

Index

a

- Abatacept (Orencia™) 497
- absorption 313–315
- AB toxins reengineering 675
- activation-induced cytidine deaminase (AID) 95, 99
- adalimumab 35, 320, 505
- adaptive immunity
 - antigen processing 393–397
 - antigen properties of 399–400
 - immunological tolerance 400–402
 - MHC-peptide complexes 397–398
 - protein engineering 398–399
- adcetris 279–281
- ADCT-301 296
- additional cell surface antigens 539
- ADP-ribosylating toxins 235
- adsorptive-mediated transcytosis (AMT) 666
- affibodies 169–171
- affinity chromatography 441–442
- AHo numbering scheme 55
- airflow obstruction 588
- airway hyperresponsiveness 588
- alemtuzumab 343
- allergic reaction 590
- alternate hit/lead discovery
 - approaches 352–354
- alternative mammalian cell hosts 428
- amphibians 97
- amyloid beta (A β) 196
- amyloid-processing enzyme
 - BACE-1 667
- AnaptysBio 134
- “anchored periplasmic expression” (APEX) 132
- andexanet alfa
 - action, mode of 628
 - immunogenicity 631
 - safety 629, 630
 - studies in patients 629
 - studies in volunteers 628
- Ang2 \times VEGF-A (vanucizumab) 568
- angiopep-2 668
- anifrolumab 510
- animal disease models 363–364
- anti-anthrax approach 635
- antibacterial immune therapy 612
- antibodies 273
 - anti-methamphetamine 631
 - chain shuffling 193
 - isotypes 56–58
 - numbering schemes 54, 55
 - retroviral B-lymphocyte display “Retrocyte Display®” 136
- antibodies from other species
 - amphibians 97
 - camel 94
 - cat/dog 88, 90
 - chicken 95
 - cow 91–92
 - pig 91
 - rat and mouse 86–89
 - sauropsida 97

- antibodies from other species (*contd.*)
 - shark 99
 - teleost 98
- antibody diversity
 - CDR-H3 diversity 65–66
 - germline VH-VL pairing 66, 67
 - junctional diversity 64, 65
 - somatic hypermutation 64
 - VDJ/VJ recombination 64, 65
- antibody fragments 316
 - Fab and Fv 61–62
 - Fc structure and fragments 56, 60, 62, 63
 - variable and constant domains 59–61
- antibody targeting of receptor tyrosine kinases (RTKs) pathways 522
- antibody therapeutics
 - development 25–27
 - future directions 45–46
 - from killing bacteria to killing human cells 43–44
 - monoclonal antibody therapeutics 33–34
 - neutralization 42–43
 - polyclonal antibodies 26, 33
 - targeting membrane receptors 44–45
- antibody-dependent cell phagocytosis (ADCP) 62
- antibody-dependent cellular cytotoxicity (ADCC) 62, 208, 209
- antibody-drug conjugates (ADCs) 683
 - adcetris 279–281
 - ADCT-301 296
 - antibody 273
 - antigen 276
 - assembling 278–279
 - duocarmycins 296–299
 - gemtuzumab ozogamycin 283
 - govitecan 291–292
 - internalisation and trafficking 277–278
 - Kadcyla 281–283
 - linker 275
 - mafodotin 286–287
 - maytansinoids 287–288
 - MEDI4276 300–301
 - mertansine 288–289
 - ozogamicin 290–291
 - pyrrolobenzodiazepines (PBDs) 292–293
 - ravtansine 289–290
 - rovalpituzumab tesirine 295–296
 - soravtansine 290
 - talirine 293–295
 - tesirine 295
 - tubulysins 299
 - vedotins 284–286
- anti-CD20
 - atumumab 35
 - rituximab 31
- anticoagulant drugs 625
- anti-digoxin Fab 622
 - action, mode of 623–624
 - cost considerations 624–625
 - dose considerations 624
 - safety 625
 - studies in patients 625
 - studies in volunteers 624
- anti-drug antibody (ADA) 320
- antidotes 622
- anti-human CD20-mouse IFN α immunocytokine 240
- anti-human lymphocyte function associated antigen-1 (LFA-1) antibody 196
- anti-infective monoclonal antibodies 617
- anti-interleukin (IL)-1 based therapies 498
- anti-interleukin (IL)-1 α mAb Xilonix™ 128
- anti-interleukin (IL)-2 receptor daclizumab 31
- anti-interleukin (IL)-4/IL-13 therapies 503
- anti-interleukin (IL)-5

