, 1536, 1537
 paclitaxel, 553, 839, 1393
Pagothenia borchgrevinki, 75, 77*f*
 pain, and opioids, 458
 paired dorsal aortae (pDA), 143, 144*f*, 145
 Paleolithic, and biomedical environment of humans, 129–33, 257
 pancreas, 173–9, 901
 pancreatic cancer, 331, 342
 pancreatic islets, 177–8
 pancytopenia, 1590
 pan-endothelial ligands, and drug targeting, 1736–7
 papillary carcinomas, 1391, 1392
 parabronchial lung, 92
 paracellin, 634
 paracellular permeability, 1017
 paracellular route, of leukocyte transmigration, 579
 paracrine functions
 of endothelium in fish, 63
 E-selectin, 1077–8
 nitric oxide, 990–1
 P-selectin, 1051–3
 vasodilation and properties of nitric oxide, 562–3
 parallel plate chamber, 1204
 paralogous genes (paralogues), 113
 parasites, and blood transfusions, 1533
 parenchyma, and normal microvasculature, 1457
 Parkinson disease, 1131, 1132
 paroxysmal nocturnal hemoglobinuria, 565, 566, 1632–3
 partial differential equations (PDEs), 1781–2
 particulate matter, and toxicity, 531
 passive targeting, of magnetic resonance imaging, 1646
 passive transport pathways, 882
 pastoralists and pastoralism, 130, 131
 pathogen-associated molecular patterns (PAMPs), 411, 430, 431, 433*f*
Pathologische Anatomie
Leiden-endothelium (PAL-E), 1433
 pathology. *See also* disease; infection; inflammation and inflammatory response
 apoptosis, 1090–3
 dietary salt intake, 1289–91
 E-selectin, 1073
 extracellular nucleosides and nucleotides, 391
 fibroblast growth factors, 294
 forkhead signaling, 838–9
 hereditary hemorrhagic telangiectasia, 1120–1
 history of medicine, 13
 ICAM-1 and VCAM-1, 1063, 1065
 microvascular blood flow, 1665–6
 snake toxins, 461–2
 sphingolipids and vascular, 407–408
 toxicity, 527–8, 529–30
 vascular endothelial growth factor, 267–8
 vascular endothelial growth factor receptors, 271–3, 274
 vascular smooth muscle cells, 550–4
 pathway diagrams, 220
 pattern recognition receptors (PRRs), 411.
See also Toll-like receptors
 paxillin, 242, 1020, 1021
 PD173074, 1393
 peg and socket contacts, 1126
 peliosis hepatis, 1229, 1233
 penthalaris, 922
 peptide(s), 62, 888, 899, 901, 902–903
 peptide growth factors, and angiogenesis, 1448*t*
 peptide-phage display libraries, 884
 PER-ARNT-SIM homology (PAS) domains, 247
 perfusion scanner, and laser Doppler flowmetry, 1662
 periarteriolar macrophage sheath, 1256
 pericardial effusion, in dog, 96
 pericyte(s). *See also* mural cells
 alignment and contact, 538
 antiangiogenic therapy, 541
 blood-brain barrier, 1126
 functions of, 539–40
 future research, 541–2
 investment, 536–8
 origins and phenotypes, 538–9
 retinal vascular development, 1157
 skin, 1432
 transforming growth factor- β and recruitment, 312–13, 538
 vascular disease, 540–1
 perinatal switch, and high endothelial venules, 1581
 periodic acceleration (pGZ), 1692–3
 peripheral angioplasty, 1605*t*
 peripheral arterial disease, 95, 1704
 peripheral artery measurements, 1660–1
 peripheral blood, and endothelial progenitor cells, 1590–1
 peripheral blood lymphocytes (PBLs), 1581
 peripheral blood mononuclear cells (PBMCs), 1616

- peripheral blood-nerve barrier, 1129
 peripheral lymph nodes (PLNs), 1570–2,
 1573–5, 1576–7, 1577–80
 peripheral node addressins, 1433
 peritoneal cavity, and aquaporin function,
 716–17
 peritonitis, and tissue factor pathway
 inhibitor, 927
 peritubular plexus, 1271, 1273*t*
 perivascular cells, 1716–17, 1718
 permeability. *See also* hyperpermeability;
 vascular permeability
 continuous endothelia, 881–2
 diabetes, 1376
 fish capillaries, 61–2
 intercellular adhesions, 1019
 lipopolysaccharide, 413–14
 platelet-endothelial cell adhesion
 molecule-1, 1043–4
 real-time imaging, 1655
 regional differences, 1016–17
 selective vectorial transport, 632
 thrombin model of increased, 1020–1
 tumor blood vessels, 1460–1
 peroxisome proliferator-activated receptors
 (PPARs)
 adipogenesis and insulin sensitivity, 707
 definition, 796
 endogenous activation, 801
 fatty acid metabolism, 799–800
 gene expression, 797
 history and evolution, 796
 as mediators of transcriptional
 responses, 802–803
 potential negative effects, 800–801
 role of in endothelium, 797–9, 800
 peroxynitrite, 1528, 1545
 Peyer Patches, 1570–1, 1575
 PF4, and immune modulators, 592, 596
 PGA-PHA grafts, 1503
 PGE synthase (PGES), 1006
 phage-based techniques, for proteomic
 mapping, 884–6
 phage display, 898–904
 phagocytosis, and protein S, 985
 pharmacokinetics, and drug targeting,
 1734, 1736
 pharmacologic preconditioning, and
 organic nitrates, 1684
 pharmacology. *See also* chemotherapy;
 drugs; pharmacokinetics; therapeutic
 implications
 angiogenesis inhibition, 1452
 erectile dysfunction, 1401
 sphingolipids, 408
 phenotypes, of endothelial cells. *See also*
 genetics
 angiopoietins, 355–6
 breast cancer, 1795
 circulating endothelial cells, 1612
 complement deficiency, 434*t*
 EC activation, 1112
 Eph receptors and ephrin ligands, 347*t*
 E-selectin, 1077
 heparan sulfate, 956
 hemodynamics, 234–8
 hepatic sinusoidal endothelial cells,
 1227–9
 high endothelial venule-like vessels,
 1420–5, 1569–70
 ICAM-1 and VCAM-1, 1062
 intermediate types of, 1768
 lectins in pulmonary circulation,
 1164–5
 pericytes, 538–9
 sickle cell disease, 1358
 skin endothelial cells, 1432–4
 thrombospondin family, 329–20
 phenotypic drift, 883, 1165
 phenotypic evolution, 27
 phenotypic plasticity, of vascular smooth
 muscle cells, 550
 phosphatase and tensin homolog deleted
 form chromosome 10 (PTEN), 870
 phosphatidylinositol 3-kinase. *See*
 phosphoinositide 3-kinase
 phosphatidylserine, 985, 1085*t*, 1091
 phosphoadenosine-5'-phosphosulfate
 (PAPS), 949
 phosphoglycerate kinase, 595*t*
 phosphoinositide 3-kinase (PI3K), 241,
 295, 354, 729–30, 934, 1674–5
 phospholipase C (PLC), 722, 723
 phospho-tyrosine mimics, 769
 photographic images, 209
 photosynthesis, 122, 246, 247*f*
 phylogenetic analysis, 116, 118
 phylogeny, molecular, 113–20
 physical barrier, of blood-brain barrier,
 1127–8
 physical deformation, and flow-mediated
 mechanotransduction, 239–40
 physiology
 cell motility, 288
 comparative biology of fish, 61–3
 diving, 44, 45
 endothelial cells and integrative, 256–60
 giraffe and gravitational, 101–102
 history of medicine, 13
 vascular endothelial growth factors, 267,
 271, 274
 vascular smooth muscle cells, 547–50
 pigment epithelium-derived factor
 (PEDF), 1154
 pillar cells, 60, 63
 pinocytosis, 664
 pioglitazone (Actos), 797
 placental expression, of E-selectin, 1072
 placental growth factor (PlGF), 115, 250–1,
 296
 placental trophoblast cells, endothelial
 mimicry of, 1479–85
 placental vasculature, and development,
 1488–96
Plague Time (Ewald), 132
plakoglobin, and β -catenin, 773
 plaques, and atherosclerosis, 1215
 plasma, 924, 986
 plasmalemmal vesicle(s), 646, 647–8,
 649–51, 680–1, 682
 plasmalemmal vesicle-associated protein
 (PLVAP), and vascular permeability,
 683–4
 plasma membrane integrity assay, 1085*t*
 plasma volume loss, and space travel, 521
 plasminogen, and platelets, 593*t*
 plasminogen activator inhibitor (PAI)-1,
 306–307, 314, 1334, 1671
Plasmodium falciparum, 1303, 1304, 1433.
