

Index

a

AbbVie's multiparametric score
(AB-MPS) 314

ABC transporter superfamily
(ABCB1) 317

Abdegs 37

aberrant splicing 249–255

ABX464 263

AceTAGs 17

adaptor or shuttling proteins 32

all-*trans* retinoic acid (ATRA) 7–8,
152, 153

alpha-synuclein 206, 208–209

alternative splicing (AS) 248, 249

AMP-activated protein kinase
(AMPK) 16, 281

antibody-based PROTACs
(AbTACs) 14, 38, 216

anticancer aryl sulfonamides 186

antisense oligonucleotides (ASOs) 247

apical-basolateral permeability (AB)
296

area under the curve (AUC) 342

Argonaute proteins (Ago1–Ago4) 260

ARV-110 (androgen receptor
degrader) 3, 12, 13, 18, 216, 290,
298, 299, 315, 318, 320,
322, 349–352

ARV-471 12, 13, 18, 291, 298, 299, 315,
322, 323, 349, 350, 353, 354

aryl sulfonamides 32, 136, 180, 183,
185–187, 189, 192, 303

ASO gapmers 260–262

ATP-binding cassette (ABC) 317

autophagosome-tethering compounds
(ATTECs) 177, 216, 277

autophagy-targeting chimeras
(AUTACs) 14, 33, 177, 216, 277

auxin-inducible degron (AID) 5,
29, 47, 32

AZD4785 262

b

bacterial protease-targeting chimeras
(BacPROTACs) 177

baculoviral IAP repeat containing 3
(BIRC3) 223

bait sequence 7

BCR–ABL (ML 2-23) 164, 225, 226

binary equilibrium binding
constants 344

branaplam 252, 253

BRD4-degrading PROTAC MZ1 153

BRD4 (ML2-14) 225

bRo5 compounds 314–316,
331, 339

BromoTag 29, 218

Bruton's tyrosine kinase (BTK) 17,
126, 218

Burkitt's lymphoma cell lines 9

C

- Caco-2 cells 296, 315, 317, 342
- catalytic knockdown 324
- C-degrons 30, 65, 66
- CDK12 inhibitors degrade cyclin K 305–306
- cell-free parallel artificial membrane permeability assay (PAMPA) 342
- cellular degradation systems 26, 28, 50
- cellular inhibitor of apoptosis protein 1 (cIAP1) and BTK 126–127
- cellular machinery controlling protein degradation 2
- cereblon-derived PROTACs 18
- cereblon modulators (CELMoDs) 216
- Chaperone-mediated autophagy (CMA) 28, 209
- chemical knockdown with affinity and degradation dynamics (CANDDY) 33
- chloroalkane penetration assay (CAPA) 342
- chloroquinoxaline sulfonamide (CQS) 187, 303
- C2H2-type zing-finger (ZF) transcription factors Ikaros (IKZF1) 184
- cisternae 47
- clustered regularly interspaced short palindromic repeats (CRISPR)/Cas9 5, 218, 306
- co-crystallization 303
- covalent functionalization followed by E3 electroporation into live cells (COFFEE) 227, 228
- covalently engineered nanobody chimeras 216
- covalent PROTAC 4 218, 220
- covalent protein degraders
 - Bruton's tyrosine kinase (BTK) 218–220
 - DCAF11 231–233
 - DCAF16 229–231
 - E3 ubiquitin ligases 224
 - epidermal growth factor receptor (EGFR) 221–223
 - ERK1/2 221–223
 - estrogen-related receptor alpha (ERR α) 221–223
 - FEM1B 227
 - HaloPROTAC 217–218
 - KEAP1 226–227
 - KRAS G12C 220–221
 - leveraging covalent chemistry 236–237
 - methionine aminopeptidase-2 (METAP2) 218–220
 - monofunctional 223
 - RNF4 224–225
 - RNF114 225–226
 - SPSB2 228–229
 - technologies for discovery 233–235
- CRBN-based androgen receptor (AR) degrader 349
- CRBN-based degraders 9, 298, 339
- CRBN-based estrogen receptor (ER) degrader 349
- cryo-electron microscopy 112, 304
- Cullin1-based E3s assemble 68
- Cullin-4-containing E3 ubiquitin ligase complex CUL4–RBX1–DDB1 254
- Cullin-RING ligases (CRLs) 30, 179, 180, 183, 306
- cullin ring ubiquitin ligases (CRLs) 68, 69, 229
- ϵ CXXCG 135
- cyanoacrylamide-based BTK PROTAC, RC-3 220
- cyanoacrylamide derivative 220
- cyclin K molecular glue degraders 180, 189–192
- CYP3A4 catalysis 320
- cysteine 12 (Cys12) 216
- cytochrome P450's (CYP450s) 153, 319
- cytoplasmatic RNA quality control mechanisms
 - incorrect splicing triggers NMD in the cytoplasm 257–259
 - RNA binding proteins 259–260

