

Index

A

- Activated folate, preparation of 72
- Acyl hydrazides, 58
- Adenosine triphosphate (ATP), 163
- A-interferon, 205
- Amine, modification of, 52, 55-57
- Analytical protocols
 - liposome antibody conjugation methods, 59-61
- Anion exchange chromatography, 282
- Anionic lipids, targeted gene transfer of, 262
- Anti-ACE MAb 9B9-conjugated catalase
 - catalase biodistribution, 251f
 - pulmonary targeting, 249-250
- Antibodies
 - antimyosin, 160, 169-173
 - liposomes, 164-165
 - bispecific. *See* Bispecific antibodies
 - cellular expression, 103-104
 - dosage, tumor:normal tissue permeability ratios and, 11 8t
 - glycosylation, 57
 - IgG
 - disulfide group introduction, 5-6
 - IT, 4
 - sulfide group introduction, IT, analysis of, 18
 - metal labeled, chelating polymers and, 160-161, 162f-164f
 - monoclonal. *See* Monoclonal antibodies
 - multi-agent targeting, 104
 - passive tumor targeting, 103-104
 - proteolytic degradation, 52
 - structure, 52
 - Antibody-antigen binding affinity
 - antibody targeting, 116--119
 - Antibody-bearing liposome chloroquine vehicles, 227-236
 - chloroquine resistance, 230, 233
 - drug treatment, 234
 - F(ab')₂ fragments, 230, 232
 - 125I labeled fragments, 230, 232-233
 - liposome/antimouse erythrocyte coupling, 230, 233
 - liposomes, 229-231
 - tissue distribution, 230-231, 234
 - in vitro binding, 231, 234-235
 - MAbF10, 229-232
 - materials, 229-231
 - methods, 231-235
 - Antibody-conjugated catalase
 - hydrogen peroxide, 250t
 - immobilized antigen, 249t
 - streptavidin, 248
 - Antibody-dependent enzyme prodrug therapy (ADEPT), 101
 - Antibody Fab fragment
 - DTPA-PL, 166f-167f
 - Antibody-liposome conjugates, 5-1-64
 - aggregation reactions, 62, 63f
 - amine modification, 52, 55-57
 - SPDP-coupling protocol, 57
 - immunoreactivity, 182-183
 - polymer, 182-183
 - radiolabeled, 182-183

- Antibody targeting
 - analysis, 115-119
 - antibody-antigen binding affinity, 116-119
 - antibody injected dose, 116, 118t
 - extravasation, 115-116, 116f, 1 17t
 - Antibody-toxin constructs, structure of, 1, 2f
 - Antibody uptake, 115-127
 - antibody targeting analysis, 115-119
 - antibody targeting modeling, 119-122
 - mathematics and computer software, 121-122, 122t
 - model expression equations, 120-121
 - model structure design, 119-120, 119f
 - combined effects, 125, 126f
 - injected dose, 124-125, 124f-125f
 - model predictions, 122-125
 - molecular size, 122-124
 - Anti-CD19 immunotoxins, quality control analysis of, 22t
 - protein
 - Antiferritin, 105
 - Antigen-binding, β -antibody-SA/ β -catalase conjugate and, in vitro assessment of 245-246
 - Antigens, passive tumor targeting and, 103-104
 - Anti-HIV immunotoxins
 - cytotoxic effects, 202f
 - experimental uses, 206-208
 - Env internalization, 207
 - HIV protein cell-surface topology, 208
 - immunotoxin-resistant variants, 207-208
 - therapeutic applications, HIV protein cell-surface topology and, 208-209
 - Antimyosin (AM)
 - antibodies, 160, 169-173
 - liposomes, 164-165
 - Fab
 - DTPA-PL, 180-181
 - labeling, 180
 - immunoliposomes (ILs), 173
 - liposomes, cell membrane sealing of, 173f
 - radiolabeled, 160
 - Antisense, HIV-infected cell targeting and, 197-198
 - Antivirals, HIV-infected cell targeting and, 197
 - Asialoorosomucoid (ASO), 260
 - Avidin, 247
 - AZT, 205
- B**
- B4, chemical structure of, 15t
 - B43, chemical structure of, 15t
 - β -antibody-SA/ β -catalase conjugate, in vitro assessment of, 245-246, 248-249
 - BCA protein assay, pure
 - characterization of 223
 - β -catalase/ β -antibody conjugate, 245
 - B-galactosidase, 278-279
 - Binding assay, pure protein
 - characterization of, 223
 - Bispecific antibodies
 - effector molecule delivery, 38f
 - acid-triggered release, 39-42
 - antibody production, 46
 - antibody refinement, 44
 - binary delivery modes, 42, 43f
 - cytotoxic assays, 47
 - materials, 44
 - methods, 44-47
 - monoclonal antibodies, 45-46
 - toxin-cell binding, 46-47
 - toxin isolation, 44-45