- efficacy and safety 602
 - programmes 601
 - targeted treatments 600–602
 - anti-interleukin (IL)-6 therapies 498–499
 - anti-interleukin (IL)-12/IL-23 therapies 501
 - anti-interleukin (IL)-17 therapies 502
 - antigen 276
 - cancer stem cell specific 277
 - processing 393–397
 - properties of 399–400
 - antigen-binding fragment (Fab) 31
 - antigen presenting cells (APCs) 590
 - antigen-specific human mAbs
 - B cells types 127
 - clinical trials 128–130
 - fragments of 322–323
 - recovery and isolation 126–127
 - strategies 128
 - antigen-target associated factors 318
 - anti-lysozyme model antibody D44.1 195
 - anti-methamphetamine antibodies 631
 - anti-PCSK9 antibody 208
 - anti-TNF- α therapies 505
 - anti-toxins 631
 - envenoming, epidemiology of 633
 - generation of 634
 - history 632
 - immunoglobulin design, effects of 633
 - safety and tolerability 637
 - specificity 635
 - anti-tumor immunity 552
 - anti-venoms 631
 - envenoming, epidemiology of 633
 - generation of 634
 - history 632
 - immunoglobulin design, effects of 633
 - safety and tolerability 637
 - specificity 635
 - asthma 588–590
 - biomarker 591–593
 - DREAM study 599
 - extrinsic 590
 - intrinsic 591
 - phenotypes of 590–591
 - Th1 pathway 593–594
 - Th2 pathway 594–595
 - atopic dermatitis (AD) 502–503
 - ATP-binding cassette (ABC) efflux transporters 666
 - autologous cell therapies 402–403
 - Avimers 172–173
 - azithromycin 594
- b**
- bacterial antibody display (BAD) system 132
 - bacterial display 132
 - B cell acute lymphoblastic leukemia (B-ALL) 403
 - B cell depletion therapies 499–500
 - benralizumab 600
 - benzylalcohol 480
 - beta-2 adrenergic receptor 589
 - B7-H3 550
 - bilin-binding protein (BBP) 167
 - binary toxin 236
 - Biologics Price Competition and Innovation (BPCI) Act 645, 648
 - biomarker
 - asthma 591
 - of eosinophilic inflammation 593
 - biosimilars 645
 - approvals 651–653
 - challenges and future trends 656–658
 - definition and interpretation of 647–648
 - development of 645, 653
 - generic small molecule drugs compared with 645

- non-clinical and clinical studies 655–656
 - products 652
 - quality 654–655
 - rationale and significance
 - cost reduction, potential for 648–650
 - opportunity to reduce cost, scale of 650–651
 - regulatory pathways for 653–654
 - biotinylated-BACE1 peptide inhibitor 671
 - bispecific antibodies
 - additive and synergistic effects 247
 - in clinical development 558
 - foreign molecules, clearance of 248
 - format 232
 - hematological malignancies 561–563
 - immunocytokines 255–257
 - immunotoxin 249–255
 - and multispecific biologics 681
 - receptor targeting 249
 - re-directed cytotoxicity 247
 - RG6013 248
 - solid tumors 563–566
 - therapeutic agents, targeted delivery of 248
 - two receptor pathways, dual targeting of 566–568
 - bispecific anti-TNF/IL-17A FynomAb (COVA322) 166
 - bispecific T cell engagers (BiTE) 365, 375
 - blinatumomab 323
 - block mutagenesis 191–192
 - botulinum neurotoxin (BoNT) 197, 676
 - broadly neutralising antibodies (bNAbs) 198
 - brodalumab 593
 - bronchospasm 589
 - butyrylcholinesterase (BChE) 631
- C**
 - camels 94
 - Canakinumab (Ilaris™) 498
 - cat/dog 90
 - cathepsin B 275
 - catumaxomab 32
 - CD4+ effector memory T-cells 346
 - CD27 (TNFRSF7) 556
 - CD28 receptors 325
 - CD40 ligand 555–556
 - CD137 (4-1BB) 554–555
 - CDR-H3 loops 70–72
 - cell lysate 430
 - cell-penetrating peptides (CPPs) 677
 - central nervous system
 - ADME 670–671
 - alternative BBB transporter targets 671
 - challenge 664–665
 - nature's solution 665–666
 - opportunity 663–664
 - path to the clinic 671
 - preclinical studies 669–670
 - targeting pathways 666–669
 - certolizumab 323, 505
 - cetuximab antigenicity 400
 - checkpoint inhibitors
 - cytotoxic T-lymphocyte antigen-4 (CTLA-4) 542–545
 - lymphocyte activation gene-3 548–549
 - programmed death-1 (PD-1) and PD-1 ligand 545–548
 - chemical degradation 470
 - chicken 95
 - chimeric and humanized mAbs 34
 - chimeric antigen receptor (CAR) T cell therapy 403, 688
 - Chinese hamster ovary (CHO) cells 425–428
 - cell engineering 439
 - directed evolution methodology 449–450
 - folding and assembly machinery 446