RNA interference (RNAi) 260–265
cytoplasmic mRNA degradation 258

d

dBET1 (BRD4 degrader) 216
DCAF11 231–233, 235
DCAF16 217, 229–231, 235
decapping by exoribonuclease protein 1 (DXO1) 255
degradation selectivity 9, 10, 161, 343, 344, 347, 348
degradation tag (dTAG) 218
degrader score (Deg_S) 314, 321
degraders, oral 313–331
degron-independent interactions 65
degronomids 313
degrons 5, 10, 29–31, 41, 47, 65–66, 69, 78, 86, 129, 130, 132–134, 136, 178, 179, 185, 187, 209
DeLinker 166–168
destabilization domains 25, 30, 46, 49
destabilizers 1, 178, 179, 188
deubiquitinases (DUBs) 78, 235, 277
deubiquitinase-targeting chimeras (DUBTACs) 17, 277
dihydrofolate reductase (DHFR) 30
DNA damage-binding protein 1 (DDB1) 138–139, 254
DNA-encoded libraries (DELs) 193
double cluster 159, 161
double minute 2 homolog (MDM2) 297
dovitinib (DOV) 264
DOV RIBOTAC 265
Drosha Ribonuclease III (Drosha)-Microprocessor complex subunit DGCR8 (DGCR8) 260
drug–drug interactions (DDI) 315, 318, 319
druggable protein targets 245
drug metabolism and pharmacokinetics (DMPK) 3, 296, 339
drug target binding 326
dystrophia myotonica protein kinase (DMPK) 255

e

E1-activating enzyme (E1) 63
E2-conjugating (E2) enzyme 63, 68
E3-agnostic positive selection assay 192
E3-ligase (E3) enzyme 63, 155
E3 ubiquitin ligases 224
 activity 66–67
 substrate recruitment & degron recognition 65–66
 ubiquitin code and targeted protein degradation 63–65
efflux ratio (ER) 317
endocytosis 35–38, 47, 49, 50
enoxacin 262, 263
epidermal growth factor receptor (EGFR) 15, 221–223
ER-associated protein degradation (ERAD) 39–46
ERK1/2 221–223
ER-localized substrate proteins 41
ER-to-lysosome-associated degradation (ERLAD) 46
estrogen receptor (ER) 2–4, 30, 298, 299, 322, 323, 349
estrogen receptor (ER α) 178
estrogen-related receptor alpha (ERR α) 9, 222
eukaryotic mRNAs, life cycle of 247–248
event-based pharmacology 345
event-driven pharmacology 1, 215, 263, 293, 323, 343
exonic splicing enhancer (ESE) 251, 252
exon junction complex (EJC) 249, 251, 257
exon ligation 248, 251
extended clearance classification system (ECCS) 317

f

FcRn receptor 37
FEM1B 227, 229
12-kDa FK506-binding protein (FKPB12) 30
focal adhesion kinase (FAK) 121–122