- BL21 (DE3), 88
 β -Mab 9B9/SA/ β -catalase conjugate, 246
BRBT, formation of, 11f
BRT, chemical structure of, 15t, 16-17
- C**
- Cancer therapy, tumor blood flow inhibition and, 134-135
Carbohydrate modification, 52, 57-59
 PDPH coupling protocol, 58-59
Carcinoembryonic antigen (CEA), 103-104, 116-117
Cardiac myosin, 165
Cardiocytes
 H9C2 embryonic, 175
 hypoxic, 173
 normoxic, 173
 transfected, ScFv and, 176f
Cardiomyocytes
 ILs, 169-176
 drug delivery, 175-176
 sealing, 169-175, 173f
Carrier molecules, plasmids and, 256
Catalase
 activity determination, and
 pulmonary vascular endothelium catalase immunotargeting, 243
anti-ACE MAb 9B9-conjugated
 catalase biodistribution, 251f
 pulmonary targeting, 249-250
antibody-conjugated
 hydrogen peroxide, 250t
 immobilized antigen, 249t
 streptavidin, 248
immunotargeting. *See* Pulmonary vascular endothelium catalase immunotargeting
 pulmonary vascular endothelium.
 See Pulmonary vascular endothelium catalase immunotargeting
radiolabeled, kinetics of, 252f
- Cationic lipids, 256
 DOPE, 286
 targeted gene transfer, 261-262
Cationic liposome/DNA complexes, 257, 284
Cationic liposomes, 257
 fusion, 286
 targeted gene transfer, 266-267
Cationic peptides, 259
Cationic polymers, 256
Caveolae, 70
CCR5, HIV-infected cell targeting and, 195
CD3, HIV-infected cell targeting and, 195
CD4, 194-195
 HIV-infected cell targeting, 195
CD 14, HIV-infected cell targeting and, 195
CD38, HIV-infected cell targeting and, 195
CD4-PE40, 208
Cell-binding domain, 12
Cell lines, HIV-infected cell targeting and, 199-200
Cell membrane sealing, AM-liposomes and, 173f
Cellular receptors, modulation of, and passive tumor targeting, 104
Cellular targets, HIV-infected cell targeting and, 198-199
Cell viability, 3H-thymidine and, 174t
Cesium chloride, gradient, 282
Chelating polymers, metal labeled antibodies and, 160-161, 162f-164f
Chemical bonds, 1
Chloramphenicol acetyltransferase (CAT), 279
Chloroquine, 227-236
 resistance, 227
antibody-bearing liposomes
 chloroquine vehicles, 230, 233