See also malaria
Plasmodium falciparum-infected
 erythrocytes, 1038
 platelet(s). *See also* platelet-endothelial cell
 adhesion molecule
 acute respiratory distress syndrome,
 1183*f*, 1187–8
 adhesion, 588–90
 burn injury, 1509
 cerebral malaria, 1306–307
 definition, 587
 endothelial communication, 590–8
 functions, 587
 therapeutic implications, 598
 trauma, 1527
 platelet-activating factor (PAF), 1378,
 1508–509
 platelet activation-dependent
 granule-to-external-membrane
 protein (PADGEM), 1049
 platelet aggregation, 587, 1525
 platelet-derived growth factors (PDGFs),
 250–1, 536–7, 1561
 platelet-derived growth factor-BB
 (PDGF-BB), 1157
 platelet-endothelial cell adhesion molecule
 (PECAM-1)
 apoptosis, 1042–3
 as biosensor, 1040–2
 drug targeting, 1739
 gene expression, 1037–9
 hereditary hemorrhagic telangiectasia,
 1115
 history of research, 1037
 inflammation, 1059*t*
 leukocyte transendothelial migration,
 1033, 1039–40
 platelet-endothelial interactions, 589
 protein tyrosine phosphatases, 768
 regulation of cell migration and
 angiogenesis, 1040
 regulation of vascular permeability,
 1043–4
 vascular targeting, 888

- platelet factor 4 (PF4), 593*t*, 1346–7
 platelet microparticles (PMPs). *See*
 endothelial microparticles
 Platyhelminthes (flatworms), and evolution
 of cardiovascular system, 33, 34*f*
 pleckstrin, 595*t*
 pleiotropic effects, of organic nitrates,
 1683–5
 pleural space, and aquaporin function,
 716–17
 plexiform lesions, 272, 1168–9, 1193, 1194,
 1196
 plexins (PLXNs), 337, 341, 361
 pluripotency, and developmental evolution
 of endothelial heterogeneity, 55
plxnd1 gene, 154
Pneumocystis carinii pneumonia, 1472
Podocoryne carnea (jellyfish), and
 phylogenetic analysis, 119, 120
 podocytes, 620–4
 podoplanin, 1560
 podosomes, 702
 point mutations, of E-selectin, 1075–6
 poly ADP-ribose polymerase (PARP), 1084,
 1373, 1666
 polybutylcyanoacrylate (PBCA), 1132
 polychaete worms, 37
 polyclads, 33
 polycyclic aromatic hydrocarbons (PAHs),
 1325, 1326
 polycystic ovary syndrome (PCOS), 1375
 polycystic transient receptor potential,
 724–5
 polyethylene glycol (PEG) liposomes, 1133,
 1734–5
 polyglycolic acid (PGA), 1503
 polyhydroxyalkanoate (PHA), 1503
 polylactic acid sponges, 1717
 polymersomes, 1735
 polymorphic light eruption, 1437*t*
 polymorphonuclear leukocytes (PMNLs),
 483, 484–6, 654, 1183*f*. *See also*
 neutrophils
 polyomavirus, 671
 polymorphonuclear neutrophil
 (PMN)-mediated acute lung injury
 (ALI), 1533
 polysaccharides, and platelet factor 4, 1347
 polysorbate 80, 1132–3
 population dynamic, of agent-based
 model, 1757
 pore theory, of capillary permeability, 13,
 644, 679, 680
 Porifera. *See* sponges
Porphyromonas gingivalis, 132, 412
 portal heart, 67, 69*t*, 71
 portal hypertension, 1242–5
 portal vein thrombosis (PVT), 1245
 portal venous blood flow, 1239
 portosystemic collateral circulation,
 1244
 positional cloning, 150
 positron emission tomography (PET), and
 vascular smooth muscle cells, 555
 post-biosynthetic processing, of heparan
 sulfate proteoglycans, 951
 postcapillary segments, 1163
 postcapillary venules, 1050
 posterior cardinal veins (PCVs), 143, 144*f*,
 145, 147
 posterior intersomitic veins (PiV), 144*f*,
 145
 postgastrulation, and vascular
 development in mammals, 161–2
 posthepatic resistance, 1246
 postnatal vasculogenesis, 1435
 postprandial hyperlipidemia, 1629
 post-transcriptional modification, and
 GATA transcription factors, 807–809
 post-translational modifications, 814, 815*f*,
 1064
 potassium and potassium channels
 in ancestral human diet, 132
 composition of blood, 259
 dietary salt, 1288
 ion channels, 725–6
 lung ischemia, 1206, 1208*f*
 power laws, and networks, 1765
 PPAR response elements (PPREs), 797
 pravastatin, 1604
 precapillary segments, 1163
 preeclampsia
 endothelial microparticles, 1630,
 1632*t*
 endothelin-1, 1604
 maternal-fetal conflict over blood flow
 control, 137–9
 placental vascular development,
 1494–6
 role of endothelium in, 1112
 toxicology, 531–2
 VEGFR1 and VEGFR2, 272
 preferential attachment, and scale-free
 network model, 1761
 pregnancy. *See also* placental trophoblast
 cells; placental vasculature;
 preeclampsia; reproduction
 cigarette smoking, 1320, 1327
 endothelin-1, 1604
 hereditary hemorrhagic telangiectasia,
 1116
 maternal-fetal interactions in human,
 135–9
 plasma levels of protein S, 986
 thrombophilia-associated complications,
 1483–5
 von Willebrand factor levels, 1602
Xenopus and test for, 142*n*1
 pregnancy-associated plasma protein
 (PAPP)-A, 1496
 pregnancy-induced hypertension (PIH),
 137–9. *See also* preeclampsia
 prehepatic resistance, 1245
 prekallikrein (PK), 444–5
 pre-patterned embryonic gut epithelium,
 176–7
 pre-proendothelin-1 promoter, 806
 prevention, of disease. *See also* diet;
 exercise; health and health care;
 obesity; public health
 coronary heart disease, 1808
 decompression sickness, 501–502
 platelet activation, 598
 role of endothelium in chronic disease,
 1810, 1811
 space travel and orthostatic intolerance,
 525
 primary capillary plexus, 25
 primary hemostasis, 909, 913
 primary lymphedema, 1562
 primary pulmonary hypertension (PHH),
 316
 prion diseases, 1533, 1534*t*, 1535
 proadhesive effects, of antiphospholipid
 antibody syndrome, 1365–6
 proangiogenic genes, 792, 1493
 probes, by magnetic resonance imaging,
 1642, 1647–8
 procedural simulation, 1805
 procoagulant effects, 415, 1324–5, 1363–5,
 1527
 proepicardium, 169
 professional APCs, 1099, 1104
 profilin, 594*t*
 progressive determination, and endothelial
 heterogeneity, 55
 progressive multifocal
 leukoencephalopathy (PML), 1252
 prohibitin, 901
 proinflammatory activation, 759, 823, 825,
 1323–4
 proinflammatory mediators, and brain
 ECs, 1146
 proliferation. *See* cell proliferation
 proline-directed protein kinases, 737
 prolyl hydroxylase(s), 248
 prolyl hydroxylase inhibitors, 624
 proof-of-principle experiments, 674
 properdin, 432, 434*t*
 Prospero protein, 1556
 prostacyclin, 564*t*, 1006–1009, 1323
 prostaglandins, 511–12, 564*t*, 1004,
 1186–7, 1542
 prostanoids, 62*t*, 63
 prostate cancer, 342, 870, 871, 903
 prostate-specific membrane antigen
 (PSMA), 890
 prosthetic vascular grafts, 1501–505,
 1700–701
 protease(s), 594*t*, 598, 1185
 protease-activated receptors (PARs), 923,
 976–7, 1185
 proteasome, 1098

- protein(s). *See also* amino acids; Crk-like proteins; glycoproteins; liver-transcription activation protein; liver-transcriptional inhibitory protein; LPS-binding protein; protein C; protein kinase C; protein S; Rho GTP-binding proteins; RNA-binding protein; slit proteins; Smad proteins
 antithrombin, 961–3
 E-selectin, 1074–5
 Ets factors and protein-protein modifications, 814
 GATA transcription factors and protein-protein interactions, 809–10
 heparan sulfate binding, 948*t*
 hereditary hemorrhagic telangiectasia, 1116–17
 integrin and structure of, 708–709
 tissue factor pathway inhibitor, 923–4
 von Willebrand factor, 916
 protein-arginine methyltransferases (PRMTs), 1282
 protein arrays, 885*t*, 886
 protein C. *See also* activated protein C (APC); endothelial protein C receptor
 activation, 974–5
 antiphospholipid syndrome, 1364–5
 deficiencies, 977
 definition, 973
 development, 978
 disseminated intravascular coagulation, 1333
 evolution, 974
 gene, 974
 hemostasis, 910, 912*f*
 history of research, 973
 identification and isolation, 939
 regulation of coagulation, 975
 regulation of expression, 978
 structural features, 973
 therapeutic considerations, 979
 protein expression, and proteomic mapping, 883–7
 protein kinase C (PKC)
 diabetes, 1372–3
 discovery, 746
 functions, 748–51
 gene family, 746–8
 hemodynamics, 237
 therapeutic implications, 751
 protein-platelet endothelial adhesion molecule (PECAM-1), 242
 protein-rich tyrosine kinase 2 (PYK2), and flow-mediated mechanotransduction, 241–2
 protein S
 anticoagulant activity, 983–4
 apoptotic cells and phagocytosis, 985
 C4B-binding protein, 984–5
 deficiency of and venous thrombosis, 985–6
 definition of, 982
 gene and synthesis of, 982
 structure of, 982–3
 protein transduction domains (PTD), 1132
 protein tyrosine phosphatases, 764–9
 proteinuria, 137
 proteoglycans (PGs), 327
 proteomic mapping, 882–7, 890–1
 prothrombin, 594*t*, 910
 prothrombinase, 962
 protochordates, and evolution of cardiovascular system, 40–1
 protonephridia, 34
 Prox1 gene, 1556, 1558
 Prxl gene, 189–90, 191, 192
 P-selectin
 atherosclerosis and deficiency of, 1219
 cerebral malaria, 1306
 diagnostic and therapeutic implications, 1054
 gene expression, 219