- fuchs endothelial corneal dystrophy (FECD) 255
- fulvestrant 3–6, 11, 178, 290, 349, 354
- g**
- Gartner hype cycle 273
- GastroPlus 330
- GlaxoSmithKline (GSK) 120, 344
- global proteomics 208, 209, 348
- GLTSCR-containing BAF complex (GBAF) 290
- GlueBody 216
- glue-like mechanism 184, 188
- gold rush 3, 19
- G protein-coupled receptors (GPCRs) 245
- green fluorescent protein (GFP) 5, 208, 262
- h**
- β -hairpin loop structure 185
- HaloPROTAC 217–218
- HaloPROTAC-E-induced VPS34 degradation 218
- Halo-tagged programmed cell death protein 4 (PDCD4) 282
- HaloTag protein 5
- H-bond donor (HBD)/H-bond acceptor (HBA) 297–298, 341
- heavy atom (HA) count 298
- HECT E3s 76
- definition and discovery 73
- insights 79
- regulation 75–78
- structure and mechanism 74–75
- subgroups 73–74
- Helios (IKZF2) 133–134, 192–193
- hereditary transthyretin amyloidosis (hATTR) 261
- heterobifunctional 153
- protein degradation beyond cancer 273–275
- proteolysis targeting chimera (PROTACs) advantageous 275
- BET proteins 275
- degradation of extracellular proteins 279
- highjacking autophagy 277
- inspired technologies 277
- modulating phosphorylation 281–282
- oligonucleotides as recruiting elements 276
- PTMs 283
- RNA degradation 281
- structures of 276
- targeted acetylation 282
- heterobifunctional degraders 186, 206, 216, 223, 298, 321, 323, 337, 339, 342, 342, 344, 348, 349, 355
- heterobifunctional targeted protein degraders
- kinases and HDACs 210–211
- misfolded proteins
- alpha-synuclein 208–209
- mHtt 209–210
- tau 206–208
- TDP-43 210
- heterogeneous nuclear ribonucleoproteins (hnRNPs) 249
- ^{15}N -heteronuclear-single-quantum-coherence (HSQC) 112
- highjacking autophagy 277–279
- HOIL-1L interacting protein 85
- hook effect 110, 301, 302, 325, 326, 343, 344
- human aldehyde oxidase (hAOX) 320
- huntingtin (HTT) proteins 33, 34, 41, 206, 209, 252, 277
- Huntington's disease 14, 206, 209–211, 252
- hydrogen bond donors (HBD) 168, 298, 299, 314, 339
- hydrophobic tagging (HyTag) 2, 5, 30, 36, 38, 46, 49, 208, 210, 216, 236
- hyponeddylated cells 305, 306
- hypoxia-inducible factor 1α (HIF1 α) 65, 260

i

ibrutinib-based PROTACs 220
 ibrutinib-thalidomide PROTAC 220
 Ikaros (IKZF1) 10, 132, 184, 192, 302
 immune modulatory imide drugs
 (IMiDs) 32
 immunosuppressants cyclosporin A
 (CsA) 301
 Inclisiran 261, 262
 Indisulam 10, 32, 137, 183, 185–187,
 254, 265, 303
 inhibitor of apoptosis proteins (IAP) 3,
 7, 126, 293, 297, 339
 Inotersen 262
 interleukin-1 receptor-associated kinase 4
 (IRAK4) 274
 intraluminal vesicles (ILVs) 36
in vitro ADME assays 342
in vitro-in vivo correlation (IVIVC)
 342
 iodoacetamide (IA)-alkyne 224, 233
 isothermal titration calorimetry
 (ITC) 112
 isotopic tandem orthogonal proteolysis-
 activity-based protein profiling
 (isoTOP-ABPP) 229, 233

k

KEAP1 208, 226–227, 229
 kinetic-proofreading 326–328, 344–346
 KRAS G12C 216, 220–221
 Kymera Therapeutics 305, 352
 Kynamro® 262

l

lenalidomide 10, 129, 130, 132, 133, 135,
 136, 163, 184–186, 205, 215, 218,
 300–302, 348
 Leqvio® 262
 lewy body dementia (LBD) 208
 ligand-centric approach 157
 linear degrons 65
 linear ubiquitin chain assembly complex
 (LUBAC) 85
 Lin-28 homolog A (LIN28A) 259

