

Index

- 1- α , 25-dihydroxy vitamin D3 547
- 5- α -reductase inhibitors 15
- AA, *see* arachidonic acid
- A β aggregation inhibitors 487
- A β plaque toxicity 481
- ABC transporters 624, 632
- absorption, distribution,
 - metabolism and excretion/
 - toxicity (ADME/Tox) 16–17, 33, 387–388, 453
- abxicimab 106
- ACE, *see* angiotensin-converting enzyme
- ACE-inhibitors 231
- acetazolamide 76–79, 86–87, 90
- acetylcholine 15, 420, 429–430, 432–433, 438, 475–478, 568, 581
- acetylcholine esterase inhibitors 15
- acetylcholinesterase (AChE) 32, 360, 388, 420, 428, 439, 476, 487
 - inhibitors 360, 428, 440, 488
- 2-acetylphenothiazine (ML171) 267–268
- AChE, *see* acetylcholinesterase
- AChE, *see* acetylcholinesterase
- acid α -glucosidase 640, 642
- acquired immunodeficiency syndrome 2
- actinic keratosis 539
- Activase® 107, 111
- activated protein C (APC) 185
- activity, 7-ethoxycoumarin hydroxylase 551
- acute lymphoblastic leukemia 172, 178, 642
- acute lymphoblastic leukemia (ALL) 172, 178, 642
- acute myeloid leukemia 7, 9, 24, 643
- acute myocardial infarction (AMI) 99, 101–102, 111, 113, 577
- acute promyelocytic leukemia (APML) 9, 622
- acyl-coenzyme A (CoA) 354, 388
- AD, *see* Alzheimer's disease
- ADA-SCID 11
- ADCs, *see* antibody–drug conjugates
- adeno-associated virus 52
- adenosine 11, 105, 568, 581, 638
- adenosine deaminase (ADA) deficiency 638
- adenosine deaminase deficiency 11
- ADI, *see* L-arginine deiminase
- ADI-PEG20 319
- ADME/Tox, *see* absorption, distribution, metabolism and excretion/ toxicity
- Adnectins 185
- Ado-trastuzumab emtansine 176
- ADP-ribosyltransferase 34
- advanced glycation end products 254
- advanced glycosylation end product-specific receptor (AGER/RAGE) 254
- AEDs, *see* antiepileptic drugs
- AEI, *see* allelic expression imbalance
- Affibodies 185, 189–190

- affinity chromatography 55–56, 61, 221, 602
- Aflatoxin B1 552
- agalsidase α 639
- agalsidase β 9, 171, 178, 639
- AGER/RAGE, *see* advanced glycosylation end product-specific receptor
- albinterferon α -2b 172, 180
- Alcalase 231–232
- Alcanivorax borkumensis* 548
- alcoholism 402
- aldehyde oxidase 34, 270, 506
- aldehyde oxidase (AOX) 34, 270, 506
- inhibitor binding 517
- nitro-reduction 525
- substrate binding 516–517
- alfimeprase 123
- alirocumab 20
- alkaline phosphatase (ALP) 640
- ALL, *see* acute lymphoblastic leukemia
- all-trans retinoic acid (ATRA) 599, 623
- allelic expression imbalance (AEI) 403
- alopecia 2
- ALP, *see* alkaline phosphatase
- alteplase 107, 111–112, 114–116
- altered biosynthesis 727
- altered glycan theory 688
- altitude sickness 75
- Alzheimer's amyloid β -protein precursor inhibitor (APPI) 192
- Alzheimer's disease 19, 31, 397, 408, 427, 473–474, 476, 478, 480, 482, 484, 486, 488, 490, 492, 494–496, 498, 679
- Alzheimer's disease (AD) 19, 31, 397, 408, 427, 473–474, 476, 478, 480, 482, 484, 486, 488, 490, 492, 494–496, 498, 679
- Alzheimer's disease, treatment 427, 479, 486, 496
- amediplase 116
- AMI, *see* acute myocardial infarction
- amino acid depletion therapies 313–314
- amino acid deprivation 312–338, 340–341
- amitriptyline 541, 544, 553
- amoxicillin 727
- AmpliChip cytochrome P450 genotyping test 33
- AMPs, *see* antimicrobial peptides
- α -amylase 655
- amyloid β ($A\beta$) peptides 420, 480
- amyloid β precursor protein (APP) 480
- amyloidogenic cascade 489
- anakinra 292
- analgesics 33, 85, 237, 240
- anaplastic lymphoma kinase 24
- anastrozole 539, 541
- androgen receptor (AR) 599
- androgens 539, 541
- angina 2, 28, 261
- angiogenesis 13, 229, 234–235, 237, 251, 550, 579, 586–587, 620, 693, 707
- angiotensin-converting enzyme (ACE) 358
- angiotensin II 258, 568, 579–582, 585
- anistreplase 107, 113
- anthracyclines 624
- anti-apoptotic proteins 600
- anti-GPCR antibodies 183–184
- anti-hypertensive drugs 230
- anti-malarial drugs 521
- anti-tuberculosis drugs 538, 557
- anti-tumor drugs 521, 523, 597, 600

- anti-tumor therapies 701
- anti-viral drugs 521
- antibodies 15, 31, 46, 55, 57, 59, 87–88, 103–104, 171, 173, 175–177, 183–185, 187–188, 292, 597, 607, 631, 642, 658, 661, 696
 - bispecific 88, 177
- antibody-dependent cellular cytotoxicity 177
- antibody-dependent cellular phagocytosis 177
- antibody fragments 46, 56–57
- antibody–drug conjugates (ADCs) 176
- anticalin 185, 187–188
- Anticalins 185, 187
- antiepileptic drugs (AEDs) 78, 81, 83
- antifungal agents 538
- antifungals 85
- antigen presentation 688, 702
- antimetabolites 624
- antimicrobial peptides (AMPs) 206, 213, 226, 232–233, 235, 237, 691–692, 696
- antioxidant response elements (ARE) 292
- antioxidants 249, 274–276, 278–279, 281, 289–290, 294, 489, 491–492
 - endogenous 249, 274–276, 290
 - enzymatic 249, 274–276, 294
 - exogenous 274, 289
 - non-enzymatic 274–276
 - polyphenolic compounds 274, 491
 - vitamins 274, 289–290
- antioxidin-RL peptide 289
- antiparasitic therapy 701
- α 2-antiplasmin 100
- antiplatelet drugs 105–106, 585
- antipsychotic agents 507
- antisense oligonucleotides 605
- antithrombin III (AT) 105
- AOX, *see* aldehyde oxidase
- AOX genes 508, 510–511, 524
- AOX isoenzymes 506–509
 - gene organization 509, 511
 - phylogenetic tree 509
 - phylogeny 509
- AP2238 445–446
- APC, *see* activated protein C
- APML, *see* acute promyelocytic leukemia
- apocynin 268
- apoptosis 12–13, 47, 85, 229–230, 238, 250–251, 266, 274, 279–280, 330, 575, 598–599, 603, 620, 626, 648, 650, 688
- apoptosis induction 229
- APP, *see* amyloid β precursor protein
- APPI, *see* Alzheimer's amyloid β -protein precursor inhibitor
- AR, *see* androgen receptor
- arachidonic acid (AA) 249, 270, 273, 568–569
- ARE, *see* antioxidant response elements
- argatroban 104
- ArgI, *see* Arginase I
- arginase (rhARGI) 313–314, 316, 323–324, 339–340
 - Co-rhArgI-PEG 326
 - rhArgI-PEG 340
- Arginase I (ArgI) 323–324
 - catalytic mechanism 322
 - structure 326–327
 - therapeutic use 325
- arginine 42, 44, 172, 178, 182, 185, 267, 312–319, 323, 339–340, 643
- arginine deprivation 340, 643

- argininosuccinate lyase (ASL) 316
- argininosuccinate synthase (ASS) 316
- aromatase 539
- arsenic trioxide 606, 623
- Artemisia annua* 724, 728
- artemisinin 559, 724, 727–730, 738
- arterial hemodynamics 248
- arterial inflammation 272
- arthritis 2, 8, 12, 15, 85–86, 173–174, 187–188, 289, 537, 703
- ascorbic acid 276, 279, 290
- Asfotase alfa 640
- ASL, *see* argininosuccinate lyase
- ASNase-I 330
- ASNase-II 330–332
- asparaginase 178, 313–314, 329, 642–643, 647, 654–655
- asparaginase (ASNase) 313–314, 329
- asparaginyln endopeptidase 701
- aspartic proteases 211–212
- Aspergillus niger* 399
- aspirin 77, 80, 86, 100, 102, 105–106, 116, 583–585
- ASS, *see* argininosuccinate synthase
- ASS234 443
- astemizole 543
- AT, *see* antithrombin III
- atezolizumab 4
- atherogenesis 271, 568, 571–572, 581, 587
- atherosclerosis 140, 248–249, 258, 263, 267, 270–271, 283, 289, 570, 573, 583–584
- atherothrombosis 140, 253–254, 570, 572, 583
- ATM–CHK2 signaling pathways 625
- atorvastatin 716–717
- ATR–CHK1 signaling pathways 625
- ATRA, *see* all-trans retinoic acid
- autoimmune diseases 78, 179, 193
- avanafil 293
- avermectins 731
- Avimers 185, 190
- 7-azaindole structure molecule, *see* GSK2795039
- AZT 280
- B-cell activation 704
- B-cell receptor 702–703
- BACE-1 inhibitors 482, 484, 494
 - LY 2811376 484
 - LY 2886721 484
- Bacillus amyloliquefaciens* 53, 132
- Bacillus brevis* 58
- Bacillus megaterium* 536, 651
- bacterial cell wall 48
- bacterial CYP enzymes 536, 538, 543, 550
- bacteriocins 227, 691
- bacteriophage P22 651
- bafibrinase 132
- barbiturates 78, 80
- BBB, *see* blood–brain barrier
- BchE, *see* butyrylcholinesterase
- BCR–ABL protein 608
- benazepril 230
- benign prostatic hyperplasia 2, 15
- Benzonase 51–52, 54
- 2-(2-hydroxy-3-methoxyphenyl) benzothiazole (BMBT) 388
- 4-benzoyl-N-butyl-1,8-naphthalimide (MPN) 389
- betaine-homocysteine methyltransferase (BHMT) 334
- bevacizumab 171
- BHMT, *see* betaine-homocysteine methyltransferase