 gene regulation, gene/protein structure, and protein trafficking, 1049–51
 history of research, 1049
 homeostasis, 1051–4
 inflammation, 1059*t*
 nuclear factor- κ B signaling, 790
 regulation, 1050–1
 skin inflammation, 1434, 1439
 von Willebrand factor, 918
 pseudoattractors, 1776
 pseudocapillarization, and hepatic sinusoidal endothelial cells, 1229
 psedotolerance, of organic nitrates, 1685
 pseudovasculogenesis, 1488, 1489, 1490*f*
 PSI-BLAST analysis, 114, 116, 118*f*, 119*f*
 psoriasis, 582, 1421*t*, 1436, 1437–8, 1439
 PTK 787/ZK222584, 1393
 PTP- β inhibitors, 769
 P2Y and P2X receptors, 388–9
 public health, and future of endothelial biomedicine, 1807–12. *See also* health and health care; prevention
 PubMed, 1445, 1450
 pulmocutaneous arch, 42
 pulmonary arterial hypertension (PAH), 272, 316, 1116, 1704–705. *See also* pulmonary hypertension
 pulmonary arteriovenous malformations (PAVMs), 1114–1115
 pulmonary circulation, and EC heterogeneity, 1161–9
 pulmonary endothelium, 1174
 pulmonary hypertension. *See also* pulmonary arterial hypertension
 apoptosis and shear stress, 1195–6
 bronchial vasculature, 1175
 cell proliferation, 1194–5
 endothelial cell heterogeneity, 1168–9
 remodeling, 1193
 viral infections, 1196
 Pulmonary Hypertension: Assessment of Cell Therapy (PHACeT) trial, 1705
 pulmonary vascular development, 181–92
 pulmonary vascular disease, 1168–9, 1704–705
 pulmonary vasculature, and drug targeting, 1739–40
 pulsatility, and shear stress, 231, 1691
 pulse wave velocity (PWV), 1661–2
 purinergic/pyrimidinergic signaling, 385
 purinergic receptors, and extracellular nucleosides and nucleotides, 387–9, 391*t*
 purines, and secondary circulation in fish, 62*t*
 purpura fulminans, 912, 977, 979
 pyogenic infections, in infancy and childhood, 432, 434*t*
 PX-478, 253
 pyrrolidine dithiocarbamate (PDTc), 933
 pyruvate kinase M2 isozyme, 595*t*
 quantum dots, 1657
 quiescent endothelial cells, 1449
 Rac signaling, 700, 1023
 radiation-induced organ injury, and apoptosis, 1092
 radioiodinated antibodies, 890, 891
 radiotherapy, and vascular smooth muscle cells, 553
 ragged mutations, and Sox genes, 864, 865
 raloxifene, 1675–6
 random network model, 1761, 1762*f*, 1763*f*
 RANTES, and platelet-endothelial interaction, 596
 rapamycin, 253, 553, 792, 999
 Rap signaling, and microfilaments, 700
 Ras-Ral signaling, and forkhead proteins, 835
 rat lung microvascular ECs (RLMVECs), 883
 Raynaud phenomenon, 1435
 reactive nitrogen species (RNS), 527, 530, 1188
 reactive oxygen species (ROS). *See also* oxidative stress; redox state
 acute respiratory distress syndrome, 1188
 apoptosis, 1089
 cytochrome P450, 377–8
 diabetes, 1370
 endothelial response, 378–9
 high altitude, 516–18
 history of research, 375
 integrative physiology, 257
 lung ischemia, 1209–10
 molecular targets, 379–80
 protein-rich tyrosine kinase 2 (PYK2), 241

- Rho GTP-binding proteins, 758–9
 shear stress, 1204
 sources, 376–7
 therapeutic implications, 380
 tissue- and vascular bed-specific differences, 378
 toxicity, 527, 530, 531
 real-time imaging, 1654–7
 rebound, and nitrate therapy, 1686
 receiver coils, and magnetic resonance imaging, 1640–1
 receptor(s). *See also* coreceptors; coupling; endothelial protein C receptor; Fc- γ receptor; G-protein coupled receptors; growth hormone receptor; lymphatic vessel endothelial receptor; mannose receptor; membrane estrogen receptors; Notch receptors; opioid receptors; pattern recognition receptors; protease-activated receptors; P2Y and P2X receptors; purinergic receptors; Roundabout receptors; signaling; sphingosine 1-phosphate receptors; sulfonylurea receptors; TNF-receptor; toll-like receptors; vascular endothelial growth factor receptors
 angiopoietins and interactions with ligands, 353–4
 extracellular nucleosides and nucleotides and purinergic, 387–9
 fibroblast growth factors, 294–5
 heparan sulfate and ligand interactions, 953–6
 hepatocyte growth factor and c-MET, 286–8
 integrins, 709
 receptor for advanced glycation end-products (RAGE), 419–26
 receptor-induced magnetization enhancement (RIME), 1643
 receptor-like protein tyrosine phosphatases (RPTPs), 764–5, 766, 767*t*
 receptor-mediated transport, of therapeutics, 1132
 receptor Smads (rSmads), 308–309
 receptor tyrosine kinases (RTK), 352, 709
 recombinant technology, 925, 927–8, 1025, 1315, 1528. *See also* genetic engineering
 recompression chamber, 480
 red blood cell(s), 563–6, 1306, 1352–3, 1525, 1537. *See also* packed red blood cells
 red blood cell microparticles (RMPs). *See* endothelial microparticles
 Redi, Francisco, 461
 redox potential, and Rho GTP-binding proteins, 757
 redox sensor, platelet-endothelial cell adhesion molecule-1 as, 1042
 redox state, 1062, 1063, 1670.
See also oxidative stress; reactive oxygen species
 re-endothelization, and statins, 1671
 regeneration, and real-time imaging, 1656.
See also vascular repair
 regression, and exercise, 510
 regulation. *See also* gene expression; thermoregulation; vasoregulation
 Akt signaling and nitric oxide synthase, 731–2
 angiogenesis, 1448*t*
 apoptosis, 1084, 1093
 blood flow in acute respiratory distress syndrome, 1186–7
 C-natriuretic peptide and vasoreactivity, 824
 contractile apparatus and barrier, 1017–19
 disseminated intravascular coagulation, 1333
 endothelial nitric oxide synthase and NO production, 563*t*
 E-selectin and gene, 1072–4
 fibroblast growth factors and vasomotor, 296–7
 forkhead proteins, 835–8
 heme oxygenase, 996
 hemoglobin and nitric oxide, 563–6, 568–70
 heparan sulfate signaling, 955–6
 hypoxia-inducible factor 1 and oxygen homeostasis, 246–8
 ICAM-1, 1063–5
 junctional and matrix adhesion in barrier, 1019–20
 modified tensegrity model for barrier, 1017, 1018*f*
 myocyte enhancer factor 2 by Ets factors, 851
 myoglobin and nitrite, 568–70
 nuclear factor of activated T cells and signaling, 828–9
 nuclear factor- κ B signaling, 787–8
 opioid receptors, 452, 454
 platelet-endothelial cell adhesion molecule-1, 1040, 1043–4
 protein C and coagulation, 975
 protein tyrosine phosphatases and cell function, 766–8
 P-selectin, 1050–1
 Rho GTP-binding proteins, 754–5
 sphingosine 1-phosphate-mediated barrier, 1024
 VCAM-1, 1063–5
 von Willebrand factor, 917
 regulators of complement activation (RCA), 432, 435
 regulatory domain, of protein kinase C, 747*f*
 Reinfusion of Enriched Progenitor Cells and Infarct Remodeling in Acute Myocardial Infarction (REPAIR-AMI), 1702
 relative activity versus endocytosis (RAVE), 454
 relaxivity, and magnetic resonance, 1642
 releasate, and platelets, 592–7
 Rel binding domain, and nuclear factor of activated T cells (NFAT), 828
 Rel homology domain (RHD), and nuclear factor- κ B signaling, 784–7, 788–9
 remodeling. *See also* vascular remodeling
 outward hypertrophic, 549
 placental vasculature, 1480–1, 1489, 1490*f*
 pulmonary hypertension, 1193
 retinal vascular development, 1157
 remote control, of leukocyte recruitment during inflammation, 1575
 renal decompensation, and portal hypertension, 1244
 renal disease, and dietary salt, 1289–91. *See also* end-stage renal disease; kidney disease; renal failure
 renal endothelium, 1271–6
 renal failure, 624, 1276. *See also* acute renal failure
 renal glomerulus, 620–1
 Rendu-Osler-Weber syndrome. *See* hereditary hemorrhagic telangiectasia
 renin-angiotensin-aldosterone system (RAAS), 1380
 reperfusion injury, 438, 1355, 1356*f*, 1357.
See also ischemia-reperfusion injury
 reperfusion-mediated lung injury, 1209–10
 replication-defective retroviruses, 168
 reproduction. *See also* embryo; pregnancy
 angiogenesis, 1449–50, 1451
 evolutionary conflict between parents and offspring, 135
 natural selection and maximization of, 123
 of shrew, 111
 vascular endothelial growth factor receptors and cycle, 271
 reptiles, 43–5, 1555. *See also* snakes and snake toxins
 repulsive vascular guidance, 365
 residual oil fly ash (ROFA), 531
 resistance, to activated protein C, 977–8
 resistance vessels, 1713
 respiratory capillaries, of amphibians, 86
 respiratory system, 109, 181–92. *See also* acute respiratory distress syndrome; asthma; lung
 restenosis, 273, 289, 424
 resveratrol, 999
 retargeting, of adenovirus for gene transfer, 1727–31
rete mirabile, 59

- reticular dermis, 1431
 retina, 541, 1154–8. *See also* retinopathy
 retinal pigmented epithelium (RPE), 1154
 retinoic X receptor (RXR), 797
 retinopathy, and protein kinase C, 751.
See also diabetic retinopathy; familial
 exudative retinopathy
 retinopathy of prematurity (ROP), 1155–6,
 1158
 retroviruses, 168, 169, 1726, 1727*t*, 1728*t*.