Lipinski's rule of five 12, 222, 223,
 307, 314
 lipophilicity 11, 296–298, 314, 315, 318,
 341, 342
 lipophilic permeability efficiency
 (LPE) 316
 LLC-PK1 315
 lysosomal targeting 27–28, 37, 47–49
 lysosome targeting chimaeras (LYTACs)
 14, 15, 18, 36, 37, 48, 50, 177, 216,
 279, 280

m

major histocompatibility class I (MHC-I)
 complex 45
 malignant rhabdoid tumors 290
 MDCKII 315
 messenger ribonucleoprotein particles
 (mRNPs) 258
 methionine aminopeptidase-2
 (METAP2) 218
 MG ternary structure 142
 microRNAs (miRNAs) 13, 246, 260–263
 microtubule formation 182
 mipomersen 262
 molecular degrader of extracellular
 proteins through (MoDE-As) 37
 molecular degraders of extracellular
 proteins through the
 asialoglycoprotein receptor
 (MoDE-As) 216
 molecular glue 10, 178, 211
 natural compounds, 179–182
 synthetic compounds, 182–183
 molecular glue degraders 178, 182, 300
 aryl sulfonamides 303
 BCL6 degrader BI-3802 303–304
 NX-2127 and KT-413 304–305
 rational discovery
 screening-based discovery 305–306
 target-based discovery 306
 to glue or not to glue 307
 thalidomide analogs 301–303
 molecular glues recruiting
 cereblon (CRBN)

- C2H2 zinc fingers
 - Helios (IKZF2) 133–134
 - Ikaros (IKZF1) 132
 - SALL4 134–135
 - ZNF692 132–133
 - CK1 α 129–130
 - GSPT1 130–131
 - molecular glues recruiting, E3 ligases
 - DDB1 and CUL4 Associated Factor 15 (DCAF15) and RBM 39 137
 - DNA damage-binding protein 1 (DDB1) and CDK12 138–139
 - molecular mechanism 2, 34, 40, 47–50, 348
 - molecular operating environment (MOE)'s 140, 158
 - monofunctional degraders 216, 223
 - monofunctional protein degraders 223
 - monomeric RING E3 ubiquitin ligases 70
 - monovalent and bivalent degraders 1
 - monovalent degraders 178, 179, 188, 192
 - muscleblind-like 1 protein (MBNL1) 255
 - mutant Huntingtin (mHtt) 14, 33, 34, 206, 209, 277
 - myotonic dystrophy type 1 (DM1) 255
- n**
- N-degron 65, 66
 - neosubstrates 10, 16, 17, 32, 65, 86, 87, 129, 130, 132, 134–136, 138, 139, 151–155, 157, 158, 160–163, 178, 282, 301, 303–305, 348, 349
 - neuronal precursor cell-expressed developmentally down-regulated protein 8 (NEED 8) 69
 - next-generation sequencing (NGS) 245
 - nimbolide 225, 226, 233
 - noncanonical BAF (ncBAF) 290
 - non-covalent PROTAC 7, 218, 220, 224
 - non-native substrates 163, 189, 347, 348
 - nonsense mediated decay (NMD) 246, 249, 257
 - nonstoichiometric agents 293
 - nuclear cap binding protein (CBP) complex 247
 - nuclear cap-binding protein subunit 1 247
 - nuclear cap-binding protein subunit 2 247
 - nuclear magnetic resonance (NMR) experiments 111, 304
 - nuclear RNA decay 248, 255, 257
 - nusinersen (Spinraza[®]) 252
- o**
- 2'-OMe or 2'-methoxyethyl (2'-MOE) 260
 - Onpattro[®] 261
 - open reading frame (ORF) 248
 - oral degraders
 - clearance rate 319–320
 - drug–drug interactions (DDI) 319
 - gaps and future perspectives 330
 - oral absorption 320–323
 - permeability 315–316
 - pharmacological processes of degraders and PK/PD aspects 323–324
 - physicochemical properties 314–315
 - PK/PD considerations during drug discovery and development 324–329
 - plasma protein binding (PPB) 318
 - solubility 318
 - translational PK/PD and human dose prediction for targeted protein degrader 330
 - transporters 317–318
 - organic-anion transporting polypeptide (OATP) transporters 317–318
- p**
- parallel artificial membrane permeability assay (PAMPA) 315, 342
 - PatchDock algorithm 159
 - Patisiran 261