- Chloroquine-laden targeted liposomes,
biologic response of, 235
- Chloroquine-susceptible *Plasmodium*
berghei, 228-229
- Chromatography
anion exchange, 282
ion exchange, fusion toxins and, 221,222
refolded recombinant protein,
recombinant RNase single-
chain antibody fusion proteins
and, 80, 84-85, 91-93
sizing, fusion toxins and, 219, 221
- Coichicine, 140
- Complementarity-determining region
(CDR), 103
- Coreceptors, HIV-infected cell
targeting and, 195
- Corticosteroids, 102
- Covalent bonds, 13f
- Covalent coupling, polylysine and,
178-179
- CRM45, 42, 44
- CRM 107, 41, 42, 44
- Cryogenic transmission electron
microscopy (CTEM), 269
- CXCR4, HIV-infected cell targeting
and, 195
- Cyclosporine, 196
- Cytotoxicity assays
bispecific antibody intracellular
targeting, 47
pure protein characterization, 223
- D**
- Dendrimers, 257, 259
- Dexamethasone, 102-103
- DgRTA
chemical structure, 1St
preparation, flow diagram of, 10f
- Diethylenetriamine pentaacetic acid
stearylamine, 168
stearylamine, 168
- Dioleoylphosphatidylethanolamine
(DOPE), 257, 259
cationic lipids, 286
- Diphtheria toxin (DT), 39, 215
- Disulfide bonds, 1
- Disulfide group, IgG antibody and, 5-6
- Disulfide linkage antibody
derivatization, ribonuclease-
antibody conjugates construction
and, 28-31
- Disulfide modification, 52, 59
- DNA
analysis, targeted gene transfer and, 262
intracellular delivery, ILs and, 183-184
isolation, 289
nontransfecting cell line, 288
protection, 272-273
purification, measure of, 283
- DNA/carrier complex, 288
- DNA delivery systems
lipid-based, 256
nonviral. *See* Nonviral DNA delivery
systems
- DNA/liposome complexes
endocytosis, 286
- DNase I, sensitivity of, 272
- Dot-blot analysis, 275
- Drug-induced tumor blood flow
inhibition, 140-148
erythrocyte velocity, 141-142
tracer uptake, 142-144
tracer washout, 144-147
- Drug treatment, antibody-bearing
liposomes chloroquine vehicles
and, 234
- DT, 39, 215
- DTPA-PL, 178
AM Fab, 180-181
antibody Fab fragment, 166f-167f
- DTPA-PL-AM-Fab
immunoreactivity, 180
purification, 179
- E**
- ECP, 77
- EDN, 77

- Effector molecule, bispecific antibodies and, 38f
- Endocytosis, DNA/liposome complexes and, 286
- Endocytotic cycling, 47
- Endosomal system, 287
- EndOtoxin, 282
- Endotoxin assay, pure protein characterization of, 223-224
- Env, 193
internalization, anti-HIV immunotoxins and, 207
- Eosinophil cationic protein (ECP), 77
- Eosinophil-derived neurotoxin (EDN), 77
- Erythrocytes, drug-induced tumor blood flow inhibition and, 141-142
- 1 -ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC), 55, 56
- 1 -ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC)-activated folate protein conjugation, 73
- 1 -ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC)-activated folic acid, 72
- Extraction ratio (ER), 142
- F**
- FAA, 136f, 137-139
xanthenone analogs, 136f, 139
- Fab' fragment, IT and, 4-5
- F(ab')₂ fragments, -antibody-bearing liposomes chloroquine vehicles and, 230, 232
- FACS, 279
- FACSIMILE/CHEKMAT package, 122
- Fc receptor, HIV-infected cell targeting and, 195
- FIA, HIV-infected cell targeting and, 204-205
- Flavone acetic acid (FAA), 136f, 137-139
xanthenone analogs, 136f, 139
- Fluorescence-activated cell-sorting (FACS), 279
- Fluorescent lipids, targeted gene transfer and, 262
- Fluorescent perfusion markers, tumor blood flow inhibition and, 146f
- Focal infectivity assay (FIA)
HIV-infected cell targeting, 204-205
- Folate
activated, preparation of, 72
EDC-activated, protein conjugation of, 73
- Folate conjugates, folate receptor-mediated endocytosis and, 70-71
- Folate receptor, tumor marker of, 69-70
- Folate receptor-mediated endocytosis, 69-75
folate conjugates, 70-71
folate receptor as tumor marker, 69-70
materials, 72
activated folate preparation, 72
protein conjugate synthesis, 72
methods, 72-74
conjugate characterization, 74
conjugate purification, 74
protein-folate preparation, 72-74
- Folic acid, 69
vs. MABs, 70-71
structure, 70f
- Fusion toxins, 196, 215-225
materials, 218-219
anion exchange columns and buffers, 21-9
inclusion body washing, 218, 224
plasmids, 218
reducing agents and buffers, 218
sizing chromatography, 219
solubilization, 218
transformation and fermentation, 218
methods, 219-224
inclusion body protein isolation, 219-220