See also antiretroviral therapy; human
 immunodeficiency virus
 Reynold's number, 37
 RGD peptide motif, 902
 RGD sequence, of thrombospondins, 329,
 330
 rheumatoid arthritis, 781, 786*t*, 902,
 1419–27, 1605*t*
 RhoA isoform, 753, 754
 RhoA/Rho-kinase pathway, and erectile
 dysfunction, 1542*f*, 1543, 1544
 Rho-associated kinase (ROCK), 242
 RhoB isoform, 753–4
 RhoGEFs, 754–5
 Rho GTPase system, 275–6, 553–4, 596*t*,
 859. *See also* Rho GTP-binding
 proteins
 Rho GTP-binding proteins
 cell cytoskeleton, 755–6
 cell migration, 756–7
 downstream effector molecules, 755
 gene expression, 757
 gene family, 753–4
 history of research, 753
 reactive oxygen species, 758–9
 redox potential, 757
 regulation of, 754–5
 shear stress, 758
 therapeutic implications, 759–60
 vasculogenesis and angiogenesis, 757–8
 ribbon worms, 33–4
 right ventricle systolic pressure (RVSP),
 1705
 rimonabant, 1329
 risk factors, for disease
 atherosclerosis, 1606*t*
 avascular necrosis, 1550
 cardiovascular disease, 1320
 RNA-binding protein, 595*t*
 RNA viruses, and hemorrhagic fevers, 1311
 rolipram, 1163
 rolling
 of leukocytes, 576–8, 790
 of platelets in inflammation, 589
 of P-selectin, 1052, 1053–4
 rosiglitazone (Avandia), 797, 799, 1220
 rotational correlation time, and magnetic
 resonance, 1642
 Roundabout (Robo) receptors, 362–3,
 365
 RU486 (mifepristone), 1677, 1678
 rule-based system, comparison of
 endothelial biology to, 215–16, 219–21
 Sabin, Florence, 14, 53–4, 161, 1554
Saccharomyces cerevisiae, 403, 1760, 1764,
 1774
 saddle thrombus, 97*n*4
 safety
 of drug targeting, 1736
 of magnetic resonance imaging, 1644–6
 salamanders (Urodeles), and skin
 breathing, 43, 86, 88
Salmonella spp., 1533
 salt, dietary intake, 1287–92
 Sanger Center (Britain), 150
 Sapporo Investigational Criteria, 1360
 sarafotoxins, 463*t*, 465
 sarcoplasmic, endoplasmic reticulum
 calcium ATPase (SERCA), 1163
 saturation diving, 497
 scale-free networks, 1760–5, 1775
 scaling, and size of mammals, 24–5, 107
 scanning electron microscopy (SEM), and
 vascular permeability, 681
 scatter factor (SF), 285. *See also* hepatocyte
 growth factor
 scavenger function, of hepatic sinusoidal
 endothelial cells, 1228
 scavenger organs, and endocardium in fish,
 81–2
 schistosomiasis, 1245
schwentine mutation, 152, 154
 Scientific Revolution, 14
 scleroderma, 540–1, 1411, 1437*t*
scl gene, 153
 SDS-PAGE, and proteomic mapping, 887
 seawater, internal circulation of in sponges,
 31–2
 sebaceous glands, 1431
 secondary circulation, in bony fishes, 61
 secondary hemostasis, 909–10, 911*t*, 913
 secondary lymphedema, 1562
 secondary lymphoid organs (SLOs), 1568
 secretion, of von Willebrand factor,
 916–17
 secretogranins, and platelets, 593*t*, 596
 secretory organs, and endocardium in fish,
 80–1
 seeding. *See* autoseeding; cell seeding
 selectins, 576–8, 588–9, 1299*t*. *See also*
 E-selectin; L-selectin; P-selectin
 selective estrogen receptor modulators
 (SERMs), 1675–6
 selective vectorial transport, 632–8
 self-contained underwater breathing
 apparatus (SCUBA), 497
 self-similarity, and complex processes, 1752
 semantic nearness, 200*f*, 201*f*
 semaphorins (SEMA), 337, 340–2, 361,
 1448*t*
 sensitivity amplification, 1772
 sepsis. *septic shock*
 acute respiratory distress syndrome,
 1182
 apoptosis, 1092
 barrier regulation by activated protein C,
 1025
 definition, 1294–5
 endothelial microparticles, 1631–2
 E-selectin, 1078
 leukocyte transmigration, 581
 neurological dysfunction, 1146–7
 platelet-endothelial cell adhesion
 molecule-1, 1041, 1044
 protein C and activated protein C, 978,
 979
 skin necrosis, 977
 systemic inflammatory response
 syndromes, 969
 therapeutic strategies, 1299
 tissue factor expression, 934–5
 tissue factor pathway inhibitor, 927–8
 use of term, 1294
 virtual patient simulation, 1804–805
 sepsis-associated encephalopathy, 1147
 septic shock, 1294, 1312
 septic vasculitis, 1437*t*
 sequestration, and cerebral malaria, 1303
 serine proteinases, 463*t*, 464, 466
 serine residues, and forkhead signaling, 835
 serine threonine kinases (ALK), 308
 serpins (serine protease inhibitors), and
 antithrombin, 963, 964, 966
 “serum effect,” and transendothelial
 transport, 882
 serum response factor (SRF), 190
 serum sickness, 439
 severe angioproliferative pulmonary
 hypertension (SAPPH), 1193–7. *See
 also* pulmonary hypertension
 severe combined immunodeficiency
 (SCID), 1218
 sexual debility, and opioid receptors, 457
 shear stress and shear forces. *See also* blood
 flow; laminar shear stress
 apoptosis, 1086
 atherosclerosis, 1220
 barrier regulation, 1021
 cytoskeleton, 699
 flow-mediated mechanotransduction,
 239, 241, 242
 hemodynamics, 231–3, 238, 910,
 1690–1
 ICAM-1 and VCAM-1, 1063–4
 lung ischemia, 1204–1208
 nitric oxide, 990
 platelet-endothelial cell adhesion
 molecule-1, 1041
 protein tyrosine phosphatases, 768
 pulmonary hypertension, 1195
 Rho GTP-binding proteins, 758
 T cells, 1103

- Tie1 and Tie2 signaling system, 353
 tissue factor expression, 933
 von Willebrand factor, 919
 short consensus repeats (SCRs), 435
 shotgun MS approaches, to proteomic mapping, 886
 SHP-1 and SHP-2, 275
 shrew, comparative biology and metabolism of, 24–5, 107–11
 SH2 domain-containing leukocyte protein of 76 kDa (SLP-76), 1560–1
 sialic acid, 1577
 sialomucins, 1433
 sickle cell disease
 avascular necrosis, 1550, 1551
 blood transfusions, 1537
 circulating endothelial cells, 935, 1354–5, 1613
 endothelial microparticles, 1607, 1632
 nitric oxide-dependent vascular homeostasis, 562, 565, 566
 nonendothelial pathogenesis, 1112
 phenotypic diversity and genomics, 1358
 P-selectin, 1054
 red blood cell adhesion, 1352–3
 therapeutic implications, 1357
 tissue factor expression, 935
 Sidell hypothesis, 76–7
 sidestream cigarette smoke, 1325
 Siemens Corp., 15
 sieve function, of hepatic sinusoidal endothelial cells, 1227–8
 sieve plates, 682, 1226
 sigmoidal input/output relationship, 1772
 signal amplification, for magnetic resonance, 1642–6
 signaling. *See also* Akt signaling; C5a signaling; C5b-9 signaling; coupling; *Delta-Notch* signaling; downstream signaling; forkhead signaling; inside-out signaling; ligand-based cell surface signaling; mutual signaling; noncanonical Wnt signaling; purinergic/pyrimidineric signaling; Rac signaling; Rap signaling; Ras-Ral signaling; receptors
 activated protein C and barrier regulation, 1025–6
 angiopoietins, 355*t*
 apoptosis, 1086–90
 cardiac myocytes, 602–606
 caveolae and ligand-based cell surface signaling, 668–9
 chemokines, 578
 dietary salt, 1288–9
 extracellular nucleosides and nucleotides, 385–6
 fibroblast growth factors, 293*f*, 295
 flow-mediated mechanotransduction, 240–1
 heparan sulfate and regulation of, 955–6
 hepatocyte growth factor and c-MET receptor, 286–8
 hereditary hemorrhagic telangiectasia and TGF- β , 1117–19
 high altitude and transduction of, 517
 ICAM-1 and VCAM-1 as transducers, 1060–3
 leukocytes and leukocyte transendothelial migration, 581, 1030–1
 lipid rafts and sphingosine 1-phosphate, 1023–4
 lung ischemia, 1207–1209
 nuclear factor of activated T cells (NFAT), 828–9
 nuclear factor- κ B signaling, 784–93
 receptor for AGE, 424–5
 regulatory properties of coreceptor modulated, 953
 steroid hormones, 1674–5
 syndecans, 397–8
 Toll-like receptors, 411–12
 transforming growth factor- β , 304, 305*t*, 308–313, 316
 signal intensity, in magnetic resonance imaging, 1638
 signal transducer and activation of transcription 3 (STAT3), 1436
 sildenafil, 1401, 1546
 silica-coated plasma membranes, 666
 simile, and metaphor, 199*n*1
 Simvastatin, 934
 single-chain antibodies (scFVs), 1728
 single photon emission computed tomography (SPECT), and vascular smooth muscle cells, 555
 sinus circulation, in hagfish, 67, 71
 sinus-lining cells, 1256
 sinusoidal dilatation, 1229
 sinusoidal endothelium, 680, 881.
 See also hepatic sinusoidal endothelial cells
 sinusoidal fenestrae, 681
 sinusoidal obstruction syndrome (SOS), 1112, 1229, 1230–3
 sinusoidal vessels, 1463
 sirolimus, 553
 site-directed delivery, of ICAM-1 and VCAM-1, 1065, 1066. *See also* vascular targeting
 “site-specific drug delivery,” 673
 6-sulfo sialyl Lewis X ligands, 1420
 6-thioguanine, 1229, 1231
 skeletal muscle(s), 110, 258–9, 1267
 skeletal muscle cells, 547
 skin. *See also* burn injury; dermis; eczema; epidermis; psoriasis; skin lesions
 angiogenesis, 1435–6
 diseases of, 1436–40
 phenotypes of endothelial cells, 1432–4
 thermoregulation, 1434–5
 vascular architecture, 1431–2
 vasodilation and local heating of, 1664
 skin breathing, in amphibians, 42–3, 85–90
 skin lesions, at heparin injection sites, 1345–6
 slip bonds, and P-selectin, 1052
 slit diaphragms (SDs), 620, 621
 slit proteins, 362–3, 365
 Smad anchor for receptor activation (SARA), 308–309
 Smad-independent signals, 310–11
 Smad proteins, 308–309, 310–11
 small integrin-binding ligand, N-linked glycoproteins (SIBLINGS), 432
 small interfering RNA (siRNA) technology, 1731
 small intestine, and aquaporin in lacteal endothelium, 717
 small ubiquitin-like modifier (SUMO)-1 and -2, 807
 small-vessel vasculitis, 1411, 1412–13, 1416
 SMART analysis, 114
 “smart skins,” 212
 “Smoke Detector Principle, The,” 124
 smoking. *See* cigarette smoking
 smoking cessation, 1328–9
 smooth muscle actin (SMA), 1157
 smooth muscle cells (SMCs), 548, 1474*t*.