- gene editing 449
 - glycosylation pathways 447–449
 - miRNAs 450
 - programmed cell death 446
 - secretory pathway 447
 - unfolded protein response 447
 - CHOmics 424
 - chronic infection, immunomodulatory agents for 618
 - chronic obstructive pulmonary disease (COPD) 594, 606
 - Churg Strauss syndrome 607
 - clinical and marketed antibodies 140–141
 - clinical proof-of-concept 410–411
 - Clostridium difficile* infection 27, 95
 - monoclonal antibodies for 616
 - colony stimulating factor 1 receptor (CSF1R) and KIT 533
 - complementarity-determining regions (CDR)
 - CDR H1 loop 69, 71
 - CDR H2 loop 71
 - CDR L1 loop 68–70
 - CDR L2 69, 70
 - CDR L3 70, 71
 - complement-dependent cytotoxicity (CDC) 62, 208, 209, 343
 - constitutively-expressed endogenous genes 434
 - container closure integrity (CCI) 474
 - container closure system (CCS) 473
 - co-stimulation, inhibition of 497–498
 - cow 91–92
 - cross-reactivity study 366–367
 - cryopyrin associated periodic syndrome (CAPS) 498
 - “cryptic” B cell epitopes 406–407
 - CTLA4-Ig 198
 - C-type lectin receptors (CLR’s) 390
 - CXCR2 receptor 594
 - cyclotides/cystine knot peptides 173–174
 - cytokine blockers 606
 - cytokine release syndrome (CRS) 403
 - cytokine storm 347–348
 - cytoplasmic proteins 391
 - cytotoxic T-lymphocyte associated Ag-4 (CTLA4) 198, 542–545
 - cytotoxic T-lymphocyte-associated protein 4 (CD152/CTLA-4) 497
- d**
- daclizumab 319
 - damage-associated molecular patterns (DAMPs) 391
 - deamidation 470
 - degradation, oxidative 479
 - degrading enzymes 623
 - dendritic cells 388–390
 - designed ankyrin repeat proteins (DARPs) 169–170
 - digoxin 622, 623
 - diphtheria toxin (DT) 235, 674
 - direct oral anticoagulants (DOACs) 625
 - directed evolution methodology 449
 - disease modifying anti-rheumatic drugs (DMARDs) 496
 - disulfide-rich scaffolds 172
 - A-domain binders 172–173
 - cyclotides/cystine knot peptides 173–174
 - kringle domain 174–175
 - Kunitz domain 172, 175–176
 - DLL4 × VEGF-A (OMP-305B83) 568
 - DMF5 YW 197
 - dose-dependent exposure 326
 - dose levels, selection of 369
 - DR5 × FAP (RG7386) 568
 - DREAM study, asthma 599
 - Drug Price Competition and Patent Term Restoration Act 646
 - drug product development 471
 - container closure system 473
 - challenges with 473–475

- drug product development (*contd.*)
 - product requirements 472–473
- dual variable domain-immunoglobulin (DVD-Ig) 233, 370
- duocarmycins 296–299
- dupilumab 503, 603, 604

- e**
- early recombinant protein
 - therapeutics
 - genetic engineering, birth of 4–6
 - human insulin gene clone 6–9
 - insulin 3
 - recombinant hepatitis B virus vaccine 18
 - recombinant human growth hormone 12–14
 - recombinant human interferons 14–16
 - recombinant tissue-type plasminogen activator 17–18
 - semisynthetic human insulin 9–11
 - yeast recombinant insulin 11–12
- EcoR1 5
- efalizumab 319
- effector function, IgG
 - ADCC 209, 212–213
 - beyond CD16A and C1q 213
 - CDC activity enhancement 203, 211–212
 - CDC activity reduction 212–213
 - general considerations 208
 - glycoengineering 210–211
 - protein engineering 203, 210
- EGFR x HER3 566
- Eligen technology 689
- embryo fetal development and pre and postnatal development 372–374
- emtansine (DM-1) 281
- engineered AB toxin system 676
- engineered bispecifics
 - ADP-ribosylating toxins 235
 - applications and clinical studies 246–249
 - binary toxin 236–237
 - bispecific antibody format 232–233
 - continuing evolution of 229
 - functional moieties, by addition of 231–232
 - IL-2 family 238–239
 - multi-domain toxins 234–236
 - non-IL-2 family cytokines 239
 - pharmacokinetic/pharmacodynamic properties 244
 - physicochemical properties and manufacturability 246
 - single domain toxins 233–234
 - tumor antigen, antibody, and fusion strategy, selection of 241–244
 - tumor necrosis factor 240
 - type I IFNs 239–240
 - type II RIPs 235
- engineered protein scaffolds
 - affibodies 169–171
 - alternative scaffolds, advantages of 177
 - DARPinS 169–170
 - lipocalins/anticalins 165, 167
 - mixed secondary structure without disulfides 172, 176
 - monobodies 164–166
 - motivation 163–164
 - nanobodies/VHH domains 165, 167–169
 - pharmacological properties 177–178
- envelope glycoproteins (Envs) 198
- enzyme-linked immunosorbent assay (ELISA) 333
- enzymes, degrading 623
- EPHR family 536–537
- epidermal growth factor receptor (EGFR) 529–530
- epigenetic regulatory elements 436
- EPO-induced immunogenicity 388

epratuzumab 508–50
 ErbB family 522–529
 erythropoietin (EPO) 16–17, 358
 etanercept (Enbrel®) 31
 etrolizumab 506
 expressed Chinese hamster elongation
 factor 1 alpha (CHEF1 α) gene
 434
 extrinsic asthma 590