- Penetrex® 262
- pentapeptide targeting motif
(KFERQ) 209
- peptide-based approaches 208–210
- peptide degron 209
- perfusion-limited PBPK model 330
- pharmacodynamics 217, 293, 313, 320,
323, 324, 328, 337, 342–347, 349,
352, 355
- pharmacokinetic (PK) 3, 12, 153, 165,
211, 220, 223, 289, 293, 296, 313,
318–320, 322, 323, 328, 330, 339,
341–342, 344, 352
- pharmacokinetic DDIs 319
- pharmacokinetic–pharmacodynamic-
efficacy (PK–PD-*efficacy*) 342
- phosphatase recruiting chimeras
(PhoRCs) 15, 282
- phosphodegrons 31, 65, 188
- 2',5'-phosphodiester-linked
oligoadenylates (2'-5'As) 264
- phosphorylation inducing chimera
(PHICS) 31, 281
- phosphorylation targeting chimeras
(PhosTACs) 16, 31, 282
- physicochemical properties 12, 16, 165,
211, 273, 296–299, 301, 304,
313–316, 319, 321, 322, 330, 337,
339–340, 355
- PK/PD considerations during drug
discovery and
development 324–329
- plasma protein binding (PPB) 315, 318,
330, 342
- poly(ADP-ribosylation)/PARylation 67
- poly(ADP-ribosylation) polymerase 67
- polyglutamine (polyQ)-containing mutant
HTT protein 252
- poly(lactic-*co*-glycolic acid) (PLGA) 293
- polyubiquitylation of proteins 63
- post-translational modification (PTM) 1,
16, 29, 31, 37, 47, 77, 78, 273, 283
- precursor (pre) messenger (m) RNA
(pre-mRNA) 245
- predator system 18
- premature termination codons
(PTCs) 249
- prostate-specific antigen (PSA)
levels 349
- PROTAC7 330
- PROTACable genome 292
- PROTAC degraders 115, 127–128, 233
- PROTAC-induced ternary complex
structures
- VHL and BRD4
BRD4^{BD1} 117–118
BRD4^{BD2} 115–117
- VHL and FAK 121–122
- VHL and SMARCA 118–120
- VHL and WDR5 122–123
- PROTAC-mediated degradation of
splicing factor 3B1 (SF3B1) 254
- PROTAC-Model 140, 161
- PROTAC-O4I2 254
- PROTAC® protein degraders
clinical case studies 349–355
in vitro ADME assays 342
pharmacodynamics 343–347
pharmacokinetics 341–342
physicochemical properties
339–340
toxicology 347–349
- protein-centric approach 157–159,
245, 265
- protein coding sequence (CDS) 248
- protein degradation probes (PDPs) 317
- protein degraders 1–6, 18, 107, 205–210,
215–237, 274, 313, 314, 319, 324,
330, 337–355
- protein homeostasis 1, 25, 35, 177
- protein kinase C (PKC) 16, 281
- protein of interest (POI) 1, 5, 107, 151,
178, 179, 190, 215, 297, 299, 300,
302, 320, 323, 324, 337, 343, 344
- protein phosphatase 2 (PP2A) 282
- protein–protein interactions (PPIs) 3,
10, 66, 67, 107, 154, 157, 159, 163,
179, 216, 245, 300, 306, 343
- protein quality control (PQC)
machinery 29, 48, 66, 72