 See also vascular smooth muscle cells
 Smurfs (Smad ubiquitin regulatory factors), 309
 snakes and snake toxins
 adaptations to gravity, 99
 direct and indirect affects, 462–7
 evolution of cardiovascular system, 43–4
 history of research, 461
 Kunitz domain, 922
 toxicity-mediated thrombosis, 529
 in vitro versus in vivo considerations, 467
 viperid venoms and envenomation, 461–2
 snake venom metalloproteinases (SVMPs), 461, 462, 463*t*, 464, 465–6
 S-nitrosated hemoglobin hypothesis (SNO-hb), 566, 567
 sodium, in ancestral human diet, 130, 132
 sodium nitroprusside, 1663, 1665
 soft lithography, 1718
 soft-tissue injuries, and combat trauma, 1523
 soluble CD40 ligand (sCD40L), 1537
 soluble E-selectin, 1604
 soluble factors, and cytoskeleton, 699–700
 soluble fms-like tyrosine kinase (sFLT-1), 138, 269, 272, 1493–6
 soluble form of EPCR (sEPCR), 943
 soluble mediators, 743, 1126
 soluble N-ethylmaleimide sensitive factor receptor (SNARE), 659–60

- soluble plasma endothelial markers, 1606*t*
 soluble thrombomodulin, 943
 soluble VEGFR2, 270–1
 somatogenesis, and Wnt signaling, 779
 S100/calgranulins, 422
sonic hedgehog (shh) signaling pathway, 157
 source domain, and metaphor, 200–201
 Sox genes
 description, 861–2
 discovery, 862
 endothelial cell phenotype and functions, 865
 endothelial disease, 866
 expression in developing blood vessels, 863
 molecular pathway, 864–5
 mutations and functions, 863–4
 phylogeny, 862
 space of Disse, 1226, 1227, 1231
 space travel, and endothelial function, 520–5
 SPARC protein, 593*t*
 spatial resolution, in magnetic resonance imaging, 1640
 spatio-temporal complexity, in
 flow-mediated mechanotransduction, 241–3
 special conditions, effects of on endothelium
 barotrauma, 489–94
 diving, 497–502
 exercise, 506–13
 fever-range thermal stress, 471–8
 high altitude, 516–18
 hyperbaric oxygen therapy, 480–6
 snake toxins, 461–7
 space travel, 520–5
 toxicology, 527–33
 specialization, and history of biomedical research, 8–10
 specification, of endothelial cells, 1167–8
 spherocytosis, 566
 sphingolipids. *See also* sphingosine 1-phosphate
 development and angiogenesis, 406
 endothelial injury, 407
 mediators of, 405
 metabolism of, 403–405
 structural roles of, 405
 vascular pathology, 407–408
 vascular permeability, 406
 vascular S1P gradient, 405–406
 vascular tone control, 407
 sphingomyelin, 1043, 1184
 sphingosine 1-phosphate (S1P).
 See also sphingolipids
 acute respiratory distress syndrome, 1184
 apoptosis, 1089
 barrier regulation and restoration, 1021–6
 cytoskeleton and soluble factors, 699–700
 lipid rafts, 1023–4
 pericyte-endothelial cell interactions, 537
 platelet-endothelial cell adhesion molecule-1, 1043
 sphingosine 1-phosphate receptors (S1PR), 1184
 spin echo sequences, in magnetic resonance imaging, 1638–9
 spleen, 1255–62
 spleen tyrosine kinase (Syk), 1560–1
 splenic mesodermal plate (SMP), 1259
 sponges, and evolution, 31–2, 951, 952
 sporadic hemolytic uremic syndrome, 1337, 1338*t*
 sprouting angiogenesis, 25, 163–4, 184, 186*f*, 1156–7
 Sprouty (Spry) phosphatase family, 295
 squamates (snakes and lizards), 43
 squid, 36
 Src-kinase, 1021
 stable arrest, of T cells, 1103
 stable heterogeneity, of cell subtypes, 1776
 stalk cells, 1448
 stanniocalcin-1 (STC-1), 890
Staphylococcus aureus, 702
 Starling forces, 62
 Starling-Landis equation, 99–100
 stasis. *See* zone of stasis
 statins. *See also* endostatin; fluvostatin; pravastatin
 Akt signaling, 733
 Alzheimer disease, 1149
 cytoskeleton, 702
 heme oxygenase, 999
 mechanisms underlying pleiotropic effects, 1668–71
 nitric oxide, 991
 re-endothelization, 1671
 tissue factor expression, 934
 vascular smooth muscle cells, 554
 stealth technology, for drug delivery, 1735
 stellate cells, 1226, 1227
 stem cells, 145–7, 165, 858–9, 1615. *see also* hematopoietic stem cells; neural stem cell(s)
 stent(s), 552–3, 1699–1701
 stent thrombosis, 273
 steroid hormones, 1674–8
 steroid response elements (SREs), 1674
 stochastic differential equations (SDEs), 1781*f*, 1782
 stochastic models, 1752
 stomata, and plasmalemmal vesicles, 648
 stomatal diaphragms (SDs), and vascular permeability, 680, 681–2, 684–5
 stomatocytosis, 566
 ST1571, 1393
 storage, of von Willebrand factor, 916–17
Streptomyces turgidiscabies, 989
 stretch-induced injury, and barotrauma, 490–1, 492–3
 stroke. *See also* cardiovascular diseases
 activated protein C, 979
 aging, 1398*t*, 1400
 blood-brain barrier, 1130
 sickle cell disease, 1357
 thrombomodulin, 1603
 stroma, and tumor vasculature, 1457–61
 stromal derived factor (SDF)-1, 873
 structural mapping, 200*f*, 201
 subacute bacterial endocarditis, 439
 subarachnoid hemorrhage-induced cerebral vasospasm, 570
 subcellular localization, of forkhead proteins, 835–7
 subcutaneous fat layer, 1431
 subendocardium, in teleosts, 82
 substrate specificity, of protein tyrosine phosphatases, 766
 SU5416, 1476
 sulfasalazine, 1357
 sulfation, of HEV proteins, 1580
 sulfonylurea receptor (SUR), 1206
 superficial vascular plexus (SVP), 1431, 1433
 superior mesenteric artery (SMA), 1248
 superoxide dismutases (SODs), 378, 595*t*, 1545, 1546
 superoxide overproduction, and diabetes, 1370–1
 supra-physiologic levels, of antithrombin, 969
 surrogate markers, 1451
 SV40, and caveolae, 671
 swim bladder, 59
 Sydney Investigational Criteria, 1360
 symmetrical dimethylarginine (SDMA), 1281
 sympathetic nervous system, of giraffe, 104–105
 sympathetic-noradrenergic fibers, in brain, 1142
 syncope, and congestive heart failure, 95
 syndecan(s)
 cell adhesion and cytoskeleton, 400
 cell-cell and cell-ECM interactions, 398–9
 development, 397, 399
 expression of, 397
 heparan sulfate and glycanation, 955
 signal transduction, 397–8
 structure of, 396–7
 syndecan-4, 295, 399–400
 Syndrome X, 123, 126
 synthetic conduit vessels, 1714
 syphilis, 1360, 1361

- systematic transcript profiling, of genes in lung, 183–4
- systemic inflammatory response syndrome (SIRS)
- antithrombin, 967–8, 969, 970
 - burn injury, 1507
 - definition of, 1294–5
 - endothelial microparticles, 1632*t*
 - nuclear factor- κ B signaling, 786*t*
 - trauma, 1527
- systemic lupus erythematosus (SLE), 1379, 1411, 1414–15, 1416, 1630–1. *See also* lupus erythematosus
- systemic vasculitis, 438, 1631
- “systems biology” approach, 46
- tacrolimus (FK506), 793
- talin, 594*t*
- tamoxifen, 871, 1393, 1675
- target domain, and metaphor, 200–201
- targeted contrast agents, and magnetic resonance imaging, 1641–8
- targeted radioimmunotherapy, 891
- target genes, 830, 831*f*, 857
- targeting, of magnetic resonance imaging, 1646–7, 1648–51. *See also* site-specific delivery; vascular targeting
- Taxol, 703
- TBLASTN analysis, 114
- TBX5* (T-box transcription factor), 150
- T cell(s), 806, 1098–103, 1105. *See also* nuclear factor of activated T cells (NFAT) transcription factors
- T cell-attracting chemokine (TARC), 1438–9
- technology, and history of endothelial biomedicine, 14–16. *See also* nanotechnology
- telangiectases, and hereditary hemorrhagic telangiectasia, 1113–14, 1120
- teleosts, heart and endocardium of, 79–83. *See also* fish
- temperature. *See also* environment
- adaptation in shrew, 110–11
 - cold exposure at high altitude, 518
 - cutaneous breathing, 89
- tenascin-C (TN-C), 183–4, 191, 890
- tensegrity-based integration, of mechanics and chemistry, 1786–91
- tensegrity model, for vascular barrier regulation, 1017, 1018*f*, 1020, 1026
- terminal arterioles, 1256
- terminology, and rule-based system, 220–1
- testosterone, 176, 1518
- tetraspanins, 658
- thalassemia, 566
- thalidomide, 531, 1476
- thapsigargin, 552, 1163, 1165
- theory, development of model into, 218
- therapeutic angiogenesis, 1716
- Therapeutic Angiogenesis by Cell Transplantation (TACT), 1704
- therapeutic implications. *See also* diagnosis; diseases; drugs; infection; health and health care; inflammation; pharmacology; treatment; vascular targeting; *specific conditions*