f

familial hypercatabolic
 hypoproteinemia 318
 Fc engineering
 beyond the IgG-FcRn affinity
 component 202
 FcRn 199–203
 general considerations 199
 IgG binding 200–201
 improved IgG-FcRn affinity and
 serum half-life 201
 serum half-life improvement
 204–208
 YTE mutations 203–204
 Fc fusion proteins 36–42
 Fc hetero-dimeric bsAbs 233
 Fc neonatal receptor (FcRn)
 199–203, 273
 mediated salvage pathway
 317–318
 recycling pathway 315
 FDA-approved therapeutic proteins
 313
 Fenton reaction 479
 fertility 372
 FGFR2 535
 FGFR2b 535
 FGFR3 535
 Firmagon® (deca-peptide) 486
 first in human (FIH) to registration
 cross-reactivity study 366–367
 dose levels, selection of 369
 embryo fetal development and pre
 and postnatal development
 372–374

fertility 372
 genotoxicity and carcinogenicity
 374
 immunogenicity 370–371
 immunotoxicity 371
 in vivo studies 367–368
 pharmacokinetics/
 pharmacodynamics 369–370
 safe starting dose 374–375
 safety pharmacology assessments
 367
 first-time-in-human studies
 409–410
 fish 98
 fluorescence-activated cell sorting
 analysis 332
 follow-on biologics, *see* biosimilars
 forced expiratory volume in one
 second (FEV1) 588
 Forkhead box P3 (Foxp3) 393
 fractional exhaled nitric oxide (FeNO)
 592
 fully human antibodies 34–36
 Fyn SH3 domain 166

g

gemtuzumab ozogamicin 31, 283
 gene editing 449
 gene encoding p40 (IL-12B) 501
 gene targeting 432
 genetic engineering 4–6
 GeneXpert® system 618
 genotoxicity and
 carcinogenicity 374
 germline VH-VL pairing 66, 67
 glial-derived neurotrophic factor
 (GDNF)-HIRMAb 669
 Global Initiative for Asthma (GINA)
 588
 glucagon-like peptide 1 (GLP-1) 689
 glucarpidase 629
 action, mode of 629
 studies in patients 630
 studies in volunteers 630

- glucocorticoid-induced TNFR-related (GITR) protein 556–557
 - glycoengineering 210–211
 - glycosylation 57, 74–76, 427
 - pathways 447
 - golimumab 35, 505, 593
 - govitecan 291–292
 - granulocyte/macrophage colony stimulating factor (GM-CSF) 358
 - green fluorescent protein (GFP) 676
- h**
- Hatch–Waxman Act 646
 - heavy chain (CDR H3) antibodies 86
 - heavy chain only antibodies (HCAbs) 85, 94
 - HEK293 cells 439
 - hematological malignancies 561–563
 - Hendra virus (HeV) attachment G glycoprotein 73
 - HER2 530–531
 - HER2 × HER3 566
 - HER3 531
 - HER3 × IGF-1R 567
 - high affinity L19 antibody 242
 - highly-potent immunotoxin 675
 - “High Stringency Antibody Mining” (SHSAMTM) 128
 - HIRMAb 669
 - homologues 360
 - human antibodies
 - success with transgenic rodents 143
 - from transgenic animals, recovery of 143
 - transgenic farm animals 144–145
 - transgenic rodents 141–143
 - human antibody discovery
 - next generation sequencing 123–126
 - single cell cloning and manipulation 126
 - human antibody libraries
 - advantage 139
 - bacterial display 132
 - from B cells 137–138
 - clinical and marketed antibodies 140–141
 - disadvantages 139–140
 - mammalian cell-based display 134
 - phage display 131
 - synthetic libraries 138–139
 - in vitro* display 131–132
 - yeast display 132–134
 - human antibody structure and function 35
 - CDR H1 loop 69, 71
 - CDR H2 loop 69, 71
 - CDR-H3 diversity 65–66
 - CDR-H3 loops 70–72
 - CDR L1 loop 68–70
 - CDR L2 69, 70
 - CDR L3 70, 71
 - CDR 54
 - Fab and Fv 61–62
 - Fc structure and fragments 56, 60, 62, 63
 - germline VH-VL pairing 66, 67
 - glycosylation 57, 74–76
 - IgE–FceRI interaction 78
 - IgG–FcyR interaction 77
 - isotypes 56–58
 - junctional diversity 64, 65
 - numbering schemes 54–55
 - penultimate constant domains 54
 - schematic 54, 55
 - variable and constant domains 59–61
 - VDJ/VJ recombination 64, 65
 - viral envelop glycoproteins 72–74
 - human anti-MERS-CoV antibody, m336 74
 - human anti-murine antibodies (HAMA) 34
 - human insulin gene clone 6–9
 - human monocyte-derived dendritic cells 389

- human prostate-specific antigen (hPSA) 95
- human recombinant proteins 341
- human therapeutic mAbs 116
- human VH and VL genes 116, 120, 121
- human VH, V κ , and V λ gene expression 121, 122
- Humira[®] 116
- hybrid genome, Paul Berg's construction of 5
- hydrophobic interaction chromatography 443