- bioactive peptides 206–218, 220, 222, 224, 226–240, 289
 - characterization methods 221
 - cytomodulatory agents 237
 - enzymatic synthesis 217
 - mechanism 211
 - food-based 289
 - immunomodulatory agents 235
 - ligation strategies 216
 - nanoformulations 225, 239
 - pharmaceutical application 227, 229, 231, 233, 235, 237, 239
 - purification 214, 217–218, 240
 - solid-phase peptide synthesis 209
 - synthesis 206–218, 220, 222, 224, 226, 228, 230, 232, 234, 236–238, 240
- biodegradability 647, 653, 656
- biofilm 226, 228, 232
- biogenic amines 398, 408–409
- biopharmaceutical manufacturing 42, 44, 49, 57, 62
- biopharmaceuticals 3, 14, 19, 41–44, 46, 48–54, 56, 58–64
- biosimilars 14, 24
- biosynthesis 89, 714–715, 720–725, 727–738
- bivalirudin 104
- BK channels 578
- blastomas 618
- blood coagulation 100, 104, 570, 587
- blood pressure 140, 230–232, 248, 258, 281, 551, 556, 578–579, 581–582
- blood–brain barrier (BBB) 32, 419, 449, 625, 692, 705
- BMBT, *see* 2-(2-hydroxy-3-methoxyphenyl)benzothiazole
- BNPP, *see* bis(4-nitrophenyl)phosphate
- bradykinin 192, 568, 573, 581
- BRD4, *see* bromodomain-containing protein 4
- BRD4-selective degrader 609
- breast cancer 24, 171, 173, 176, 230, 320, 548, 625, 628, 658
- breast cancer stem cells 628
- breast tumors 600
- brentuximab vedotin 176
- bromodomain-containing protein 4 (BRD4) 600
- Bruton's tyrosine kinase (BTK) 602
- BTK, *see* Bruton's tyrosine kinase
- BuChE, *see* butyrylcholinesterase
- budesonide 7–8
- burosumab 7
- buspirone 543
- butyrylcholinesterase (BchE) 360, 388, 420, 429, 476
- butyrylcholinesterase (BuChE) 360, 388, 420, 429, 476
 - inhibitors 360
- C-reactive protein (CRP) 287, 359, 388
- C-type lectin receptors 704
- CAD, *see* coronary artery disease
- CADD, *see* computer-aided drug discovery
- CAIs, *see* carbonic anhydrase inhibitors
- camphor 549
- camptothecin 389, 624, 660
- cancer 2, 4–7, 13, 15, 17, 19, 24–25, 28, 30, 85–88, 171, 176, 228–230, 237–238, 288, 311–314, 316–318, 320, 322–324, 326, 328–332,

- 334–336, 338–341, 355–356, 419, 520–521, 523, 538, 586–587, 610–611, 618–632, 642–643, 650, 652, 655–656, 658, 660–661, 695, 703, 706–708
- immunotherapy 88, 623
- cancer stem cells 229, 619, 622–623, 627–630
- cancer therapy 28, 87, 229, 312–313, 330, 334, 356, 661
- canertinib 606
- capillary electrophoresis (CE) 221
- capsular polysaccharides 50, 52, 54
- CAR, *see* chimeric antigen receptor
- CAR-T cells 632
- carbamazepine 83–84, 551, 556
- carboligase 719
- carbonate dehydratases 73
- carbonic anhydrase inhibitors (CAIs) 74, 76–78, 80, 82, 84, 86, 88, 90
- carbonic anhydrases (CAs)
- catalytic mechanism 86
 - inhibitors
 - antitumor agents 86
 - mitochondrial isoforms 75
- carboplatin 88, 540–541
- carboxylesterases (CES) 349, 351–354, 356, 363, 366–367, 369, 371, 373, 376, 380, 382, 385–386, 388
- carboxypeptidase A 46, 55
- carboxypeptidase B 46, 55–56, 212
- carcinomas 171, 177, 316, 324, 523, 617
- cardiovascular disease (CVD)
- 102–103, 141, 247–248, 250–254, 256, 258, 260, 262, 264, 266, 268–270, 272, 274, 276, 278, 280–282, 284, 286, 288, 290, 292, 294
 - experimental therapeutics 250, 281
- cardiovascular diseases 2, 104, 107–108, 206, 253, 568, 571–573, 575, 577, 579, 581, 583, 585–586
- cardiovascular homeostasis 568, 570, 572, 574, 576, 578, 580, 582, 584, 586, 588
- cardiovascular therapeutics 173, 184
- β -carotene 290, 732
- CAs, *see* carbonic anhydrases
- CAS, *see* cationic active site
- cascades 255, 482–483, 489, 492, 713, 718–719, 738
- casein kinase 1 α 602
- caspase 3 85, 648
- caspases 230, 648
- catalase 280
- catalytic mechanism 74
- cathelicidin 232–233
- cathepsin B 34
- cationic active site (CAS) 430
- catumaxomab 171, 177
- CD4+T cells 700
- CD44 receptor 707
- CD47 peptides 661
- CE, *see* capillary electrophoresis
- celecoxib 84–86, 90
- cell apoptosis 13, 230, 238, 250, 279–280
- cell cycle 225, 274, 316, 330, 618, 626
- cell cycle control factors 626
- cell disruption 45, 48
- cell lysis 44, 48, 58, 61
- cell-penetrating peptides (CPP) 238
- CellPrime® rLysozyme 49
- cellular IAP1 (cIAP1) 599

- cellular retinoic acid binding protein-II 599
- cellulase 62
- cembranoid β -cembrenediol 545, 554
- central nervous system (CNS) 31, 77, 90, 420, 429, 521, 675
- cerebral infarction 252, 572
- cerebral stroke 268
- CES, *see* carboxylesterases
- CES1, *see* human carboxylesterase 1
- CES2, *see* human carboxylesterase 2
- cetuximab 176
- Chagas disease 538
- checkpoint inhibitors 5, 619, 623, 631–632
- checkpoints 88, 630
- chemokine receptor (CCRs/CXCR) inhibitors 292
- chemotaxis 270, 572
- chemotherapy 228, 319–320, 384, 541, 625, 631–632, 643, 653, 660
- chimeric antigen receptor (CAR) 5
- chimeric fusion genes 620–621
- chitinases 45, 48
- chitosan 646, 653–654
- chlorzoxazone 544, 553
- cholinergic neurons 428, 432, 434
- cholinergic pathways 428, 433
- cholinesterase activity 445, 478, 489
- cholinesterase inhibitor 31, 384, 474–477, 479, 482–484, 487, 489, 497
- cholinesterases 386, 420, 428–429, 431, 450
 - isoforms 428
- chromene analogues 487
- chromosomal translocation 619–621
- chronic obstructive pulmonary disease (COPD) 253
- chronic pancreatitis 177, 640
- chymosin 62
- cIAP1, *see* cellular IAP1
- CLEA, *see* cross-linked enzymatic aggregates
- clioquinol 495–496
- clopidogrel 106, 350, 356, 358, 368–369, 379
- clorgyline 414–415, 417
- CLUSTAL omega algorithm 509
- CNS, *see* central nervous system
- CoA, *see* acyl-Coenzyme A
- coagulation 100–101, 104, 140, 174–175, 184, 237, 331, 570, 587
- coagulation factors 100, 174–175
- coevolutionary analysis 168
- collagenase 177, 212, 644
- combinatorial 34, 170, 189, 676, 678, 683, 713–714, 729, 731–732
- combinatorial approach 170
- combinatorial biosynthesis 729, 731–732
- competitive inhibition 412, 517, 526
- complex syntheses 714–738
- computational designing 167, 170
 - de novo 167
 - rational 167–168
 - structure-based 169
- computational techniques
 - inverse docking 681
 - molecular docking 681, 683
- computer-aided drug discovery (CADD) 675
- congenital sucrase-isomaltase deficiency (CSID) 639
- conversions, single-step 714–715, 717

- COPD, *see* chronic obstructive pulmonary disease
 coronary artery disease (CAD) 272, 286–287, 572–573
 corticosterone 537, 540
 cortisol 548
 cortisone 536
 coumarin 103, 411, 445–449
 coumarin conjugates 447–448
 coumarin derivatives 103, 445
 coumarin-tacrine hybrid 446
 coumarines 491
 coumarin–piperazine hybrid 446
 COX-2, *see* cyclooxygenase-2
 COX inhibition 583
 COX1, *see* cyclooxygenase 1
 CP-31398 626
 CPT-11, *see* irinotecan
 CRBN-recruiting degraders 608
 CRISPR 605, 649
 CRISPR-CAS 605
 crizotinib 603
 CRL1 β -TRCP 601
 CRL2VHL 601, 610–611
 CRL4CRBN 602, 606, 610–611
 CRLs, *see* Cullin RING E3 ubiquitin ligases
 Crohn's disease 11–12, 174
 cross-linked enzymatic aggregates (CLEA) 645
 CRP, *see* C-reactive protein
 cryptolepine 523
 CSID, *see* congenital sucrase-isomaltase deficiency
 Cullin RING E3 ubiquitin ligases (CRLs) 600
 curcumin 288, 491, 625
 curcuminoids 491
Curvularia lunata 558
 CVD, *see* cardiovascular disease
 cyclooxygenase (COX) pathway 568–569
 cyclooxygenase 1 (COX1) 105
 cyclooxygenase inhibitors 583
 cyclosporine 78, 80, 541
 cyclotides 190–191
 cyclooxygenase-2 (COX-2) 85
 CYP, *see* cytochrome P450
 CYP enzymes 34, 534–539, 542–543, 549–553, 555, 557–560, 568, 587
 immobilized 558, 560
 CYP epoxigenase 568, 574–575, 578
 CYP fusion enzyme 550
 CYP ω -hydroxylases 569
 CYP pathways 568
 CYP1A 550, 556
 CYP1A1 544, 553
 CYP1A2 33, 477, 544, 553
 CYP1A9 551
 CYP1B1 540, 544, 553
 CYP2B 550, 552
 CYP2B35 552
 CYP2C 550, 556, 570, 573, 575, 577, 587
 CYP2C19 33–34, 82, 543, 553
 CYP2C8 570, 575, 577, 580
 CYP2C9 33, 82, 85–86, 88, 544, 553, 570, 575, 577, 580
 CYP2D6 33–34, 85, 544, 553
 CYP2E1 537
 CYP2J2 570, 574–575, 577–578, 580
 CYP3A4 556
 CYP3A4/5 541
 CYP3A5 33
 CYP4A11 551, 579, 582
 CYP4F2 579, 582
 CYP5A1 569–572, 587
 CYP8A1 569–572, 587
 CYP19 539, 541
 CYP51 538
 CYP71D445 539