- activated protein C, 979
- adipose tissue endothelium, 1268
- angiogenesis, 1452
- angiopoietins, 356–7
- antithrombin, 969–70
- β -catenin, 781
- blood endothelial cells, 1616–18
- brain ECs, 1147, 1149
- carbon monoxide, 999–1000
- caveolae, 672–4
- cigarette smoking, 1327–9
- cytoskeleton, 702–703
- endothelial microparticles, 1628–33
- E-selectin, 1078
- Ets factors, 816
- extracellular nucleosides and nucleotides, 391
- fibroblast growth factors, 298–9
- heme oxygenase, 999
- hemolytic uremic syndrome, 1341
- heparan sulfate, 956
- hepatic macrocirculation, 1245–6
- hepatocyte growth factor, 288–9
- hepatocytes and liver regeneration, 613–14
- high endothelial venule-like vessels, 1426–7
- high proliferative potential-endothelial colony forming cells, 1594–5
- hypoxia-inducible factor 1, 252–3
- ICAM-1, 1065–6
- Id proteins, 873–4
- integrin functions, 711
- Krüppel-like factor-2, 825
- leukocytes, 581–2
- luminal glycocalyx, 693
- lymphatic system, 1562–3
- nitrite and nitric oxide, 570, 991
- nuclear factor- κ B signaling, 792–3
- opioid receptors, 456–8
- platelets, 598
- podocytes, 624
- prostacyclin, 1009
- protein kinase C, 751
- protein tyrosine phosphatases, 768–9
- P-selectin, 1054
- reactive oxygen species, 380
- renal endothelium, 1275–6
- Rho GTP-binding proteins, 759–60
- sepsis, 1299
- sickle cell disease, 1357
- slit proteins, 365
- sphingolipids, 406
- thrombomodulin, 944
- thrombospondin, 330–2
- thrombotic thrombocytopenic purpura, 1341
- thyroid endothelium, 1392–4
- tissue factor pathway inhibitor, 927–8
- vascular guidance cues, 365
- vascular smooth muscle cells, 554
- VCAM-1, 1065–6
- Wnt signaling, 781
- thermodilution technique, and blood flow measurement, 1659–60
- thermogenesis, in shrew, 110–11
- thermoregulation, and skin, 1434–5
- thiazolidinediones (TZDs), 797, 799
- thiobarbituric acid reactive substances (TBARS), 421
- thioredoxin (TRX), 253, 378
- thiosulfate, 568
- thoracic duct, 63
- thorotrast, 1229
- 3-*O*-sulfates, 950
- thrombin. *See also* antithrombin
- Alzheimer disease, 1149
 - hemostasis, 910
 - lung microvascular ECs, 1165
 - neutralization, 963
 - permeability, 1020–1
 - prostacyclin production, 1007–1008
 - protein kinase C, 748
 - Weibel-Palade bodies, 660
- thromboangiitis obliterans, 1414
- thrombocytopenia, and filovirus infection, 1314
- thromboembolic disease, 979
- thrombolysis, 1328
- thrombomodulin (TM)
- acute respiratory distress syndrome, 1185
 - blood clotting, 939
 - circulating soluble markers, 1603
 - development, 942
 - diagnostics, 943
 - evolution, 941–2
 - fibrinolysis and complement activation, 939–40
 - genes and gene expression, 940–1, 943
 - hemostasis, 910, 911, 912*f*
 - inflammation, 939
 - protein C, 942–3, 973, 974
 - therapeutic implications, 943–4
- thrombophilia-associated pregnancy complications, 1483–5
- thrombosis. *See also* portal vein
- thrombosis; stent thrombosis;
 - thrombotic thrombocytopenia purpura; toxicity-mediated thrombosis; venous thrombosis
 - acute respiratory distress syndrome, 1184
 - apoptosis, 1091
 - atherosclerosis, 1215

- thrombosis (*Cont.*)
 heterogeneity in development, 977
 Krüppel-like factor-2, 823–4
 magnetic resonance imaging, 1644*t*,
 1649
 platelet microparticles, 591
 real-time imaging, 1656
 tissue factor pathway inhibitor, 927
 Virchow's triad, 910–11
- thrombospondins (TSPs)
 angiogenesis, 1449
 cloning and sequencing, 325*t*
 development, 326
 evolution, 325–6
 history of research, 324–5
 Id proteins, 873
 ligand-receptor interactions and
 signaling, 327–9
 phenotypes, 329–30
 platelet releasate, 593*t*
 therapeutic implications, 330–2
 transforming growth factor- β activation,
 307
- thrombospondin type 1 repeats (TSRs),
 325, 332
- thrombotic microangiopathy, 1337–41
- thrombotic regulation, and aging, 1398
- thrombotic thrombocytopenia purpura
 (TTP)
 antiendothelial cell antibodies, 1415
 apoptosis, 1092–3
 complement signaling, 438
 endothelial microparticles, 1629–30,
 1632*t*
 nitric oxide-dependent vascular
 homeostasis, 566
 platelet aggregation, 587
 thrombotic microangiopathy, 1337,
 1339–41
 von Willebrand factor, 917
- thromboxane, 564*t*, 1186, 1525
- thymosin β 4, 594*t*
- thyroid cancers, 331, 1391–2
- thyroid gland, 1386–94
- thyroiditis, 1390–1
- ticlopidine, 391, 1339
- Tie1 and Tie 2 signaling pathways
 development, 352–3
 discovery, 352
 downstream signaling, 354–5
 evolution, 352
 gene regulation, 353
 phosphorylation, 355
 protein tyrosine phosphatases,
 766–7
- time, and clock as metaphor, 206–207
- time scale, of human evolution, 130*t*
- Tinbergen, N., 122
- tip cells, 1448
- tissue cell-derived signals, and vascular
 development, 174–5
- tissue environment, in microvessel
 structure, 1717
- tissue factor (TF), 909–10, 911, 926–7,
 932–6, 1614*f*. *See also* tissue factor
 pathway inhibitor
- tissue factor pathway inhibitor (TFPI)
 acute respiratory distress syndrome,
 1185
 alternatively spliced form, 925
 definition, 922
 development, 923
 diagnostic and therapeutic implications,
 927–8
 disseminated intravascular coagulation,
 1333
 endothelial microparticles, 1626–7
 evolution, 922
 gene regulation, 923
 hemostasis, 910, 911, 912*f*
 lipid rafts, 925–6
 location and endothelial association,
 924–5
 luminal glycocalyx, 692
 protein structure and function, 923–4
 thrombosis and factor V Leiden, 927
 tissue factor activity, 926–7
- tissue inhibitors of metalloproteinase 2
 (TIMP)-2, 328, 902
- tissue-type plasminogen activator (t-PA),
 444, 1604–605, 1726
- titin, 594*t*
- TNF. *See* tumor necrosis factor
- TNF-receptor (TNFR1)-1, 1082–3, 1088
- TNFR1-associated DD (TRADD), 1082,
 1083
- TNP-70, 1476
- tobacco abuse, 132
- Toll-like receptors (TLRs), 410–12, 1098,
 1100, 1182, 1297
- topical opioids, 457–8
- toxicity-mediated thrombosis, 527, 529
- toxins and toxicology. *See also* exotoxins;
 snakes and snake toxins
 mechanisms of toxicity, 527–8
 model systems for study, 530
 nuclear factor- κ B blockade, 793
 pathological consequences, 529–30
 selected toxic agents, 530–1
 uremic, 1278
 vascular development, 531–2
 vasomotor control, 529
- trade-offs, in evolution, 123–4, 135
- trans*-acting factors, and forkhead
 signaling, 835, 836–7
- transactivation, of opioids, 455
- transcapillary fluid balance, 99–100
- transcellular metabolism, and eicosanoid
 synthesis, 1006
- transcellular transport, 634–5, 637–8
- transcriptional targeting, and gene transfer,
 1728–9, 1731
- transcription and transcriptional activity.
See also Ets factors; myocyte enhancer
 factor 2; post-transcriptional
 modification; Sox genes
 eicosanoids and cyclooxygenase-2,
 1008–1009
 forkhead signaling, 837–8
 GATA transcription factors, 806–10
 lung ischemia, 1209
 nuclear factor of activated T cells
 (NFAT), 828–33
 nuclear factor- κ B signaling, 788–9
 peroxisome proliferator-activated
 receptors, 802–803
 thrombomodulin, 943
 tissue factor expression, 932
 Vezf1, 855–9
- transcytosis, 680, 701, 1128
- transdifferentiation, and endothelial
 development, 147
- transduction. *See* mechanotransduction;
 transduction pathways
- transductional targeting, and gene transfer,
 1727–8
- transduction pathways, 1062–3, 1769–70
- transendothelial channels (TECs), and
 vascular permeability, 679–80, 681,
 683
- transendothelial electrical resistance
 (TEER), 1125, 1315–16, 1317
- transendothelial migration, and high
 endothelial venules, 1575–6
- transforming growth factor- β (TGF- β)
 activation, 304–308
 angiogenesis, 313–14
 atherosclerosis, 315–16
 dietary salt intake, 1287–8, 1289, 1290,
 1291
 endothelial-mesenchymal
 transdifferentiation during cardiac
 cushion development, 314–15
 hereditary hemorrhagic telangiectasia,
 1116, 1117–19
 human hereditary vascular disorders,
 316
 ligand traps, 308
 pericyte investment, 538
 signaling, 304, 305*t*, 308–313, 316
 vascular development, 311–13
- transfelin, 594*t*
- transfusion-related acute lung injury
 (TRALI), 1179, 1534*t*, 1536–7.