- i**
- ibritumomab tiuxetan 31
- ICH M3(R2) 349
- ICH Q11 349
- ICH Q6B 349
- ICH S1A 349
- ICH S5(R1) 349
- ICH S6(R1) 349
- ICH S 7A 349
- idarucizumab
 - action, mode of 626
 - anti-coagulant/pro-thrombotic properties, absence of 627
 - bleeding cessation 628
 - immunogenicity 627
 - safety 627
 - studies in patients 627
 - studies in volunteers 626
- idiopathic pulmonary fibrosis (IPF) 607
- IgA1–Fc α RI interaction 77, 78
- IgE–Fc ϵ RI interaction 78
- IgG1/IgA2 antibody 79
- IgG–Fc γ R interaction 77
- ¹²⁵I-labeled anti-CEA single chain Fv (scFv) fragments 201
- IMGT numbering system 55
- immunocytokine 255–257
 - IL-2 family 238
 - non-IL-2 family cytokines 239
- tumor necrosis factor superfamily 240
- type I IFNs 239
- immunogenicity 370–371
 - adaptive immunity 393
 - autologous cell therapies 402–403
 - clinical proof-of-concept 410–411
 - “cryptic” B cell epitopes 406–407
 - definition 387
 - EPO-induced immunogenicity 388
 - first-time-in-human studies 409–410
 - IND-enabling safety studies 408–409
 - induced clearance change 320–322
 - innate immunity 388
 - linkage to product life-cycle 405
 - product quality 407–408
 - regulatory context 403–405
 - risk assessment 405
- immunoglobulin (Ig) 85, *see also* human antibody structure and function
 - design effects of 633
- immunoglobulin D2 (IgD2) genes 97
- immunoglobulin E (IgE) 590, 595–597
- immunoglobulin G (IgG) 56
- immunoglobulin new antigen receptor (IgNAR) 100
- immunological tolerance 400–402
- immunologix 136
- immunomodulatory agents, chronic infections for 618
- immunotoxicity 371
- immunotoxins 249
 - ADP-ribosylating toxins 235
 - binary toxin 236
 - moxetumomab pasudotox 675
 - multi-domain toxins 234
 - single domain toxins 234
 - type II RIPs 235

- IND-enabling safety studies 408–409
 - infectious diseases
 - antibacterial immune therapy 612
 - novel immunotherapeutics 612
 - prophylaxis & precision medicine 611
 - inflammatory bowel disease (IBD)
 - anti-TNF- α therapies 505–506
 - IL-12/ IL-23 therapies 507
 - integrin inhibitors 506–507
 - pathophysiology 504–505
 - inflammatory phenotypes 591
 - inhaled corticosteroids (ICS) 589
 - innate immune receptors 391–393
 - innate immunity
 - dendritic cells 388–390
 - proteins endocytosis 390–391
 - receptors 391–393
 - innate lymphoid cells (ILCs) 504
 - innate lymphoid cells type 2 (ILC-2) 595
 - innovative targeting solutions (ITS) 137
 - insect cells 429
 - insulin 3
 - insulin receptor (IR) 667
 - insulin-like growth factor 1 receptor 532
 - integrin inhibitors 506
 - interleukin 2 (IL-2) 344
 - interleukin 4 (IL-4) 602–614
 - interleukin 5 (IL-5) 597
 - interleukin 6 (IL-6) 496
 - interleukin 7 (IL-7) 345
 - interleukin 9 (IL-9) 606
 - interleukin 12/23 (IL-12/ IL-23) therapies 507
 - interleukin 13 (IL-13) 604–606
 - interleukin 15 (IL-15) 238
 - interleukin 21 (IL-21) 239
 - international nonproprietary names (INNs) mutagenesis 191
 - internalization and trafficking 277–278
 - intracellular biologics
 - AB toxins reengineering 674–677
 - alternative delivery strategies 677–678
 - challenge 672–674
 - opportunity 672
 - outlook 679–680
 - potency 678–679
 - intrinsic asthma 591
 - in vitro* display 131–132
 - in vivo* expressed biologics 684–688
 - in vivo* studies 367–368
 - ion exchange chromatography 442
 - IonTorrent system 124
 - IR/MAR amplification system 438
- k**
- Kadcyla 281–283
 - KB001-A (Kalabios) 615
 - kineret 324
 - knock-out mutations 201
 - kringle domain 174–175
 - Kunitz domain, 172 175–176
- l**
- latrotoxin 633
 - lebrikizumab 604
 - lepidopteran host cells 429
 - lipocalins/anticalins 165, 167
 - look-through mutagenesis (LTM) 191
 - low-density lipoprotein receptor (LDLR) 668
 - lymphocyte activation gene-3 548–549
- m**
- MabThera® 486
 - MAdCAM-1 506
 - mafodotin 286–287
 - mammalian cell-based display 134
 - mammalian cell based manufacturing process 423
 - mammalian cell transfection
 - bioprocess application 431–432