- CYP86 539
- CYP101A1 549
- CYP102A 537
- CYP102A1 536
- CYP105 546
- CYP105 family 546
- CYP105A1 538, 540, 547
- CYP105A3 546
- CYP106A1 537
- CYP106A2 547
- CYP153 538, 540
- CYP153A 548–549
- CYP726A27 539
- CYP947 539
- CYPBM3 536–537, 540, 543–546, 549, 554
- CYPcam 549
- cystatin 229, 287
- cysteine protease 57, 124–125, 701
- cysteine proteases 124, 211–212
- cystic fibrosis 7, 29, 51, 172, 177–178, 253, 640, 644
- cytochrome b-245 light chain (p22phox, CYBA) 256
- cytochrome C 648
- cytochrome CYP2C9 88
- cytochrome P-450
 - mono-oxygenases 521
- cytochrome P450 (CYP) 33–34, 534, 536, 538, 540, 542, 544, 546, 548, 550, 552, 554, 556, 558, 560, 567, 569, 643, 651
 - polymorphisms 33–34
- cytochrome P450 (CYP) family 533
- cytochrome P450 enzymes 534, 536, 538, 540, 542, 544, 546, 548, 550, 552, 554, 556, 558, 560
 - activity 534, 542, 544–545, 550–556, 560
 - engineering 534–535, 546–547, 551–553, 555, 560
 - limitations 534–535, 557
 - substrate diversity 541
- cytokines 88, 172, 175, 179–181, 235, 253, 291, 572, 624, 629, 702
 - recombinant 179, 181
 - therapeutic 88, 172, 179–181
- cytomegalovirus (CMV) infection 8
 - terminase 8
- D-amino acid oxidase (DAAO) 399
- D-Amphetamine 414
- D-luciferin methyl ester (DME) 356, 372, 389
- DAA, *see* D-amino acid oxidase
- dabigatran etexilate 104
- daltroban 584
- DAPase 46, 55
- DARPinS 185, 188–189
- dasatinib 608
- data mining 411
- DC-SIGN receptor 704
- DE, *see* directed evolution
- defense regulator peptides (IDRs) 693
- dehydroepiandrosterone (DHEA) 538, 540
- delta plasmin 121–122
- deltamethrin (DMT) 358, 379, 381, 389
- dendritic cell 702, 704
- 2-deoxy-ribose-5-phosphate
 - aldolase (DERA) 716
- 11-deoxycorticosterone (DOC) 537, 540, 548
- deoxycorticosterone acetate (DOCA) 582
- 11-deoxycortisol 537, 540, 547–548, 555
- deprenyl (selegiline) 402–403, 414–417

- DERA, *see* 2-deoxy-ribose-5-phosphate aldolase
- derivative chromosomes 620
- desmoteplase 107, 113, 116–118
- DHEA, *see* dehydroepiandrosterone
- diabetes mellitus type 2 15, 248, 253, 272
- diabetes type 1 89
- diabetes type 2 2, 19
- diabetic cardiomyopathy 253, 271
- diabetic foot ulcers 234
- diabetic nephropathy 15
- diabetic neuropathy 252
- Dicer 626
- diclofenac 280, 368–369, 544, 553
- diffuse large B-cell lymphoma 5
- 3,5-dimethyl-8-methoxycarbonyl-BODIPY (DMCB) 389
- dipeptidyl-aminopeptidase I 55
- dipeptidyl peptidase 4 inhibitors 15
- dipeptidyl peptidase-IV 238
- directed evolution 30, 161–163, 167, 170, 542, 548, 550, 558, 643
- directed evolution (DE) 30, 161–163, 167, 170, 542, 548, 550, 558, 643
- Discovery Studio software 680–681
- DMCB, *see* 3,5-dimethyl-8-methoxycarbonyl-BODIPY
- DME, *see* D-luciferin methyl ester
- DMT, *see* deltamethrin
- DNA 2, 15, 33, 45, 50–53, 56, 58, 79, 85, 109, 141, 160, 164, 166, 178, 189–190, 230, 240, 250–252, 257, 275, 279, 282, 324, 333–334, 437, 486, 543, 550, 556, 620, 624–626, 644, 646, 648–650, 729, 736
- mitochondrial 279
- DNA methylation 333–334
- DNA nanostructures 649
- DNA origami 649
- DNA repair capacity 624
- DNA shuffling 166, 543, 550, 556
- DNase 45, 51–52, 172, 178, 620, 644
- DNase I 51, 172, 178, 620
- DNDi, *see* Drugs for Neglected Diseases initiative
- DOC, *see* 11-deoxycorticosterone
- DOCA, *see* deoxycorticosterone acetate
- docetaxel 86, 540–541
- docking, molecular 453, 681–682
- donepezil 438–444, 447, 453, 455, 457, 463, 474, 476, 489
- donepezil derivatives 440
- donepezil-lazabemide 442
- donepezil-pyridil hybrid 444
- dopamine 84, 397, 407–408, 418, 420, 434–435, 437, 475, 485–486
- dopamine oxidation 437
- dopaminergic cells 409
- dopaminergic neurons 408
- dorzolamide 76, 79
- downstream processing 41–44, 46, 48–54, 56, 58, 60–64, 715, 718
- glycosylation 59–60
- inclusion bodies 42
- microbial cell-based 53
- doxorubicin 85, 87, 280, 325, 541, 625
- toxicity 87, 280, 325
- driver mutations 619
- drug delivery 224, 237, 240, 607, 638, 646
- drug design 34, 89, 398–399, 404, 417, 440, 451, 477, 482, 489, 497, 587, 674–676, 678, 680, 682–684

- computer-aided 34, 674–676, 678, 680, 682, 684
- ligand-based 34, 675, 678, 684
- structure-based 34, 404, 675, 680, 684
- drug-drug interactions 32, 76, 86
- drug metabolites 533–535, 537, 539–540, 552–553, 555, 557–558
- drug re-profiling 676
- drug-repurposing 676
- drug resistance 237, 541, 604, 624
- Drugs for Neglected Diseases initiative (DNDi) 29, 34
- dual BACE-1 and AChE inhibitors AP 2243 485
- coumestrol 485
- dual cholinesterase and MAO Inhibitors 488
- Dupuytren's contracture 177
- dutylase 115–116
- dynamic kinetic resolutions 718

- E3-ligase 606, 625
- E3-ligase modulators 606
- E3 ubiquitin ligases 598, 600, 610–611
- ebselen 252
- Ecballium elaterium* trypsin inhibitor (EETI-II) 191
- ECLT, *see* euglobulin clot lysis time
- ECM, *see* extracellular matrix
- eculizumab 175
- edaravone 252
- edema 75, 112
 - cerebral 75, 112
 - retinal 75
- EDHF, *see* endothelial-derived hyperpolarizing factor
- EETI-II, *see Ecballium elaterium* trypsin inhibitor

- EETs, *see* epoxyeicosatrienoic acids
- eGFP, *see* enhanced green fluorescent protein
- EGR1 transcription factor 628
- eicosanoid synthesis 568
- eicosanoids 569, 571, 583, 587
- EL35, *see* Polyoxyl 35 castor oil
- elastin-like polypeptides (ELP) 55
- ELP, *see* elastin-like polypeptides
- EMA, *see* European Medicines Agency
- embryonic stem cell genes 627
- Eminase® 113
- endo- β -*N*-acetylglucosaminidases 60
- endoglycosidases 60
- endopeptidases 48, 53
- endoplasmic reticulum (ER) 349, 389, 521, 582, 688
- endoproteases 55, 211
- endothelial adhesion molecules 258
- endothelial-derived hyperpolarizing factor (EDHF) 573
- endothelial nitric oxide synthase (eNOS) 273
- engineered proteins 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192
- enhanced green fluorescent protein (eGFP) 650
- enhanced permeation and retention effect (EPR) 656
- enkephalin 692, 698
- eNOS, *see* endothelial nitric oxide synthase
- ensaculin 445–446
- enzyme inhibitors 1, 11, 13–15, 31, 34, 41, 73, 99, 159, 205, 247, 311, 349, 358, 397, 427, 473, 505, 533, 567, 597, 603–604, 617, 637, 673, 687, 713

- enzyme promiscuity 737
- enzyme replacement therapy (ERT)
 - 16, 30–31, 177, 638
- eotaxin-3 8
- Epicurian coli* XL1-red 164
- epigenetic regulation 403
- epigenomic machinery 32
- epilepsy 75, 82, 84, 551
- epinephrine 434, 437, 486
- epithelial sodium channels 578
- epothilone 538
- epothilone polyketides 538
- epoxyeicosatrienoic acids (EETs)
 - 568–569
 - EET analogs 579, 582, 585–587
 - EET antagonist 575
 - EET-B 582
 - EET metabolites 578
 - EET modulators 586
- EPR, *see* enhanced permeation and retention effect
- ER, *see* endoplasmic reticulum
- ER α , *see* estrogen receptor α
- erectile dysfunction 2, 28
- ERR α , *see* estrogen-related receptor α
- error prone PCR 164
- ERT, *see* enzyme replacement therapy
- erythromycin 538, 540, 557
- erythromycin A 714
- erythromycin D 557
- erythropoietin 15, 184, 690
- Escherichia coli* 45, 53, 56, 58–59, 112, 114, 120–122, 192, 213–214, 227, 330, 336, 517, 519, 536, 538, 550, 556, 643, 696–697, 700, 732–733
- Escherichia coli* BL21 732
- Escherichia coli* cells 53
- ESCRT-system 630
- esomeprazole 543, 553
- estrogen receptor α (ER α) 507, 599
- estrogen receptor modulators 507
- estrogen-related receptor α (ERR α)
 - 601
- estrogens 539–541, 557
- etanercept 173, 292
- eteplirsen 5, 605
- ethinylestradiol 83
- 7-ethyl-10-hydroxy-camptothecin (SN38) 389
- etoposide 541
- Euclidean distance 676
- euglobulin clot lysis time (ECLT)
 - 139
- eumiliin 125
- Euphorbia lathyris* L 539
- European Medicines Agency (EMA)
 - 3, 6–7, 48
- evasin-3 292
- EVB calculations 418
- event-driven strategy 603–604
- evolocumab 20
- exonuclease 45, 53, 164
- exoproteases 55, 211
- exosomes 624, 628–630, 632
- extracellular matrix (ECM) 186, 268, 581, 618, 629
- Fabry disease 171, 178, 639
- FACS-phenotyping experiments
 - 627
- Factor Xa 46, 55, 100, 104–105
- Factor Xa inhibitors 104–105
- FAD 397–402, 404, 406, 408, 410, 412, 414–416, 418, 420, 434–436, 451, 453, 456, 460, 505–506, 513–517, 519, 526, 545
- FAD-containing monoamine oxidases 398–420