- proteolysis targeting chimeras (PROTACs)
 activity and early examples 152
 advantageous 275
 BET proteins 275
 computationally designing and optimizing 164–168
 degradation of extracellular proteins 279
 design and optimization 162–164
 drug discovery in
 increase in, potency 293
 prolonged duration, of effect 293–294
 selective inhibition, of isoforms 292
 targeting proteins 289–292
 hijacking autophagy 277–279
 inspired technologies 277
 modulating phosphorylation 281–282
 oligonucleotides as recruiting elements 276
 routes of application 294–296
 rule-of-five 152
 structures of 276
 substoichiometric amounts of 152
 tackling DMPK challenge 296–300
 ternary complexes 153–156
 ternary structure 141
 proximity-induced protein degradation 300
 Pumilio-rich elements (PRE) 259
- R**
- RBR E3 ligases 27, 85
 receptor-mediated endocytosis 37
 receptor tyrosine kinases (RTKs) 38, 258
 regulatory target recruitment 26, 28–31
 ribonuclease targeting chimeras (RIBOTAC) 13, 263, 281
 ribonucleoprotein (RNP) 248, 249, 258
 Ring1 (Really Interesting New Gene 1) 67
 RING domain-containing protein 68
 RING E3 ligases
 definition and discovery 67–68
 insights into regulation and function 72–73
 subgroups 68–72
 RING–IBR–RING (RBR) 85
 RING-type zinc-finger (RNF)
 domain 70
 Risdiplam (Evrysdi®) 252, 265
 Risdiplam's MoA 252
 RNA binding Fox-1 homolog 1 (RBFox1) 259
 RNA binding proteins 246, 248, 254, 259, 263, 276
 RNA interference (RNAi) 245, 260, 281
 RNA recognition motif 2 (RRM2) domain 254
 RNA repeat expansions 255
 RNF4 70, 183, 224–225, 229
 RNF114 183, 225–226, 229, 233
 Rosetta software 160
 round the clock occupancy-based inhibition 347
- S**
- S37 mutant β -catenin 306, 307
 SC formulation 345
 scientific vector language (SVL) 158
 SD-36 (STAT3 degrader) 216
 selected off-target proteome (SOTP) 348
 selective estrogen receptor degraders (SERDs) 2–3, 30
 serine and arginine-rich (SR) proteins 249
 Shield-1 (48–50) 30
 short interfering (siRNAs) 260
 SimCyp 330
 Skp1-Cullin-F box (SCF) complex 6
 small molecule-assisted shutoff (SMASH) methodology 30
 small-molecule-based targeted protein degraders 107