- gene targeting 432–433
 - methodologies 430–431
 - mammalian synthetic biology 425
 - mannitol 478
 - maytansinoids 287–288
 - Medi3902 616
 - MEDI4276 300–301
 - melanotransferrin (p97) 668
 - membranes 443
 - mepolizumab 597–600
 - Mepolizumab as Adjunctive Therapy in Patients with Severe Asthma (MENSA) trial 600
 - mertansine 288–289
 - MET × EGFR 567
 - methicillin-resistant *Staphylococcus aureus* (MRSA) 614
 - methotrexate (MTX) 496, 629
 - MHC-Associated Peptide Proteomics (MAPPS) 394
 - MHC-peptide complexes 397
 - microRNAs (miRNAs) 450
 - mixed mode chromatography 443
 - mixed secondary structure without disulfides 172, 176
 - monobodies 164–166
 - monoclonal antibodies (mAbs) 189, 614, 616, 649
 - anti-infective 617
 - for *Clostridium difficile* infection 616
 - renal clearance of 324
 - for respiratory disease 587
 - respiratory uses of 606–607
 - to staphylococcal infections 614
 - therapeutics fusion proteins 36
 - for viral infections 613
 - monoclonal antibody therapeutics
 - chimeric and humanized mAbs 34
 - Fc fusion proteins 37–42
 - fully human antibodies 34–36
 - monospecific mAb-based therapeutics 229
 - Morphogenics™ 130
 - multi-domain toxins 234
 - multiple myeloma 318
 - murine monoclonal antibodies (mAbs) 34, 342
 - muromonab-CD3 26
 - Mylotarg 283–284
- n**
- nanobodies/VHH domains 165, 167–169
 - natalizumab 506
 - neutralization 42–43
 - new lead optimization methods 354–360
 - next generation sequencing 123–126
 - N-linked glycosylation 74
 - non-coding RNAs 424
 - non-IL-2 family cytokines 239
 - non-mammalian expression systems 428–430
 - “non-traditional” antibodies
 - antibody-drug conjugates 683–684
 - bispecific antibody and multispecific biologics 681–683
 - notch signaling pathway 537–538
- o**
- “off target”/“chemically related” toxicity 341
 - OKT3 347
 - O-linked glycans 74
 - omalizumab 320, 333, 595
 - oncology
 - additional cell surface antigens 539
 - B7-H3 550
 - CD137 (4-1BB) 554–555
 - CD40 ligand 555–556
 - colony stimulating factor 1 receptor (CSF1R) and KIT 533
 - cytotoxic T-lymphocyte antigen-4 (CTLA-4) 542–545
 - EGFR 529–530
 - EPHR family 536–537

oncology (*contd.*)

- ErbB family 522–529
- FGFR2 535
- FGFR2b 535
- FGFR3 535
- glucocorticoid-induced
 - TNFR-related (GITR) protein 556–557
- hematological malignancies 561–563
- HER2 530–531
- HER3 531
- insulin-like growth factor 1 receptor 532
- lymphocyte activation gene-3 548–549
- notch signaling pathway 537–538
- OX40 552–554
- PDGFR–PDGFR α 532–533
- programmed death-1 (PD-1) and PD-1 ligand 545–548
- proto-oncogene c-MET 535–536
- recepteur d'Origine nantais (RON) 535
- RTKs pathways, antibody targeting of 522
- solid tumors 522, 563–566
- targeting immune modulators, *see* targeting immune modulators
- T cell immunoglobulin and mucin protein 3 549–550
- T cell immunoreceptor with immunoglobulin and ITIM domains 551–552
- two receptor pathways, dual targeting of 566–568
- V-domain Ig suppressor of T cell activation (VISTA) 550–551
- TRAILR1 538–539
- TRAILR2 538–539
- VEGFR1 533–534
- VEGFR2 533–534
- VEGFR3 533–534
- Wnt–FZD pathway 538
- opalescence 472

- oral biologics 688–690
- Orthoclone-OKT3[®] 34
- OX40 552–554
- oxidative degradation 479
 - ozogamicin 290–291
 - of polysorbate 479

p

- PacBio system 123
- panitumumab 35
- pathogen-associated molecular patterns (PAMPs) 391
- PCSK9 333
- PDGFR–PDGFR α 532–533
- pegintron 324
- periostin 592
- phage display 131
- pharmacodynamics 369–370
- pharmacokinetics 369–370
 - absorption 313–315
 - Akaike's Information Criterion value 331
 - biopharmaceuticals 331
 - CD28 receptors 325
 - characteristic time 330
 - clearance 328
 - curve fitting 330
 - cytokines 326
 - dissociation rate constant 329, 330
 - distribution 315–316
 - dose-dependent exposure 326
 - drug-receptor complex 329
 - drug-target complex 330
 - elimination rate constant 330
 - enzyme-linked immunosorbent assay 333
 - free receptor turnover 327
 - metabolism and elimination 316–317
 - Michaelis–Menten model 331
 - monoclonal antibody, concentration of 328
 - no-observed-adverse-effect level 325
 - omalizumab 333