- FAD-containing oxidases 398–420
 FAEs, *see* fatty acid ethyl esters
 familial adenomatous polyposis (FAP) 7
 familial hypercholesterolemia 21
 FAP, *see* familial adenomatous polyposis
 fatty acid ethyl esters (FAEs) 354, 389
 fatty acid ω -hydroxylase 548
 FD, *see* fluorescein diacetate
 FDA, Food and Drug Administration (USA) 1–8, 16–17, 20, 22–25, 27–29, 31, 33, 50–51, 63, 86, 104–107, 111–112, 121, 124, 171, 177–178, 181, 224, 314, 331, 410, 419, 438, 440, 543, 605, 607, 643, 674, 731
 fenamic acid 544, 553
 fenbufen 77
 Fenton type reactions 486
 FFAs, *see* free fatty acids
 fibrin 100–102, 107–108, 110–114, 116–121, 123, 129, 134, 139, 644
 fibrinogenolysis 118, 123, 125, 128–129, 132–133, 137
 fibrinolysis 2, 30, 100–101, 108, 112, 115, 118, 120, 129, 137, 139–140
 fibrinolytic enzymes 100, 102, 104, 106–108, 110, 112, 114, 116, 118–120, 122–134, 136–138, 140, 644
 fibroblasts, cancer-associated 629
 fibrolase 123
 FLAG tag 55
 flavonoids 252, 274, 277, 375–376, 378, 387
 flavourzyme 231–232
 fluorescein diacetate (FD) 356, 372, 377, 389
 Fondaparinux 105
 formaecin 692
 fragment-based or de novo design 676, 683
 fragment-based or de novo design approaches
 chimera 682
 design tools 683
 fusion 682
 hybrid 683
 fragment condensation 207, 215
 fragments of antigen binding 175
 free fatty acids (FFAs) 253–254
 free radical species 250
 fulvestrant 606
 Fumitremorgin C 625
 fungal infections 232
 furosemide 78–81, 86
 fusion peptides 213
 fusion proteins 119, 141, 559
 fynomers 186–187
 G-CSF, *see* granulocyte colony-stimulating factor
 G-protein coupled receptor (GPCR) 183, 238, 571
 GA, *see* glycyrrhetic acid
 GAGs, *see* glycosaminoglycans
 α -Gal 639
 β -Gal, *see* β -galactosidase
 galactose-6-sulfate sulfatase 641
 β -galactosidase (β -Gal) 648–649
 α -galactosidase A 639
 galantamine 438, 474, 476
 gamma-delta T cell type (CD3+) 701
 gamma secretase inhibitors 494
 gastrointestinal cancer 320
 gastrointestinal diseases 2
 Gaucher disease 171, 178, 639–640, 647

- GDEPT, *see* gene-directed enzyme prodrug therapy
- gefitinib 603
- gemcitabine 87, 356, 540–541
- gene-directed enzyme prodrug therapy (GDEPT) 644
- gene-fusion 543, 550
- gene mutations 618, 621
cancer-specific 618
mutational landscape 618
- Generally Regarded As Safe (GRAS) 49, 731
- genetic diseases 688
- genetic knockdown technologies 605–606
- genistein 550, 555
- germ cell tumors 617
- GH, *see* growth hormone
- Ghosal hemato-diaphyseal syndrome 572
- Girentuximab 88
- GKT136901 (pyrazolopyridine derivatives) 268
- GKT137831 (pyrazolopyridine derivatives) 268
- glaucoma 75–77
- glioblastoma 87, 318, 325, 334, 523
- Glucagon Receptor Element 403
- glucanases 45, 48
- β -glucocerebrosidase 639
- glucose oxidase (GOx) 649, 660
- glucose-6-phosphate dehydrogenase 650
- α -glucosidase 640, 642
- glutamate-cysteine ligase 288
- γ -glutamyl transpeptidase 34
- glutathione 34, 55, 213, 274–280, 283, 287–288, 333, 486, 650
- glutathione peroxidase 275
- glutathione S-transferase 55
- glutathione transferase 34, 213
- glycans 687–690, 693, 696–702, 704–706, 708–709
high-mannose type 687
- glycobiology 689, 692, 705
- glycocin-F 690–691, 693
- glycocode 688, 708
- glycoengineering 690
- glycogen branching enzyme 640
- glycogen debranching enzyme 640
- glycogen phosphorylase 640
- glycogen storage disease 178, 640, 642
- glycogen synthase 640
- glycome 687, 705
- GlycoMine 706
- glyconanoparticles 691
- glycoprotein 59–60, 105–106, 114, 175, 640, 689, 697, 700, 702, 706
- glycosaminoglycans (GAGs) 641
- glycosidases 48, 688, 705
- glycosylation 46, 59–60, 115, 224, 254, 329, 353, 459, 655, 687–693, 695–701, 705–709
types 689
- glycosylation of proteins 691
C-linked 688–689
N-linked 688–689
O-linked 689
S-linked 688, 690
- glycosylation type 688–689
- glycosyltransferases 690, 696, 698–699, 705
- glycotransferase SunS 690
- glycyrrhetic acid (GA) 370–371, 389
- GlyTouCan 698, 706
- Gordonia alkanivorans* 548
- GOx, *see* glucose oxidase
- granulocyte colony-stimulating factor (G-CSF) 180–181, 184
- granzyme B 648

- GRAS, *see* Generally Regarded As Safe
- green chemistry 716
- growth hormone (GH) 174, 181–183
- GSK2190915 (5-LOX activating protein (FLAP) agonist) 271
- GSK2795039 (7-azaindole structure molecule) 268
- Haemophilus influenzae* 52
- hallmarks in cancer 620
- hAOX 1 507, 512–520
- hAOX1
oxidation mechanisms 518
structure 512
- Haploinsufficiency 626
- harmine 413–414, 460, 462
- 27-HC, *see* 27-hydroxycholesterol
- HCC, *see* hepatocellular carcinoma
- HCEC, *see* human epithelial colon cells
- HDL-c, *see* high-density lipoprotein cholesterol
- HDPs, *see* host defense peptides
- heart failure 2, 269, 271–272, 287, 398, 585
- heart failure (HF) 2, 269, 271–272, 287, 398, 585
- Heberkinasa® 110
- hematological tumors 619–621
- hemophilia 9, 174, 184–185
- hemostasis 100–101
- heparin 102–105, 116
- heparin-induced thrombocytopenia (HIT) 103
- hepatitis C 4–5, 12, 172, 179–180, 237, 291, 630
- hepatitis C virus 4–5, 237, 630
- hepatocellular carcinoma (HCC) 314, 316, 326, 658
- Herpes simplex virus 228, 233
- 20-HETE, *see* 20-hydroxyeicosatetraenoic acid
- HETE, *see* hydroxyeicosatetraenoic acid
- HF, *see* heart failure
- HIF-1 α , *see* hypoxia-inducible factor- α
- high-density lipoprotein cholesterol (HDL-c) 254
- high-dose hook effect 603
- high-performance liquid chromatography (HPLC) 218–220, 700
- high-throughput screening (HTS) 160, 162, 268, 389
- hirtin 125
- hirudin 104, 119
- His tag 55
- HIT, *see* heparin-induced thrombocytopenia
- HLC, *see* human liver cytosol
- HLM, *see* human liver microsomes
- Hodgkin's lymphoma 10, 171, 316
- homoisoflavonoid 457–458
- homologous recombination 166–167
- horizontal gene transfer 731
- horseradish peroxidase 648–649, 651
- host defense peptides (HDPs) 693
- HPLC, *see* high-performance liquid chromatography
- HTS, *see* high-throughput screening
- human carboxylesterase 1 (CES1) 350–351, 388
- human carboxylesterase 2 (CES2) 350, 388
- human epithelial colon cells (HCEC) 229

- human genome 597, 626
- human liver cytosol (HLC) 389
- human liver microsomes (HLM) 355, 389
- Humulin 181
- Hunter disease 172, 178
- Hunter syndrome 641
- Huntington's disease 238, 480
- Hurler-Scheie syndrome 178
- Hurler syndrome 171
- hyaluronan 707–708
- hybrid proteins 118
- 27-hydroxycholesterol (27-HC) 379, 389
- 20-hydroxyecosatetraenoic acid (20-HETE) 273, 551, 556, 569
- hydroxyecosatetraenoic acid (HETE) 273, 551, 556, 568–569
- 20-HETE 569–570, 572, 574, 579–583, 587
- 20-HETE inhibitor 583
- HETE deficiency 582
- (R)-4-hydroxyisophorone 555
- 17 α -hydroxyprogesterone 537
- hydroxytamoxifen 600, 653
- hypercholesterolemia 21, 248
- hyperglycaemia 253, 255, 284, 331, 340
- hyperinsulinemia, hypertension 253
- hyperpigmentation 232–233
- hypertension 9–10, 28, 79, 230, 240, 248–249, 253, 257–259, 262, 265, 268, 282–285, 288, 291, 572, 578–582, 585
- hypertensive heart disease 247
- hyperuricemia 15, 269, 287
- hypophosphatasia 9, 640
- hypoxia 86, 258, 268–269, 586, 601
- hypoxia-inducible factor 86
- hypoxia-inducible factor- α (HIF-1 α) 601
- hypoxic tumors 75
- IAP, *see* inhibitor of apoptosis protein
- IAP antagonists 600
- ibuprofen, diflunisal 77
- ICAM-1, *see* intracellular adhesion molecule
- ICU, *see* intensive care unit
- Idraparinux 105
- IDRs, *see* defense regulator peptides
- ifosfamide 541, 544, 553
- IgG function 688
- IKAROS family transcription factors 602
- imatinib 603, 621
- imidacloprid 525–526
- immune checkpoint inhibitors 5
- immune system 175, 179, 272, 624, 631, 660–661, 688–689, 691–692, 700–702, 704, 708
- immunity 13, 235, 240, 660, 692
- immunoglobulins 175, 661, 699, 703
- immunons 704
- immunosenescent peptides 701
- immunosuppressive drugs 521
- in silico approaches 676
- in silico studies 675
- in silico techniques 675
- in vitro recombination 165–166
- incremental truncation for the creation of hybrid enzymes (ITCHY) 167
- indisulam (E7070) 87–88, 606
- Indolicidin 228, 233
- indolotacrine analogues 460