- small-molecule protein
 - degraders 1, 3
 - small molecules (SMOLs) 1–10, 16, 18, 19, 29–31, 33, 65, 66, 77, 86, 87, 107, 152, 156, 177, 182, 186, 188, 189, 193, 205, 206, 208, 209, 211, 215, 216, 224, 225, 227, 247, 254, 255, 262, 279, 281, 289, 292, 296, 298–300, 306, 307, 313–315, 319, 323, 324, 330, 337, 341, 342, 348, 355
 - small nuclear RNAs (snRNAs) 248
 - SMOL-ASO conjugates 247, 263
 - SMOL chimeric probes 247
 - soluble decoy RTKs (sdRTKs) 258
 - solute carrier (SLC) transporters 38, 317
 - spalt-like transcription factor 4
 - (SALL4) 134
 - specific and nongenetic IAP-dependent protein erasers
 - (SNIPERs) 126, 216
 - splice switching oligonucleotides (SSOs) 253
 - splicing regulation 249–252
 - SPSB2 227, 229
 - stable ternary complex formation 156, 300, 326, 347
 - survival of motor neuron 2
 - (SMN2) 252
 - sweeping antibodies 14, 36, 37
 - switching gears 2
 - synovial sarcomas 290
 - SyntaLinker 167, 168
 - synthetic molecular glue
 - degraders
 - BCL6 degraders, 188
 - hijacking CRL4CRBN
 - broad target
 - accommodation 184–186
 - high shape
 - complementarity 186–187
 - intentional developments
 - β -catenin molecular glue
 - degraders 188–189
 - cyclin K molecular glue
 - degraders 189–192
 - prospective discovery of IKZF1 192
 - structure-guided development, of Helios (IKZF2) 192–193
- t**
- tandem mass tag (TMT)-ABPP-based method 233
- tankyrase (TNKS) 67
- targeted protein degradation (TPD) 177, 215, 307
 - cytosol and the nucleus
 - engaging the proteasome 32–33
 - regulatory target recruitment 29–31
 - ubiquitination machinery 31–32
 - development of
 - fulvestrant 4–6
 - human clinical trials 11–13
 - molecular glues 10
 - PROTACs 6–7
 - proteasome 13–14
 - small molecule degraders achieve in vivo PoC 8–9
 - SNIPERs and peptidomimetic VHL binders 7–8
 - endoplasmic reticulum (ER)
 - ERAD 39, 45–46
 - ERLAD 46–47
 - Golgi apparatus 47–49
 - field of 2
 - heterobifunctional targeted protein degraders 206
 - lysosomal targeting 27–28
 - lysosomes 33–34
 - molecular glues 211
 - plasma membrane (PM) and the extracellular space
 - endocytosis 35
 - ubiquitination 37–39
 - UPS 26–27
- targeted protein degraders 107, 205–210, 313, 324, 330

- target protein removal 324
 - TDP-43 210
 - Tegsedi® 262
 - ternary complexes of PROTAC- and MG-induced complexes
 - affinity and cooperativity 108–110
 - binding pose 108
 - biophysics 111–112
 - flexible 111
 - mechanism of degraders through ternary complexes 108
 - plasticity 110–111
 - prediction of 140
 - principle 143
 - residency 110
 - stoichiometry 110
 - structural biology 112–113
 - thalidomide 8, 10–12, 18, 32, 124, 129, 130, 132, 134, 135, 163, 178, 183–186, 220, 221, 254, 301–304, 317, 341, 348
 - time-resolved fluorescence energy transfer (TR-FRET) 192
 - toxicology 347–349, 355
 - transcription factor 4 (TCF4) 134, 255
 - transcription factor targeting chimeras (TRAFTACs) 216
 - transcriptome-wide splicing regulation 251
 - translational PK/PD and human dose prediction for targeted protein degrader 330
 - transporters 28, 294, 299, 315, 317–320, 330
 - Trim-away 216
 - trimethoprim (TMP) 30
 - tristetraprolin (TTP) 259
 - triptophan pocket 129
 - trough of disillusionment 273, 277
- u**
- ubiquitination machinery 26, 29–32, 34, 38, 39, 47, 108, 110
 - ubiquitination pathway 151, 152
 - ubiquitination, PM 37–39
 - ubiquitin code and targeted protein degradation 63–65
 - ubiquitin conjugating enzyme (E2) 151
 - ubiquitin E3 ligases targeting Golgi 41, 48
 - ubiquitin–proteasome system (UPS) 26–27, 177, 215, 324, 326
 - ubiquitin protein ligase (E3) 74, 75, 313
 - ubiquitin variants (UbVs) 77
 - U-Box 72
 - undruggable target space 313
- v**
- vascular endothelial growth factor 2 (VEGFR2) 259
 - von Hippel–Lindau disease tumor suppressor (VHL) ubiquitination complex 260
 - von Hippel–Lindau (VHL)-degraders 316
 - von Hippel–Lindau protein (VHL) 114
 - Bcl-xL 120
 - BRD4^{BD1} 117–118
 - BRD4^{BD2} 115–117
 - focal adhesion kinase (FAK) 121–122
 - SMARCA 118–120
 - Von Hippel–Lindau tumor suppressor (VHL) 65, 297
- w**
- Western blot analysis 5, 218
- z**
- zinc finger protein 692 (ZNF692) 132–133