See also acute lung injury
- transfusion-related immunomodulation
 (TRIM), 1533, 1534*t*, 1535
- trans-Golgi network, and P-selectin,
 1051
- transient receptor potential (TRP)
 channels, 721, 722–5
- transketolase activity, and diabetes, 1373,
 1382

- transmigration. *See also* leukocyte
 transendothelial migration
 of endothelial microparticles, 1627–8
 of leukocytes, 579–80
 skin inflammation, 1434
- transmigratory cups, 701, 1576
- transmission electron microscopy (TEM),
 and vascular permeability, 680
- transparency, and agent-based models,
 1757
- transplantation. *See* bone marrow
 transplantation; organ
 transplantation; xenotransplantation
- Transplantation of Progenitor Cells and
 Regeneration Enhancement in Acute
 Myocardial Infarction
 (TOPCARE-AMI), 1702
- transport and transportation networks
 active and passive, 882
 blood vessel structure, 1712
 carrier-mediated, 1128, 1132
 D-glucose, 637
 junctional, 651–2
 mitochondrial electron chain, 1370–1
 receptor-mediated, 1132
 transcellular, 634–5, 637–8
 urban design as metaphor, 211–14
 vesicular, 649–51
- transplant-linked hemolytic uremic
 syndrome, 1337–8
- transport/metabolic barrier, of blood-brain
 barrier, 1128–9
- transrepression, and glucocorticoids,
 1676
- transthyetin, 595*t*
- transvascular exchange, and caveolae,
 670–2
- trauma, 1513, 1523–9. *See also* wound
 healing
- treatment. *See also* drugs; health and health
 care; pathology; pharmacology;
 therapeutic implications
 alteration of hemodynamic forces,
 1690–4
 drug targeting, 1734–42
 blood vessel building, 1712–20
 gene transfer and expression in vascular
 endothelium, 1725–31
 organic nitrates, 1682–7
 stent- and nonstent-based cell therapy,
 1698–1706
- TREEVIEW analysis, 117*f*
- Trematopus bernacchii*, 80*f*
- Trimeresurus* spp., 465
- tripeptides, 899, 902
- triphosphate diphosphohydrolase,
 389–90
- trophoblast, 136, 1074. *See also* placental
 trophoblast
- Trypanosoma cruzi*, 1533
- tuberculosis, 935*t*, 936
- Tubifex*, 37
- tubular structures, and MAPK cascade,
 741–2
- tubulin, 594*t*
- tumor(s). *See also* cancer
 agent-based model of angiogenesis,
 1793–7
 angiogenesis, 1451–2, 1461–3
 angiogenic switch, 898, 1451
 angiopoietins, 356
 aquaporin 1, 718
 blood-brain barrier, 1131
 blood vessels, 1457–67
 DNzyme inhibition of, 819–20
 Eph/ephrin system, 348
 E-selectin, 1077
 heparan sulfate, 956
 hepatic arterial flow, 1241
 hepatocyte growth factor, 288–9
 ICAM-1 and VCAM-1, 1065
 Id proteins, 868–70
 nanomedicine, 673
 neovascularization, 882
 nuclear factor- κ B signaling, 792
 opioid receptors, 458
 radiation, 1092
 splenic endothelium, 1260–1
 thrombospondins, 330–2
 tissue factor expression, 935
 transforming growth factor- β , 314
 vascular endothelial growth factor
 receptors, 272
 vascular targeting, 891
 Wnt signaling, 781
- tumor-angiogenesis factor (TAF), 1445,
 1793
- tumor-associated ECs, 898
- tumor necrosis factor (TNF), and cerebral
 malaria, 1304, 1305–306
- tumor necrosis factor (TNF)- α , 902, 968,
 1082–3, 1088–9
- tumor vascular endothelium, 882
- tumor vasculature, and drug targeting,
 1741
- tumstatin, 711
- TUNEL staining, 1085*t*
- tunicates, 71
- Turbellaria, 33
- turbulent flow, in cephalopods, 37
- turbulent shear stress (TSS), 236–7
- Turkey, and opioids, 451
- turn-motif site, and protein kinase C, 747
- turtles, and evolution of cardiovascular
 system, 43–4
- twin pregnancies, and preeclampsia, 137,
 139
- two-dimensional (2D) gel analysis,
 886–7
- two-event model, of transfusion-related
 acute lung injury, 1536–7
- “two stage” grafts, 1502, 1503
- type 2M vWD, 918
- tyrosine kinases, 379, 709, 1446–7.
See also protein-rich tyrosine kinase 2
- tyrosine phosphatases, 379. *See also* protein
 tyrosine phosphates
- tyrosine phosphorylation, 1019, 1023,
 1041
- Uganda, and Kaposi’s sarcoma, 1472
- UHF, and heparin-induced
 thrombocytopenia, 1346, 1348
- ulcerative colitis (UC), 1248, 1249, 1251,
 1252, 1421*t*
- Ulex europaeus* agglutinin-1 (UEA-1),
 1432
- ultrastructural characteristics, of splenic
 endothelium, 1258
- ultrastructural diversity, and
 morphological heterogeneity, 881–2
- ultrastructure, of high endothelial cells,
 1572
- umbilical cord, and endothelial progenitor
 cells, 1590–1
- Unc DCC signaling pathway, 363–4
- Unc5B* gene, 155
- uncoupler proteins (UCPs), 257
- uncoupling, and eNOS, 377
- undisturbed flow (UF), 235–6
- unfractionated heparin (UFH), 1344
- unimodal population, and cell fate
 dynamics, 1768
- Uniramia, 38
- universal grammar, of language, 203
- universality, principle of, 1751–2
- universities, and history of biomedicine, 6
- University of Oregon, 150
- upper arm occlusion, 1660
- urban design, as metaphor, 211–14
- urea, 1280
- uremia, 1278–83. *See also* hemolytic uremic
 syndrome (HUS)
- uremic toxins, 1278, 1280, 1281–2
- urethane, 1229
- Urochordata (tunicates), 40
- urokinase-type plasminogen activator
 (u-PA), 444, 807
- urticaria, 1437*t*
- U73122, 274
- uteroplacental blood flow, 135–9
- vagus nerve, 1144
- validation, of models, 1756–7, 1783
- vanilloid transient receptor potential,
 724
- Van Leeuwenhoek, Antoni, 8
- varanid lizards, 44
- variant Creutzfeldt-Jakob disease (vCJD),
 1534*t*
- varicella infections, and protein S, 986
- vascular adhesion protein (VAP)-1,
 1576

- vascular architecture
 of kidney, 1271–4
 of skin, 1431–2
 of tumors, 1458–61
- vascular bed-specific gene regulation, and
 Ets factors, 813–14
- vascular bubbles, and diving, 497–501
- vascular cell adhesion molecule-1
 (VCAM-1)
 atherosclerosis, 1217, 1219
 drug targeting, 1740–1
 E-selectin, 1078
 expression pattern, structure, and
 domains, 1059–60
 history of research, 1058–9
 leukocyte transendothelial migration,
 1031–2
 platelet-endothelial cell adhesion
 molecule-1, 1041
 regulation of, 1063–5
 as signal transducer, 1060–3
 skin, 1434
 as therapeutic target, 1065–6
- vascular development. *See also*
 development; vascular system;
 vasculogenesis
 cell differentiation in mammals, 161–5
 complementary approaches to study, 25
 Eph receptors and ephrin ligands, 345–6
 evolution and comparative biology, 50–7
 fibroblast growth factors, 295–6
 neuropilins, 339–40
 placental vasculature, 1488–96
 pulmonary endothelium, 181–92
 retina and hyaloid vasculature, 1154–8
 semaphorins, 340–1
 transforming growth factor- β , 306*t*,
 311–13
 vascular endothelial growth factor, 267
Xenopus, 142–5
 zebrafish, 150–7
- vascular disease, 540–1, 1676–8,
 1698–1706. *See also* cardiovascular
 disease; vasculitis
- vascular endothelial cadherin
 (VE-cadherin), 242–3, 768, 1019,
 1024, 1033, 1164
- vascular endothelial growth factor (VEGF).
See also vascular endothelial growth
 factor receptors; vascular permeability
 factor
 angiogenesis, 250–2
 apoptosis, 1089
 bronchopulmonary dysplasia, 192
 cardiac myocytes, 603
 developmental and pathological
 angiogenesis, 165
 diabetes, 1378–9
 EC proliferation and differentiation, 360
 endothelial development in *Xenopus*, 145
 gene expression, 266–8
 glomerular development, 622–4
 hepatic sinusoidal endothelial cells, 1227
 history of research, 266, 1445–6
 liver regeneration, 611, 612*t*, 614
 lung vascular homeostasis, 1195,
 1199–1200
 lymphatic system, 1559, 1562–3
 mutual signaling and development of
 pancreas and liver, 173, 174, 177–8
 neuropilins, 338–9
 pancreatic tumors and upregulation, 324
 phylogenetic analysis, 115–20
 renal injury, 1276
 retinal expression, 1156
 thrombospondins, 328, 332
 tissue factor expression, 932, 933
 transforming growth factor- β and
 synthesis, 314
 vascular targeting, 888
 vasculogenesis in zebrafish, 152, 153–4,
 156–7
- vascular endothelial growth factor-A
 (VEGF-A), and tumor blood vessels,
 1462, 1463–7
- vascular endothelial growth factor-like
 proteins (VEGF-like proteins), 463*t*,
 465
- vascular endothelial growth factor
 receptors (VEGFRs). *See also* vascular
 endothelial growth factor (VEGF)
 development, 269–70
 discovery, 268
 flow-mediated mechanotransduction,
 242–3
 gene expression, 269, 273–4
 lymphatic system, 1558–9
 physiology and pathology, 274
 placental vasculature development,
 1491–3
- vascular endothelial zinc finger 1 (Vezf1),
 855–9
- vascular endothelium, 55
- vascular growth phase, of tumor, 1797
- vascular guidance assays, 364–5
- vascular labeling, 202–203
- vascular lumen, and atherosclerosis, 1214
- vascular malformations, and tumor blood
 vessels, 1466–7
- vascular memory, and Weibel-Palade
 bodies, 661
- vascular mimicry, 1463*t*, 1467, 1489, 1490*f*
- vascular patterning, 311–12, 341, 360–5
- vascular perfusion, of gut, 1249
- vascular permeability. *See also*
 permeability; vascular permeability
 factor
 cytoskeleton, 700–702
 description, 679–80
 function of organelles, 684–5
 history of research, 680–1
 ion channels, 727
 luminal glycocalyx, 691–2
 molecular structure of organelles,
 683–4
 ontogenetic considerations, 681–2
 protein kinase C, 750–1
 protein tyrosine phosphatases, 767–8
 sphingolipids, 406
 ultrastructure of organelles, 682–3
- vascular permeability factor (VPF), 266,
 1462. *See also* vascular endothelial
 growth factor
- vascular reactivity measurements, 1659
- vascular remodeling. *See also* remodeling
 Akt signaling, 729–33
 heme oxygenase and carbon monoxide,
 998
 Notch genes, 370, 371
 space travel, 522–5
 vascular smooth muscle cells, 549
- vascular repair, and cell therapy, 1698–9
- vascular smooth muscle cells (VSMCs)
 atherosclerosis, 1215
 development, 546–7
 diagnostics, 554–5
 history of research, 545–6
 pathology, 550–4
 physiology, 547–50
 shear stress, 233
 therapeutic implications, 554
 transforming growth factor- β , 312–13,
 315–16
 vasodilation, 1659
- vascular system, 6*f*, 337–8, 361–4.