- inflammatory disorders 537, 708
 inflammatory mediators 270
 infliximab 292
 influenza virus 52
 ingenol mebutate 539
 inhibitor binding 516
 inhibitor of apoptosis protein (IAP) 598
 inhibitors, multi-targeted 443
 innate immune system and 701
 insulin 13, 46, 56–57, 63, 172–173, 181–182, 184, 189, 234, 253–255, 283–284, 288, 574
 insulin receptor substrate 1 (IRS1) 253–254
 integrase inhibitors 15
 intelectins 691
 intensive care unit (ICU) 272
 intracellular adhesion molecule (ICAM-1) 571
 5-iodo-2-deoxyuridine 523
 iproniazid 410, 437
 iPS cells 628
 iPS technology 627
 irciniastatin A 717–718
 irinotecan (CPT-11) 350, 355–356, 358, 379, 388
 IRS1, *see* insulin receptor substrate 1
 ischemia 249, 267, 272, 291, 574–577, 583
 Isocarboxid 414
 isocitrate dehydrogenase 24
 isothiocyanates 491
 ITCHY, *see* incremental truncation for the creation of hybrid enzymes
 ivermectins 731–732

 K channels 578
 kallikrein 186, 192
 Kaplan-Meier curves 622
 KEAP, *see* Kelch-like ECH-associated protein 1
 KEAP 1-recruiting degrader 610
 KEGG, *see* Kyoto Encyclopedia of Genes and Genomes
 KEGG Cancer database 695
 Kelch-like ECH-associated protein 1 (KEAP) 292
 11-keto- β -boswellic acid (KBA) 537
 ketoprofen 77
 kinase inhibitors 621
 knottins 190–191
 KRAS 608
 kringle domains 111, 120–121, 191–192
 Kunitz domain 185, 192
 Kyoto Encyclopedia of Genes and Genomes (KEGG) 32, 512

 L-amino acid oxidase (LAAO) 399
 L-ARG, *see* arginine
 L-ARG deprivation 316, 318, 320, 324–325
 L-arginine deiminase (ADI) 313–314
 catalytic mechanism 314
 structure 314
 therapeutic use 318
 L-asparaginase 647, 654
 L-DOPA 402
 α -L-iduronidase 641
 L-methionine 314, 333–334
 LAAO, *see* L-amino acid oxidase
 lactic dehydrogenase 650
 Lactoferrin 227
 ladostigil 420, 450–452, 493
 lanoteplase 115

- lansoprazole 553
- lanthipeptides 693
- LDL, *see* low-density lipoprotein
- lebetase 123
- lectin 688, 691, 700, 704
- lectin receptors 688, 704
- leishmaniasis 2
- lenalidomide 11
- lentivirus 52
- lepirudin 104
- letermovir 7–8
- letrozole 539, 541
- leukemia disease subtypes 620
- leukemias 617, 620–621
- leukocyte migration 292, 688
- leukocyte rolling 705
- leukotriene receptor antagonists (LTRAs) 271
- leukotriene receptors 270
- levan 654
- Levemir 173, 182
- lidocaine 544, 553
- ligand-based pharmacophore model 678
 - available software 679
- ligand-based techniques 678
- ligand-pharmacophore modelling 273
- LIGSITE 676
- lipid-linked oligosaccharide (LLO) 698
- lipocalins 185, 187
- lipogenesis 89
- lipoic acid 252, 275, 277, 281, 288
- lipopeptides 233
- lipopolysaccharide 690, 697
- lipopolysaccharides (LPS) 49
- lipoprotein lipase 690
- liposome 225, 646–648
- lipoxins 271
- lipoxygenase (LOX) pathway 568–569
- lipoxygenases (LOXs) 249, 270
 - 12/15-LOX 270
 - 5-LOX 270
- (R)-lisofylline 556
- liver toxicity 415, 525
- LLO, *see* lipid-linked oligosaccharide
- LMWHs, *see* low-molecular-weight heparins
- low-density lipoprotein (LDL) 190, 254, 281
- low-molecular-weight heparins (LMWHs) 103
- lower urinary tract symptoms 15
- 5-LOX activating protein (FLAP) agonist, *see* GSK2190915
- LOXs, *see* lipoxygenases
- LPS, *see* lipopolysaccharides
- LTRAs, *see* leukotriene receptor antagonists
- lumbrokinase 107, 123–124
- lumiflavin 418
- lunasin 229
- lymphomas 238, 314, 329, 617, 620–621
- lysosomal storage diseases 2
- lysozyme 45, 48–49, 63, 176, 653
- macrophages 235, 237, 253, 255, 262, 264, 288, 355, 571, 629, 639–640, 653, 660, 691, 701
- magainin peptide 234
- major histocompatibility complex (MHC) 175, 693, 700–704
- Malaria 29
- malignant pleural mesothelioma 316, 320
- maltose binding protein (MBP) 55, 189
- mammalian CYP enzymes 536, 542–543, 550–551

- mannanases 45, 48
- mannose-binding lectin (MBL) 691
- mannoside *N*-acetylglucosaminyltransferase 5 703
- MAO, *see* monoamine oxidase
- MAO A 398–399, 402–404, 406–417
- MAO-A-immunoreactive neurons 437
- MAO B 397–404, 406–418, 437
- MAO-B inhibition 447–448, 454, 457, 486
- MAO inhibition 410, 419, 446, 452, 455–456, 459, 486
 - antidepressant effect 410
 - irreversible 410
 - reversible 410
- MAO inhibitors (MAOI) 398, 410, 415, 440, 445, 461, 482, 488
- MAOI, *see* MAO inhibitors
- MAOs, *see* monoamine oxidases
- MAP kinase 279
- MAPK, *see* mitogen-activated protein kinase
- Marinobacter aquaeolei* 548–549
- Maroteaux-Lamy syndrome 178
- matrix metalloproteinases (MMPs) 571
- MBL, *see* mannose-binding lectin
- MBP, *see* maltose binding protein
- MCM, *see* multiple-compound medication
- meclofenamic acid 544
- mediated drug metabolism 33, 551
- medicaid 25
- medicare 25–26
- mefenamic acid 544
- melphalan 87
- memantine 438–439, 474, 476, 479–480
- memoquin 493
- 6-mercaptopurine 521
- mertansine 176
- mesenchymal cells 629
- metal chelators 495–496
- metalloproteases 123, 128–137, 140, 211–212
- METase, *see* methionine- γ -lyase
- metastatic melanoma (MM) 179, 181, 316
- metastatic pancreatic ductal cancer 87
- mETC, *see* mitochondrial electron transport chain
- metformin 28
- methionine aminopeptidase 2 601
- methionine- γ -lyase (METase/MGL) 313–314
 - catalytic mechanism 314
 - structure 336, 337
 - therapeutic use 335
- methotrexate 81, 521, 624
- methylene blue 413–414
- methylthioadenosine phosphorylase (MTAP) 334
- MHC, *see* major histocompatibility complex
- MI, *see* myocardial infarction
- micelles 646–647
- microbial thrombolytic enzymes 119
- microplasmin 121
- microwave technology 215
- midazolam 79, 90, 542
- minicircle (MC) DNA vectors 58
- minicircle vector purification 46
- miniplasmin 120–121
- mipomersen 605
- mitochondrial complex II 255
- mitochondrial electron transport chain (mETC) 249, 254–255, 279

- mitochondrial neurogastrointestinal encephalomyopathy 641
- mitogen-activated protein kinase (MAPK) 189, 282, 575
- MitoQ, *see* mitoquinone
- mitoquinone (MitoQ) 290
- mitoxantrones 624
- MM, *see* metastatic melanoma
- MMPs, *see* matrix metalloproteinases
- MMT, *see* multiple-medication therapy
- moclobemide 414
- mogamulizumab 173, 184
- molecular dynamics (MD) simulation study 682
- Molecular Operating Environment (MOE) software 703
- molybdoflavoenzymes 505
- monoamine oxidase (MAO) 15, 31, 84, 397–420, 428, 430, 432, 434–440, 442–463, 482, 485–488, 522
 - active site 400–401, 404, 412–414, 416–418, 435–436, 448, 451, 456, 460, 462
 - function 433–435, 438, 442, 485
 - isoforms 434
 - mechanism 84, 399–401, 405, 411, 415–418, 439
 - structure 398–399, 401, 404, 411, 416, 418, 434–435, 440, 443, 446, 454, 461, 488
- monoamine oxidase inhibitors 15
- monoamine oxidases (MAOs) 31, 397–398, 400, 402, 404, 406, 408, 410, 412, 414, 416, 418, 420
 - FAD-containing 400
- monobodies 186
- monoclonal 8, 15, 59, 88, 175–177
- monoclonal antibodies 15, 59, 88, 175–176
- monocyte differentiation 255
- monomethyl auristatin E 176
- monteplase 116
- morphine 99
- Morquio syndrome 641
- MPN, *see* 4-benzoyl-N-butyl-1,8-naphthalimide
- MPO, *see* myeloperoxidase
- MPO inhibitor, *see* PF-1355
- MPS, *see* mucopolysaccharidosis
- MSA, *see* multiple sequence alignment
- MTAP, *see* methylthioadenosine phosphorylase
- MTDL, *see* multitarget drug ligand
- Mucin-6 protein 699
- mucopolysaccharidosis (MPS) 641
- multidrug resistance 227, 624
- multiple-compound medication (MCM) 674
- multiple-medication therapy (MMT) 674
- multiple myeloma 10, 355, 602
- multiple sclerosis 4, 29, 171, 673
- multiple sequence alignment (MSA) 168
- multistep conversions 714–715, 718, 738
- multitarget directed ligands 674
- multitarget-directed ligands 31
- multitarget drug design (MTDD) approach 398, 417, 477, 482–483, 489, 497, 673–674, 677, 679–680, 683
- multitarget drug designing (MTDD) 674–677, 679–681, 683
- multitarget drug ligand (MTDL)
 - AD therapy 453
 - design 682
 - semicarbazone derived 459
 - thioxanthone derivatives 460
- multitarget drugs 398, 417, 419–420