- PCSK9 333
- percent-free monocyte $\alpha_5\beta_1$ integrin response 332
- quasi-equilibrium model 329
- soluble low-molecular-weight target 331
- target-mediated drug disposition (TMDD) 326, 327
- TGN1412 325, 326
- total free receptors 328
- volociximab 332
- Phase I anti- α -synuclein candidate, BIIB054 128
- Phase III clinical candidate mAbs 119
- pH dependent antigen binding 206, 207
- point-by-point (PxP) mutagenesis 198
- point mutagenesis 190–191
- polyclonal antibodies 26, 33
- polymerase chain reaction (PCR) 618
- poly N-acetyl glucosamine (PNAG) 615
- polysaccharide intercellular adhesion (PIA) 615
- polysorbate, oxidative degradation of 479
- porcine immunoglobulin heavy chain locus 91
- product quality 407–408
- proenzyme plasminogen 17
- programmed cell death (PCD) 446
- programmed death (PD-1) 545, 618
- progressive multifocal leukoencephalopathy (PML) 506
- pro-inflammatory cytokines 496
- proprotein convertase subtilisin kexin type 9 (PCSK9) 206
- protective antigen (PA) 236, 635, 676
- protein-coding sequences 437
- protein drugs 314
- proteins, endocytosis of 390–391
- protein engineering 398–399
 - affinity 193
 - block mutagenesis 191–192
 - Fc engineering 199–208
 - IgG effector function 208–214
 - pH dependent antigen binding 206, 207
 - point mutagenesis 190–191
 - rational design 192–193
 - specificity 196–199
- protein folding and assembly machinery 446
- protein formulation
 - analytical panel 482–484
 - composition 476–480
 - dosage form 475–476
 - stability testing 480–482
- protein local optimization program (PLOP) 196
- protein purification
 - affinity chromatography 441–442
 - clarification 441
 - economics 444–445
 - future trends 445
 - hydrophobic interaction chromatography 443
 - ion exchange chromatography 442
 - membranes 443
 - mixed mode chromatography 443
- protein stability 469–471
- proteomic approaches 671
- Protexia® 631
- proto-oncogene c-MET 535–536
- Pseudomonas aeruginosa* 615
- Pseudomonas* exotoxin A (PE) 235
- psoriasis
 - anti-IL-12/IL-23 therapies 501–502
 - anti IL-17 therapies 502
 - TNF- α antagonist therapy 500–501
- pyrrolobenzodiazepines (PBD) 292–293, 684

q

quasi-species 425

r

random mutagenesis 190

rat and mouse

antibody isotypes 89–90

antibody organization 89

lymphoid system 89

passive transfer 86–89

ravtansine 289–290

raxibacumab 617

recepteur d'Origine nantais (RON)

535

receptor-mediated transcytosis (RMT)

666

receptor targeting 249

recombinant biopharmaceutical

production

alternative mammalian cell hosts

428

CHO cell 425–428, 445–446

CHOmics 424

mammalian cell based

manufacturing process 423

mammalian cell transfection 430

mammalian synthetic biology

425

non-coding RNAs 424

non-mammalian expression systems

428–430

protein purification 440

quasi-species 425

recombinant gene expression

433–437

selection/amplification systems

437–438

transient production systems

438–439

recombinant DNA delivery

mechanisms 439–440

recombinant gene expression

epigenetic regulatory elements

436

promoters 434

protein-coding sequences 437

untranslated regions 435

utilizable elements 433

recombinant hepatitis B virus (HBV)

vaccine 18

recombinant human

growth hormone 12–14

human interferons 14–16

recombinant tissue-type plasminogen

activator 17–18

re-directed cytotoxicity 247

Reed Sternberg cells 280

regulatory guidance 349–350

Repatha® 485

repertoire shift 193

reslizumab 600

respiratory disease, monoclonal

antibody for 587

respiratory syncytial virus (RSV)

infection 613

restricted access barrier systems

(RABS) 479

reversal agent 622

approach, clinical testing in 631

Reverse Translational Medicine™

(RTM™) 128

RG6013 248

rheumatoid arthritis (RA)

anti IL-6 therapies 498

anti-IL-1 based therapies 498

B cell depletion therapies 499–500

co-stimulation, inhibition of 497

disease modifying anti-rheumatic

drugs 496

IL-6 496

pathophysiologic mechanisms

496

pro-inflammatory cytokines 496

TNF- α antagonists 496–497

ribonucleases (RNAses) 233

Riloncept (Arcalyst™) 498

rituximab 499, 508

rontalizumab 510

rovalpituzumab tesirine 295–296

S*Saccharomyces cerevisiae* Aga1p/2p α -agglutinin system 133

safe starting dose 374

safety considerations for biologics

alternate hit/lead discovery

approaches 352–354

animal models disease 363

cross-reactivity study 366–367

dose levels, selection of 369

embryo fetal development and pre

and postnatal development

372–374

fertility 372

genotoxicity and carcinogenicity

374

homologues 360

immunogenicity 370

immunotoxicity 371

in vivo studies 367–368

new lead optimization methods

354–360

new targets/pathways 350–352

nonclinical safety assessment 361

pharmacokinetics/

pharmacodynamics 369–370

safe starting dose 374–375

safety pharmacology assessments

367

small molecules versus large

molecules 342–344

toxicity related to exaggerated

pharmacology 344–347

toxicity unrelated to exaggerated

pharmacology 347

transgenic and knockout animals

364–366

safety pharmacology assessments

367

SAR279356 (F598) (Sanofi/Alopecx)