See also circulatory system; vascular
 development; vascular cell adhesion
 molecule-1; vascular development;
 vascular disease; vascular endothelial
 growth factor; vascular endothelial
 growth factor receptors; vascular
 endothelial zinc finger 1; vascular
 patterning; vascular permeability;
 vascular remodeling; vascular smooth
 muscle cells; vascular targeting;
 vascular tone
- vascular targeting
 drug delivery, 673–4, 887–91, 1734–42
 phage displays, 900, 901–904
 thyroid endothelium, 1392–3
 tumor blood vessels, 1467
- vascular tone, 407, 726–7, 1121
- vascular wall, and vascular smooth muscle
 cells, 549
- vascular zip codes, 175, 879, 901
- vasculature. *See* microvasculature; vascular
 architecture
- vasculitis, 1405, 1632*t*. *See also* small-vessel
 vasculitis; systemic vasculitis
- vasculogenesis. *See also* vascular
 development
 β -catenin, 780
 definition, 1444–5, 1446*t*

- endothelial cell differentiation in mammals, 162
- evolution of vascular development, 53–4
- fate mapping, 167
- fibroblast growth factors, 296
- placental, 1488–9
- pulmonary vascular development, 184–5, 188–90
- Rho GTP-binding proteins, 757–8
- skin, 1435
- study of development and, 25
- transforming growth factor- β , 311–12
- vascular smooth muscle cells, 547
- vasculoprotectiveness, of thrombomodulin, 943
- vasculosyncytial membranes, 1491
- vasoactive drug delivery, 1662–3
- vasoactive intestinal peptide (VIP), 1142
- vasoconstriction and vasoconstrictors, 1194, 1195, 1434, 1435, 1516
- vasodilation and vasodilators
- bronchial vasculature, 1173
- endothelium-dependent versus endothelium-independent, 1659
- erectile dysfunction, 1401
- local heating of skin, 1664
- nitric oxide, 562–3
- organic nitrates, 1683
- skin and thermoregulation, 1434–5
- trauma-hemorrhage, 1515–16
- vasomotor control, 529, 997–8
- vasomotor regulation, and fibroblast growth factors, 296–7
- vasomotor tone, 1173, 1398–9, 1656, 1670
- vasoreactivity, and Krüppel-like factor-2, 824
- vasoregulation, 1250–1, 1321–3, 1355–6
- VCAM-1. *See* vascular cell adhesion molecule-1
- VE-cadherin. *See* vascular endothelial cadherin
- vector systems, for gene transfer, 1725–6
- vegetation patterns, computer models of, 215, 217–19
- VEGF. *See* vascular endothelial growth factor
- veil cells, 1432
- veins. *See also* blood vessels; jugular vein; posterior cardinal veins; posterior intersomitic veins; venous circuits; vessel wall
- pulmonary vasculature, 181, 1161–3
- thyroid gland, 1388
- venous drainage from brain, 1140
- venogenesis, 1245, 1719
- veno-occlusive disease, 1246
- venous circuits, 155, 360
- venous drainage, from brain, 1140
- venous plethysmography, 1659
- venous thrombosis, 965, 985–6, 1345
- venous tree, and composition of endothelial cells, 257–60
- ventilator-induced lung injury (VILI), 489–91, 492*t*, 1179
- ventral blood island (VBI), 143
- venules, and normal microvasculature, 1458
- Venus statuettes, from Paleolithic, 131
- versican, 1572
- vertebral arteries, 1140
- vertebrates, and evolution of cardiovascular system, 40–5. *See* mammals
- very-low-density lipoproteins (VLDLs), and adipose tissue blood flow, 1266
- Vesalius, Andreas, 7, 230, 1240*t*
- vesicular transport, and electron microscopy, 649–51
- vesiculation, and endothelial microparticles, 1621
- vesiculo-vacuolar organelles (VVOs)
- caveolae, 672
- electron microscopy, 645
- normal microvasculature, 1458
- sphingolipids, 405
- tumor blood vessels, 1460, 1463–4
- vascular permeability, 683, 685
- vessel cooption, 1445
- vessel-derived endothelial cells, 1593–4
- vessel wall. *See also* blood vessels
- AGE and structural integrity of, 420–1
- cell seeding, 1699–1701
- Eph/ephrin system, 349
- Kawasaki disease, 1405–406
- Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group (VA-HIT), 800
- Viagra, 457
- videomicroscopy, and T cells, 1103
- vimentin, and cytoskeleton, 698, 699, 700, 701
- vinculin, 594*t*
- Vipera lebetina obtusa*, 466
- Viper ammodytes ammodytes*, 465
- Viperidae, 461–2
- viral hemorrhagic fever (VHF), 1311–17
- Virchow, Rudolph, 9, 231, 1171, 1255
- Virchow's triad, 910–11, 913
- “virtual organism,” and agent-based modeling, 1756
- virtual patient simulation, 1801, 1802*t*, 1803–805
- virus(es). *See also* adenoviruses; cytomegalovirus; filoviruses; Hanta virus; herpesvirus; infection; lentiviruses; retroviruses; RNA viruses
- blood transfusions, 1533
- Eph/ephrin system and Nipah, 349
- gene transfer, 1726–31
- metaphor, 202
- oncogenes in spleen, 1261
- pulmonary hypertension, 1196
- visual metaphor, 206–209
- vitamin C, and endothelial dysfunction from smoking, 1328
- vitamin D binding protein, 593*t*
- vitamin E, and endothelial dysfunction from smoking, 1328
- vitamin K-dependent protein S, 594*t*
- vitronectin, 975
- voltage-gated calcium channels, and lung ischemia, 1207
- volume-sensitive anion channels (VRAC), 726
- von Hippel-Lindau tumor suppressor protein (VHL), 248, 267
- von Willebrand disease (vWD), 915
- von Willebrand factor (vWF)
- adhesion, 918–19
- cell culture, 15
- circulating soluble markers, 1602–603
- definition of, 915
- endothelial microparticles, 1628, 1629–30
- evolution of hagfish, 72
- gene encoding of human, 915–16
- hemodilutions, 1525
- history of research, 915
- hemostasis, 911
- pericytes, 539
- platelets, 593*t*
- protein, 916
- regulation, 917
- storage and secretion, 916–17
- structure and function, 917–18
- transcriptional targeting, 1729
- Weibel-Palade bodies, 657, 659*f*
- Voronoi diagram, 183
- V-PYRRO/NO, 1232
- Waardenburg-Shah syndrome, 861
- wall tension, and vascular smooth muscle cells, 549
- warfarin-induced skin necrosis, 909, 911, 912, 977
- WASP family verprolin-homologous protein (WAVE), 756
- water, and composition of blood, 259. *See also* drinking water; seawater
- weather, comparison of endothelial biology to, 215, 216–17
- Wegener granulomatosis (WG), 1412–13, 1437*t*
- Weibel-Palade bodies
- alpha-granules, 658
- cargo loading, 658–9
- contents, 657–8, 659*f*
- discovery of, 657
- electron microscopy, 15, 646, 647
- exocytic machinery, 659–61
- gill vessels of fish, 60
- hagfish endothelium, 72
- P-selectin, 1051

- Weibel-Palade bodies (*Cont.*)
 pulmonary circulation, 1164
 vascular memory, 661
- West Nile Virus, 1533
- Wharton jelly, 1491
- What Makes Biology Unique* (Mayr), 122
- white dot syndrome. *See* heparin-induced thrombocytopenia
- whole body periodic acceleration, 1691, 1692–3
- Wilms tumors, 1230
- Wiscott-Aldrich syndrome protein (WASP), 756
- Wnt signaling pathway, and β -catenin, 773–4, 776–81
- World Health Organization, 1599, 1807
- wound healing. *See also* burn injury
 combat trauma, 1523
 hyperbaric oxygen therapy, 480–6
 older persons and impaired, 1397, 1398*t*, 1400–401
 opioid receptors, 457
 vascular endothelial growth factor receptors, 271
- Wuchereria bancrofti*, 1562
- xanthine dehydrogenase (XDH), 377
- xanthine oxidase (XO), 377, 1061, 1188
- Xase complex, 961, 962*f*
- xenobiotics, and selective vectorial transport, 638
- Xenopus laevis* (African clawed frog)
 β -catenin, 773
 lymphatic system, 1554, 1555
 as model for study of endothelial development, 142–8
 vascular development in embryo, 152, 153, 546
- xenotransplantation, 438
- XIIIa-positive dendrocytes, 1432
- Yanamamo (Venezuela), 132
- YC-1, 253
- Y-27632, 1543
- Zaire ebolavirus* (ZEBOV), 1311, 1312
- ZD6474, 1393
- zebrafish (*Danio rerio*)
 fate mapping, 167, 169, 170
Hex homologue *hHex*, 189
 lymphatic system, 1554–5
 neuropilins, 340
 phylogenetic analysis, 118–19
 protein C, 974
 semaphorins, 341
 thoracic duct, 63
 vascular development, 150–7, 340, 341
 vascular endothelial growth factor receptors, 269
 vascular smooth muscle cells, 546
- zidovudine, 1132
- zinc finger domain, 855, 857. *See also*
 vascular endothelial zinc finger 1
- zone of coagulation, 1506–507
- zone of hyperemia, 1507
- zone of stasis, 1507, 1508–509
- zonula occludens (ZO) family, 1019, 1127
- zyxin and zyxin-related protein (ZRP-1), 594*t*, 1117