- multitarget ligand design 475, 477, 483, 485, 487, 489, 491, 493, 495
- multitarget QSAR Models 679
- multitargeted inhibitors 444
- multivesicular body (MVB) 630
- mutagenesis 118, 164–165, 181, 185–186, 337, 517, 542–544, 546–553, 555–559, 643
 - chemical 164, 554–555, 557, 559
 - focused 164–165, 181
 - random 164–165, 542, 544, 546–547, 550–551, 553, 555, 557–558
- mutasynthesis 727, 734, 736–738
- mutasynthons 736–738
- MVB, *see* multi-vesicular body
- Mycoplasma arginini* 320
- myeloperoxidase (MPO) 272, 287
- myocardial infarction (MI) 2, 99–102, 111–114, 184, 273, 573, 577, 580

- N*-acetylgalactosamine-4-sulfatase 641
- N*-acetylglucosamine 48, 689, 705
- N*-acetylglucosaminidase 697
- N*-acetylmuramic acid 48
- N*-acetyltransferases 34
- NADPH antagonists 259
- NADPH oxidases 249, 258
 - isoforms (NOX1, NOX2, NOX3, NOX4, NOX5) 258
- nano-emulsions 225, 234
- nanobioreactors 645–647, 649–655, 657, 659
 - tissue targeting 655
 - active 657
 - efficiency 655
 - passive 656
- nanobodies 188
- nanocages 649–650
- nanocarriers (NCs) 237, 638, 646, 656, 691
 - multifunctionality 659
 - multitargeting 660
- nanodisc system 560
- nanoencapsulations 225
- nanomedicine 637–638
- nanoparticles (NPs) 225, 230, 232, 239, 638, 645–646, 650, 653–654, 656
 - core-shell 650
 - PEGylated 648
 - virus-like 651
- nanotechnology 159, 230, 240, 637
- nanotubes 649
- α -naphthoflavone activity 551
- naproxen 543–544, 553
- nargase 45, 54
- native biosynthesis 720, 722–725, 729–730
- native chemical ligation (NCL) 216
- nattokinase 107, 132, 134, 137, 139–140
- NCAMs, *see* neural cell adhesion molecules
- NCL, *see* native chemical ligation
- NCs, *see* nanocarriers
- Neisseria meningitidis* 52
- neoplastic transformation 629
- neural cell adhesion molecules (NCAM) 236
- neurodegenerative diseases 2, 31, 240, 252, 397–398, 420, 473, 673
- neurotransmitter metabolism 407–408
- neutrophil cytosol factor 2 (p67phox, NCF2) 256
- neutrophil cytosol factor 4 (p40phox, NCF4) 256

- neutrophils 235, 237, 260, 660
- new molecular entities (NMEs) 3, 674
- NF- κ B (NF-kappaB) antagonists 293
- NFE2L2, *see* nuclear factor erythroid 2-related factor 2
- NGlycPred 707
- nicking endonuclease 58
- nifedipine 573
- nitric oxide 100, 231, 250, 252, 254, 273, 282, 287–288, 413, 581
- nitrogen dioxide 252
- nivolumab 607
- NMDA receptor 438–439, 475, 479–480, 482–483, 497
- NMDA receptor antagonist 438–439, 479–480
- NMEs, *see* new molecular entities
- non-Hodgkin's lymphoma 5, 12, 314, 316, 320
- non-homologous recombination 166–167
- non-nucleoside reverse transcriptase inhibitors 625
- non-ribosomal peptides 729
- non-small cell lung cancer (NSCLC) 24, 320, 540
- non-steroidal anti-inflammatory drugs/NSAIDs 544
- noradrenaline 408
- norepinephrine 420, 434–435, 485–486
- NPs, *see* nanoparticles
- NSCLC, *see* non-small cell lung cancer
- nuclear factor erythroid 2-related factor 2 (NFE2L2) 292
- nucleoside reverse transcriptase inhibitors 625
- nusinersen 5, 605
- OA, *see* oleanolic acid
- ocriplasmin 121
- OGT, *see* oligosaccharyltransferase
- Ojima lactone 728
- oleanolic acid (OA) 369, 371, 389
- oligonucleotide therapeutics 605–606
- oligosaccharyltransferase (OGT) 697
- omega-3 PUFA family 570
- omega-6 PUFA family 570
- Oncaspar 178, 331
- ONCOFID-P 707
- ONCOFID-S 707
- oncogenes 50, 618, 620
- oncogenic proteins 597–600, 602–603, 605–606, 608, 611
- oncogenic signaling pathways 621
- OPs, *see* organophosphates
- organophosphates (OPs) 386, 389
- ornithine transcarbamylase (OTC) 317, 323
- orphan drugs 1, 7, 9, 24
- OSCARR 165
- OSMAC 723–724
- osteoporosis 547, 673
- osteosarcoma 541
- OTC, *see* ornithine transcarbamylase
- ototoxic drugs 81
- oxidative stress 75, 248–250, 252–254, 256–258, 260, 262, 264, 266, 268, 270–272, 274–276, 278–290, 292, 294, 333, 436–437, 439, 462, 480–481, 486, 490, 492, 496, 582, 660
- drug induced 250, 278–280

- experimental therapeutic agents 250, 281–283, 288
- Oxyipurinol 270

- P-selectin 268, 571
- P2Y12 receptor inhibitor 106
- p22phox, CYBA, *see* cytochrome b-245 light chain
- p40phox, NCF4, *see* neutrophil cytosol factor 4
- p53 pathway 624
- p53 protein 625–626
- p53 tetramers 626
- p67phox, NCF2, *see* neutrophil cytosol factor 2
- P450 family 409
- P450 hydroxylases 251, 273
- P450 isoflavone synthase 1 550
- PACE, *see* phage assisted continuous evolution
- paclitaxel 540–541, 724, 727–729, 738
- PAI-1, *see* plasminogen activator inhibitor 1
- PAIs, *see* plasminogen activator inhibitors
- pamiteplase 115
- PAMPs, *see* pathogen-associated molecular patterns
- pancreatic cancer 320, 643
- pancreatic carcinoma 316, 325
- pancreatic enzyme replacement therapy 177
- pancreatic tumors 640
- Pantoea ananatis* 732–733
- papain 46, 57, 212
- paracetamol 253, 278, 280
- parental plasmid (PP) 58
- pargyline 410, 414–417

- Parkinson's disease 2, 15, 84, 238, 291, 398, 402, 409–410, 417, 480, 486
- PARP, *see* poly ADP ribose polymerase inhibitors
- partial thromboplastin time (PATT) 139
- PAS, *see* peripheral anionic site
- PASS 676
- passenger mutations 619
- patent ductus arteriosus (PDA) 7
- pathogen-associated molecular patterns (PAMPs) 700
- PATT, *see* partial thromboplastin time
- PCSK9, *see* proprotein convertase subtilisin kexin 9 inhibitors
- PD-1/PD-L1 pathway 607
- PDA, *see* patent ductus arteriosus
- PDTC, *see* pyrrolidine dithiocarbamate
- pectinase 62
- pegaptanib 605
- pegfilgrastim 172
- PEGylated protein 639
- PEGylation 178, 180, 188, 652, 661
- penicillin G 734
- penicillin V 734–735
- Penicillium chrysogenum* 128, 546, 735
- pepsin 46, 57–58, 63, 212, 227, 231
- peptide-mimetic 237
- peptide-nanoparticle hybrids 230
- peptide vaccines 237
- peptides 205–216, 218, 220, 222, 224, 226–240, 691–693, 695, 697
 - animal derived 206, 231
 - food derived 227, 231
 - marine-derived 237
 - plant derived 206, 231

- peptidoglycan 48–49, 54
- peptidoglycan *N*-acetylmuramoylhydrolase 48
- PERFORM study 584
- perillyl alcohol 538, 540
- peripheral anionic site 430
- peroxisome proliferator-activated receptor gamma (PPARG) 254–255, 268
- peroxynitrite 250, 252
- personalized medicine 621
- pesticides 536, 731
- PET, *see* positron emission tomography
- Pexiganan 234
- Peyronie's disease 644
- PF-1355 (MPO inhibitor) 273
- PGI2, *see* prostacyclin
- PH2, *see* prostaglandin
- phage assisted continuous evolution (PACE) 166
- phage display 186–187, 189, 192
- pharmaceutical discoveries 721
- pharmacophore modeling 678–680
 - complex-based 680
 - structure-based 678, 680
 - target (only)-based 680
 - available databases 681
- pharmacy benefit managers 26
- phase I drug metabolism 506, 508, 510, 512, 514, 516, 518, 520, 522, 524, 526
- Phenelzine 401–402, 414, 416
- phenylalanine hydroxylase 642
- Phenylketonuria 642
- phosphatidylinositide 3-kinase (PI3K) 254
- phosphodiesterase type 4 inhibitors 15
- phosphodiesterase type 5 (PDE-5) inhibitors 81
- phospholipase A2 (PLA2) 273, 568, 655
- phospholipids 251, 273, 568–569
- phthalazines 513, 516–518, 524
- phyto-peptides 229
 - anti-cancer agents 229
- PI3K, *see* phosphatidylinositide 3-kinase
- PI3K-Akt pathway 253
- Pichia pastoris* 57, 121, 186, 227, 404, 709
- Pictet-Spenglerase 719
- pirlindole 414
- piscine 551
- PKA, *see* protein kinase A
- PKC, *see* protein kinase C
- PKD, *see* polycystic kidney disease
- PLA2, *see* phospholipase A2
- plasmid DNA vectors 52
- plasmin 100–101, 107–113, 115, 117–122, 128–129, 132, 139–141, 644
- plasmin inhibitors 108, 113
- plasminogen activator inhibitor 1 (PAI-1) 100, 114, 254
- plasminogen activator inhibitor 1 (SERPINE1) 100, 114, 254
- plasminogen activator inhibitors (PAIs) 119
- plasminogen activators 100–101, 107–111, 113, 116, 118–119, 122–123, 132, 139, 141
- PLAT, *see* tissue-type plasminogen activator
- platelet-activating factors 31, 100
- platelet aggregation 100, 105–106, 123, 139, 570, 572, 586
- platelet-derived growth factor 267, 572
- PML-RARA fusion protein 622–623
- POLDIP2, *see* polymerase delta-interacting protein 2