615

SARS CoV receptor binding domain

(RBD) 73

sauropsida 97

Secukinumab (AIN457/Cosentyx)

502

selection/amplification systems 437

semisynthetic human insulin 9–11

serum amyloid protein (SAP) 365

serum derived bovine

immunoglobulin protein isolate

(SBI) 93

serum therapy 617

shark 99

shiga toxins 235

short-acting beta-2 agonists (SABA)

589

single cell cloning and manipulation

126

single chain Fv (scFv) 232

single domain toxins 234

small molecules versus large molecules

342–344

solid tumors 563–566

solute carriers (SLCs) 666

somatropin 12

soravtansine 290

spatial aggregation propensity (SAP)

193

Src-homology 3 (SH3) domain 166

domains/fynomers 166–167

staphylococcal infections, monoclonal

antibodies to 614

Staphylococcus aureus 614

sweeping antibodies 138

synthetic libraries 138–139

synthetic promoters 435

systemic anaplastic large-cell

lymphoma (ALCL) 281

systemic lupus erythematosus (SLE)

B cells survival, regulators

of 509

epratuzumab 508

rituximab 508

type I interferons 510

t

talirine 293–295

targeted mutagenesis 194

- targeting immune modulators
 - adaptive immune system 540
 - anti-tumor immunity 552
 - CD27 (TNFRSF7) 556
 - CD40 ligand 555–556
 - CD137 (4-1BB) 554–555
 - glucocorticoid-induced
 - TNFR-related (GITR) protein 556–557
 - lymphocyte activation gene-3 548
 - OX40 552
 - targeting membrane receptors 44–45
 - target-mediated tissue distribution 315–316
 - target-mediated drug disposition (TMDD) 318–320, 326, 327
 - T cell immunoglobulin and mucin protein 3 549–550
 - T cell immunoreceptor with immunoglobulin and ITIM domains 551–552
 - T cell receptors (TCRs) 197
 - teleost 98
 - tesirine 295
 - TGN1412 325, 345
 - Th1 pathway, asthma 593–594
 - Th2 pathway, asthma 594–595
 - Th2 targeted therapies 595–597
 - therapeutic monoclonal antibodies (mAbs) 115
 - thermal unfolding 470
 - thymic stromal lymphopoietin (TSLP) 392
 - tissue-type plasminogen activator (t-PA) 17
 - TNF- α antagonists 496–497, 500–501
 - tocilizumab (TCZ) 499
 - toxicity related to exaggerated pharmacology 344
 - toxicity unrelated to exaggerated pharmacology
 - cytokine storm 347–348
 - unexpected toxicity 348–349
 - T7 phage gene 2 protein 172, 176
 - TRAILR1 538–539
 - TRAILR2 538–539
 - tralokinumab 132, 605
 - transferrin receptor (TfR) 666
 - transgenic and knockout animals 364–366
 - transgenic farm animals 144–145
 - transgenic rodents 141–143
 - transient gene expression (TGE) 438
 - transient production systems
 - CHO cell engineering 439
 - HEK293 cells 439
 - process and media optimization 440
 - recombinant DNA delivery mechanisms 439
 - TGE 438
 - transpo-mAb display 136
 - trastuzumab 198
 - True Human Antibody™ 128
 - tryptophan (Trp) residue 470
 - tubulysins 299
 - tumor necrosis factor (TNF) superfamily 240
 - type I interferons (IFNs) 239, 510
 - type I ribosome-inactivating proteins (RIPs) 233, 235
- u**
- unexpected toxicity 348–349
 - unfolded protein response 447
 - Ustekinumab (Stelara™) 501
- v**
- vaccinex 136
 - variable and constant domains 59–61
 - vascular cell adhesion protein 1 (VCAM-1) 506, 534
 - vascular endothelial growth factor receptor 1 (VEGFR1) 533–534
 - vascular endothelial growth factor receptor 2 (VEGFR2) 533–534

vascular endothelial growth factor
 receptor 3 (VEGFR3)
 533–534
V-domain Ig suppressor of T cell
 activation (VISTA) 550–551
vedotins 284–286
viral envelop glycoproteins 72–74
viral infections, monoclonal
 antibodies for 613
volociximab 332

W

West Nile virus-specific neutralizing
 antibodies 125
Wnt–FZD pathway 538

X

xenopus 97
Xilonix™ 128

Y

yeast 429
 display 132–134
 expression plasmid 12
 recombinant insulin 11–12
YTE mutations 203–204

Z

zinc crystals, recombinant human
 insulin of 10