- polmacoxib 84–86
- poly ADP ribose polymerase
 - inhibitors (PARP) 15
- polyamine oxidase 399
- polycystic kidney disease (PKD) 583
- polyketide synthase cluster 732
- polyketides 538, 729, 731
- polymerase delta-interacting
 - protein 2 (POLDIP2) 256
- polymorphisms 33–34, 272, 403, 519, 521, 568, 580, 582, 587
- Polyoxyl 35 castor oil (EL35) 383–384
- polyoxyl 40 hydrogenated castor oil (RH40) 383–384, 389
- polypharmacology 674
- polyunsaturated fatty acid (PUFA) 568
- Pompe disease 178, 642
- positron emission tomography (PET) 191, 403
- potential ligand as MTDLs 676
- potential target proteins 676
- PP, *see* parental plasmid
- PPARG, *see* peroxisome proliferator-activated receptor gamma
- prasugrel 106, 356, 358
- pravastatin 546–547, 554
- precursor-directed biosynthesis 727, 734, 736
- pregnenolone 538
- PRIMA-1 626
- pro-apoptotic proteins 280, 626
- pro-drugs 523
 - AOX1-dependent activation 523
- prodigiosin 732–733, 737–738
- prodrug 104, 335, 356, 539, 644, 651–653, 658, 660, 662
- prodrugs 355–356, 358, 536, 643–644
- progesterone 536–537, 540, 547–548, 551–552, 555–556
- proinsulin 46, 56, 62
 - recombinant 46, 56–57
- Proleukin 172, 181
- Prolyse® 112
- pronase E 45, 54
- propargylamine 400, 417–418, 420, 442–443, 449–453, 455, 463
- propargylamine inactivators 418
- propargylated compounds 449
- propranolol 83, 356, 543
- proprotein convertase subtilisin kexin 9 inhibitors (PCSK9) 15
- prostacyclin 100, 568–570
- prostacyclin (PGI₂) 100, 568–570
- prostacyclin (PGI₂) synthase 570
- prostaglandin (PH₂) 79, 105–106, 255, 264, 282
- prostaglandin E₁ 714
- prostaglandin G/H synthase 1 (PTGS1) 255
- prostaglandin synthase 105
- prostaglandins 85, 273, 535
- prostanoids 568, 570–571
- prostate cancer 2, 4, 15, 28, 320, 326, 610, 643, 658
- prostate carcinomas 316
- PROTACs 598, 601–610
- proteases 53–55, 107, 119–120, 122–125, 127, 129, 132, 176, 180, 191–192, 210–212, 214, 229, 232, 234, 353, 640, 651
- proteasomal degradation 599, 601, 606
- protein clearance 53
- protein engineering 160–161, 163, 165, 167, 169, 171, 173, 175, 184, 192, 546–547, 559, 644, 701
- protein fusions 46, 55
- protein hormones 181

- protein kinase A (PKA) 236
- protein kinase C (PKC) 254, 265, 580
- protein kinase C isoforms 254
- protein libraries 162
- protein opsonization 661
- protein phosphatase 2A 581
- protein refolding 42
- protein therapeutics 160–162, 175, 177, 179, 181, 183–185, 193
 - market 160, 193
- proteinase K 45, 54
- protein–glycan coupling technology 689, 696
- proteome homeostasis 315
- proto-oncogenes 618, 620
- prourokinase 112
- prunifoleine 461–462
- pseudogenization 511, 523–524, 526
- Pseudomonas putida* 317, 335, 538, 732
- Pseudomonas putida* KT2440 733, 738
- psoriasis 2, 4, 12, 15, 187–188
- psoriatic arthritis 2, 12, 15, 187
- PTGS1, *see* prostaglandin G/H synthase 1
- PUFA, *see* polyunsaturated fatty acid
- pulmonary disease 249, 253
- pulmonary fibrosis 249
- pulmonary hypertension 9, 262, 268
- Pulmozyme 51, 172, 178
- pyrrolidine dithiocarbamate (PDTC) 293
- quantitative structure-activity relationship (QSAR) 389, 679
- quercetin 281, 491, 625
- quinine oxidase 523
- R-6-hydroxybuspirone 543
- R3C 46
- RAC1, *see* ras-related C3 botulinum toxin substrate 1
- random mutagenesis 164–165, 542, 544, 546–547, 550–551, 553, 555, 557–558
- random mutation 729
- randomized clinical trials 21
- rapamycin 731–732, 734, 737
- ras-related C3 botulinum toxin substrate 1 (RAC1) 256
- RAS-targeted therapeutics 608
- rational drug design (RDD) 674
- RDD, *see* rational drug design
- rDNA technology 213–214
- reactive nitrogen species (RNS) 249, 252
- reactive oxygen species (ROS) 235, 249–250, 254, 271, 333, 437, 481, 486, 525, 575, 653
 - mitochondrial ROS (mtROS) 255
- ROS-mediated pathways 250
- real-world data 22
- real-world evidence (RWE) 23
- receptor-interacting serine-threonine kinase 2 (RIPK2) 601
- receptor tyrosine kinases 602
- recombinant DNA technology 15, 56, 109, 141, 160, 324
- recombinant proteins 44, 46, 50, 55, 59, 180, 646
 - glycosylation 46, 59
- redox homeostasis 249, 274–275, 277
- Q-SiteFinder 676
- QSAR, *see* quantitative structure-activity relationship
- QSAR-perturbation approach 680

- renovascular disease (RVD) 580
- renovascular hypertension 578, 581
- respiratory chain 277, 409
- respiratory problems 249
- resveratrol 31, 283, 461, 723–724
- reteplase 107, 114
- retinitis pigmentosa 75
- Reversan 625
- reversed-phase HPLC (RP-HPLC) 220–221
- RH40, *see* polyoxyl 40 hydrogenated castor oil
- rhARGI, *see* arginase
- rhein 281, 288
- rheumatic heart disease 2
- rhinovirus 3C proteases 55
- Rho kinase 580
- Rhodobacter capsulatus* B10S 732–733
- riboflavin 400, 722
- RIPK2, *see* receptor-interacting serine-threonine kinase 2
- rituximab 14
- rivastigmine 420, 438–439, 450, 474, 476–478
- RNA binding motif protein 39 606
- RNA interference 605
- RNase 45, 52–53, 63, 690
- RNS, *see* reactive nitrogen species
- ROS, *see* reactive oxygen species
- ROS signaling 275
- Rotarix 47
- RP-HPLC 220
- RUNX1 transcription factor 629
- RVD, *see* renovascular disease
- RWE, *see* real world evidence
- Saccharomyces cerevisiae* 56, 404, 639, 729–730
- Saccharopolyspora erythraea* 538
- safinamide 410, 413–414
- Sanfilippo syndrome 641
- SAR, *see* structure-activity relationship
- sarcomas 617
- saruplase 112–113
- SCARB1, *see* scavenger receptor class B member 1
- scavenger receptor class B member 1 254–255
- scavenger receptor class B member 1 (SCARB1) 254–255
- Scheie syndrome 178
- SCLC, *see* small cell lung cancer
- SDM, *see* site directed mutagenesis
- SEER's database 617
- selectins (P-, E-, L-) 258, 292, 705
- selegiline 402, 409–410, 414, 417, 452–453, 463, 486
- semicarbazide-sensitive amine oxidase (SSAO) 398
- semisynthesis 727–730, 736
- sequence saturation mutagenesis (SeSAM) 165
- serine protease inhibitors (SERPINS) 122
- serine proteases 107, 111, 117, 120–122, 124–125, 127–134, 136–137, 139, 192, 211–212
- serotonin 85, 397, 403, 407–408, 410, 413, 420, 434–435, 475, 485–486, 521
- serpin 122, 229
- SERPINE1, *see* plasminogen activator inhibitor 1
- SERPINS, *see* serine protease inhibitors
- serrapeptase 140
- Serratia marcescens* 732–733, 737
- SeSAM, *see* sequence saturation mutagenesis

- SGLT-2, *see* sodium–glucose cotransporter 2 inhibitors
- SHC1, *see* signalling adapter SHC-transforming protein 1
- she, *see* soluble epoxide hydrolase
- sialic acids 699, 704, 708
- Siglec receptors 704, 708
- signal transduction 33, 235, 249, 253, 275, 278
- signalling adapter SHC-transforming protein 1 (SHC1) 254
- sildenafil 28, 81, 293
- simvastatin 234, 382–383, 727
- single guide RNA 649
- single nucleotide polymorphisms (SNPs) 403
- single-step conversions 738
- site-directed glycosylation 696
- site saturation mutagenesis (SSM) 165
- skin burns 233–234
- skin cancers 233
- skin disease treatment 235, 240
- skin explants 524
- skin infections 232–233
- SLC-0111 87
- SLC2A4/GLUT4, *see* solute carrier family 2, facilitated glucose transporter member 4
- SLS, *see* sodium lauryl sulfate
- small cell lung cancer (SCLC) 24, 320, 540
- small ubiquitin-related modifier (SUMO) 213
- SN38, *see* 7-ethyl-10-hydroxy-camptothecin
- SNIPER(ER) 600
- SNIPERs 597–600, 602–610
- SNPs, *see* single nucleotide polymorphisms
- SOD, *see* superoxide dismutase
- sodium lauryl sulfate (SLS) 383–384, 389
- sodium-potassium-chloride (NKCC2) transporter 581
- sodium–glucose cotransporter 2 inhibitors (SGLT-2) 15
- soft tissue sarcoma 5, 320
- solid phase peptide synthesis (SPPS) 698
- solid tumors 88, 174, 187, 618–619, 621–622, 632
- solinase 115
- soluble epoxide hydrolase (sEH) 569–570
- inhibitors
AR9281 585
GSK2256294 585–586
- solute carrier family 2, facilitated glucose transporter member 4 (SLC2A4/GLUT4) 254
- somatic cells 618, 628
- sorafenib 86, 603
- spinal muscular atrophy 5, 7
- splenomegaly 621, 639
- SPPS, *see* solid phase peptide synthesis
- SSAO, *see* semicarbazide-sensitive amine oxidase
- SSM, *see* site saturation mutagenesis
- St. John's Wort 542
- staggered extension process (StEP) 166
- staphylokinase 107, 113, 118, 132
- statins 716
- stealth strategies 657, 661
- StEP, *see* staggered extension process
- steroids 187, 535, 537, 540, 557–558, 567
- sterol demethylase 538
- Streptag II 55
- streptococcal pharyngitis 734
- Streptococcus pneumoniae* 52
- streptokinase 106–110, 112–113, 118, 122, 132, 141, 644

- Streptomyces avermitilis* 731
Streptomyces coelicolor CH999 538
Streptomyces hygroscopicus 731–732
 streptozotocin (STZ) 267–268, 271
 structure-activity relationship (SAR) 389, 435, 440, 679
 structure-based drug design 404, 675
 STZ, *see* streptozotocin
 subtilisin 15, 20, 62, 132, 137, 139
 subtilisin family 139
 sulfaphenazole 577
 sulfonamides 76–81, 83, 365–366, 454
 diuretic drugs 79
 drug interactions 76–77, 79
 sulthiame 81–83
 SUMO, *see* small ubiquitin-related modifier
 superoxide dismutase (SOD) 274–276, 655
 SuperProDesigner 63
 SURFNET 676
 synthetic peptides 207, 209, 215, 234
 Szeto-Schiller (SS) family peptides 291

 t-AUCB 574
 T-cell receptors 688
 T-cell signaling 700
 T-cells 276, 630–631, 699, 703
 t-PA, *see* tissue plasminogen activator
 T4 lysozyme 653
 TAC, *see* total antioxidant capacity
 tacrine 31, 438, 440, 446, 452–453, 455, 457–458, 460–461, 463, 474, 476–477
 toxicity 453, 477
 tadalafil 293
 TAFI, *see* thrombin-activatable fibrinolysis inhibitor
 tamoxifen 651–653
 Tanimoto similarity coefficient 676
 Taq DNA polymerase 164, 189–190
 tarenflurbil 494
 tau protein 481
 taxol 538–539, 557, 724, 727–728
Taxus baccata 728
Taxus brevifolia 724, 727
Taxus chinensis 538
 TCA cycle 255
 tenecteplase 107, 114, 116
 terpenoids 491, 549
 TERT gene 628
 terutroban 584
 testosterone 537, 540, 544, 548, 553
 tetracycline 714
 TEV 46
 thalidomide 11, 602
 thalidomides 602, 606
 therapeutic antibodies 607
 therapeutic enzymes 1, 11, 13, 15, 30–31, 106, 141, 638, 645, 651, 658
 therapy with living drugs 623
 Thioredoxin 79, 213
 thioridazine 507, 513, 516–517, 526
 Thomsen–Friedenreich (TF) antigen 696, 699
 threonine proteases 211
 thrombin 46, 55, 100–101, 103–105, 122
 thrombin-activatable fibrinolysis inhibitor (TAFI) 100
 thrombin inhibitors 104–105
 thrombolytic drugs 107, 109, 111, 113, 115, 117, 119, 121, 123,

- 125, 127, 129, 131, 133, 135, 137, 139
- plasmin-like 119
- thrombolytic enzymes 102, 108, 119, 124–125, 129, 133, 141
 - algal sources 125
 - bacterial 133
 - earthworm 119
 - fungal 129
 - microbial 119, 141
 - non-microbial 119
 - plant-based 124
 - snake venom 119
- thrombosis 644
- thromboxane-A synthase 106
- thromboxane A2 105, 568, 570–571
- thromboxane A2 (TxA2) 105, 568, 570–571
- thromboxane A2 synthase 570
- thromboxane modulators 583
- thymic stromal lymphopoietin 8
- thymidine phosphorylase 641
- ticagrelor 106
- ticlopidine 106
- tirofiban 106
- tissue plasminogen activator (t-PA) 100, 107, 112, 644
- tissue-type plasminogen activator (PLAT) 107, 254
- TKI 621, 624
- TME, *see* tumor microenvironment
- Tn antigen 699–700
- Tn glycan 699–700
- TNF- α , *see* tumor necrosis factor- α
- tobacco etch virus protease 55
- α -tocopherol 277, 291
- tolfenamic acid 544
- topiramate 81, 83, 89–90
- topoisomerase inhibitors 624
- topotheacan 624
- total antioxidant capacity (TAC) 282
- TP53 mutations 627
- transgenic plants 536
- translation termination factor 602
- transposase 733
- tranylcypromine 401–402, 409–410, 412, 414–416
- TREX-system 731–733
- triphenylphosphonium (TPP+) derivatives 291
- trypanosomiasis 2
- Trypsin 44–46, 212
 - recombinant 44, 46, 213
- tryptamine 434, 486
- tuberculosis 2, 415
- tumor angiogenesis inhibition 229
- tumor cells 176, 191, 603, 606, 617–620, 622–632, 643–644, 652–653, 691, 700, 707
 - multidrug resistance 624
 - stem cell like features 627
 - therapy resistance mechanisms 625, 627
- tumor-initiating cells 627
- tumor microenvironment (TME) 86
- tumor necrosis factor α (TNF- α) 179, 184, 189
- tumor suppressor genes 50, 618
- tumor suppressors 618
- tumor therapy 600
- tumorigenesis 586–587, 707
- tumors 2, 4, 32, 75, 86, 88, 173–174, 178, 187, 191, 597, 600, 617–622, 627–629, 631–632, 640, 648, 655, 662, 696, 699
 - immunotherapies 623
 - patient outcome 622

- treatment 2, 88, 178, 619, 621–622, 631–632, 648
- Turner Syndrome 182
- TxA2, *see* thromboxane A2
- tyramine 408–409, 414, 416, 434, 437, 486
- tyrosine kinase 24, 186, 580, 602, 621, 702, 704
- tyrosine kinase inhibitors 621
- tyrosine kinase pathway 702, 704

- UA, *see* ursolic acid
- ubiquitin-proteasome system (UPS) 598
- ubiquitylation 598–599, 601–602
- UDP-glucuronosyl transferase 34
- UDP-*N*-acetylglucosamine 2-epimerase/*N*-acetylmannosamine-kinase 708
- UGT, *see* uridine diphosphateglucuronosyltransferase
- ulcerative colitis 11–12
- UPS, *see* ubiquitin-proteasome system
- uric acid 251, 269–270, 274–275, 277, 287, 638
- uridine diphosphateglucuronosyltransferase (UGT) 389
- urokinase 107, 110, 112–113, 116, 121–123
- urolithins 491
- ursolic acid (UA) 369, 371, 389

- valdecoxib 84–86
- vancomycin 737
- Vanilla planifolia* 722

- vanillin 524
- vardenafil 293
- Vascular Adhesion Protein-1 398
- vascular cell adhesion molecule (VCAM) 571
- vascular inflammation 258, 571
- VCAM, *see* vascular cell adhesion molecule
- VDEPT, *see* virus-directed enzyme prodrug therapy
- verapamil 382–383, 543, 625
- vesicular reuptake system (VMAT2) 407
- VHL, *see* von Hippel-Lindau
- VHL-recruiting degrader 608
- virtual screening procedures (VSP) 273
- virus-directed enzyme prodrug therapy (VDEPT) 644
- virus-like particles 52, 651
- visomitin 291
- vitamin D 554
- vitamin D2 538, 540, 547, 554
- vitamin K antagonists 103
- VMAT2, *see* vesicular reuptake system
- von Hippel-Lindau (VHL) 601
- von Willebrand factor (vWF) 100
- VSP, *see* virtual screening procedures
- VTNR polymorphism 403
- vWF, *see* von Willebrand factor

- WHO, *see* World Health Organization
- whole genome sequencing 618, 621
- wild-type CYP enzymes 534, 537, 539, 542
- World Health Organization (WHO) 27, 50

- wound healing 100, 179, 232, 234, 237, 696, 701
- X-linked hypophosphataemia 8
- xanthine dehydrogenase 270, 514
- xanthine oxidase 15, 258, 267, 269, 514, 526
- xanthine oxidase inhibitors 15
- xanthine oxidases 249
- xanthine oxidoreductases 507
- Yescarta 5–6
- zeaxanthin 732–733
- zinc finger protein 602
- ziprasidone 523
- zonisamide 81, 83–84, 89–90

“This book is an important addition to the literature in this field. It not only summarizes the importance of enzymes as targets for pharmaceutical drug research in the past but also shows that there is still enormous potential in the future. Motivated by Peter Grunwald, a large group of experts have shared their specialist knowledge. The book a treasure for anyone working or doing research in the field.”

Prof. Theo Dingermann
Goethe University, Germany

“This book represents an outstanding scientific work. It covers the state of the art, challenges, and key achievements of research focusing on the use of enzymes for therapeutic purposes. It discusses the fundamentals of enzyme function and its applications and shows how this fantastic research field has been explored in drug discovery and innovation for gaining a better understanding of enzymes and their use for a better quality of life.”

Prof. Cláudio Viegas Jr.
Universidade Federal de Alfenas, Brazil

This book provides an overview of the world market of therapeutic enzymes and enzyme inhibitors, rare diseases, orphan drugs, the costs of drug development and therapies, and enzymes in downstream processing of pharmaceuticals. It discusses carbonic anhydrase inhibitors and their multiple drug interactions, carboxylesterase inhibitors for pharmaceutical applications, employment of inhibitors for the treatment of neurodegenerative diseases, use of engineered proteins, bioactive peptides, and fibrinolytic enzymes for thrombolytic therapy, and enzymes important for the design and development of new drugs/drug metabolites such as aldehyde oxidases and cytochrome P450 enzymes and the role the latter play in vascular biology and pathophysiology. The treatment of cancer is explored in connection with enzymatic amino acid deprivation therapies and new drugs that act as chemical degraders of oncogenic proteins. The book also introduces the resistance mechanisms of cancer. Furthermore, it provides an insight into the relationship between pathological conditions of cardiovascular disease and oxidative stress. The text also focuses on the potential use of nanoparticles as carriers for enzymes with medical relevance, computer-aided drug design for the identification of multi-target directed ligands, and the development of improved therapeutics through a glycan-“designer” approach. It concludes with an introduction to the chemoenzymatic synthesis of drugs.



Peter Grunwald studied chemistry at the Universities of Saarbrücken and Hamburg, Germany. He graduated in the field of high-frequency spectroscopy and then became a staff member of the Institute of Physical Chemistry. After receiving his PhD in physical chemistry, he founded a biotechnology research group. He was appointed professor in 2001. His research interests focus on immobilized biocatalysts, kinetics of enzymes in organic solvents, and interactions between biocatalysts and heavy metal ions. Prof. Grunwald is also interested in chemical education, including curriculum development. He has authored a textbook on biochemistry and is an editorial board member of *Catalysts*.



JENNY STANFORD
PUBLISHING

V709
ISBN 978-981-4800-61-7



9 789814 800617