- inclusion body solubilization, 220
 - ion exchange chromatography, 221
 - ionic strength, 220-221
 - plasmid preparation, 219
 - pure protein characterization, 222-224
 - refolding, 220
 - sizing chromatography, 221, 222f
 - transformation, 219
- G**
- Gag proteins, 194
 - Gelonin, 39
 - Gene splicing, overlap extension and, 81f, 82
 - Gene therapy
 - goal, 255
 - HIV-infected cell targeting, 197-198
 - Gene therapy vectors, viruses and, 255-256
 - Gene transfer, lipid-based. *See* Lipid-based gene transfer
 - Gp41, 194, 207
 - Gp120, 194, 207
 - Gramicidin S, 259, 268
- H**
- H9C2, 176, 184
 - H9C2 embryonic cardiocytes, 175
 - (α H) cholesteryl hexadecyl ether (CHE), 59
 - HD37, chemical structure of, 15t
 - HeLa cells, 204
 - Helper lipids, 257
 - High affinity, UR and, 127
 - Hirt lysis procedure, 275
 - HIV envelope protein, 193
 - HIV-envelope protein, internalization of, and anti-HIV immunotoxins, 207
 - HIV-infected cell targeting, 193-209
 - materials, 198-202
 - cell lines, 199-200
 - cellular targets, 198-199
 - primary cell cultures, 200-201
 - targeted agents, 198
 - materials targeted, 196-198
 - antivirals, 197
 - nucleic acids, 197-198
 - toxins, 197
 - viruses, 198
 - methods, 201-205
 - cytotoxicity, 201-202
 - virus production inhibition, 202-203
 - modes, 194-196
 - CD4, 195
 - cell surface HIV-encoded structures, 194
 - coreceptors, 195
 - IL-2 receptors, 196
 - MAbs, 193-195
 - HIV-LTR, 193
 - HIV tropism, molecular basis of, 199
 - H1-J.C53, 205
 - α H-leucine, 19
 - H9/NL4-3, 202-203
 - Hoechst 33342, 143-144
 - α H-thymidine, 19
 - cell viability, 174t
 - Humanization
 - passive tumor targeting, 103
 - Human transferrin receptor-positive target cells, 47
 - Hydralazine, 136-137, 136f
 - Hydrogen peroxide
 - antibody-conjugated catalase, 250t
 - β -antibody-SA/ β -catalase conjugate in vitro assessment, 245-246
 - Hypaque-Ficoll density gradient centrifugation, 200
 - Hypoxia, tumor vasculature and, 133-134
 - Hypoxic cardiocytes (HC), 173
- I**
- IgG
 - maleimide group introduction, 8
 - modification sites, 52, 53f

- oxidation, 64
- SATA, 8
- SMCC, 9f
- IgG antibodies
 - disulfide group introduction, 5-6
 - IT, 4
- sulfide group introduction, 6-8
- ¹²⁵I labeled fragments, antibody-bearing
 - liposomes chloroquine vehicles and, 230, 232-233
- IL-2 receptor, HIV-infected cell
 - targeting and, 195
- Image manipulation, plasma targeting
 - molecules and, 99
- 2-iminothiolane, 6-8
- Immune reactions, passive tumor
 - targeting and, 103
- Immunoliposomes, stabilized, 260
- Immunoliposomes (ILs), 164-166
 - cardiomyocytes, 169-176
 - drug delivery, 175-176
 - sealing, 169-175, 173f
 - DNA, intracellular delivery of, 183-184
- Immunosuppression, passive tumor
 - targeting and, 103
- Immunotargeting, catalase, and pulmonary vascular endothelium.
 - See Pulmonary vascular endothelium catalase immunotargeting
- Immunotoxin (IT)/monoclonal antibody (MAb)binding, 19f
- Immunotoxin-resistant variants, anti-HIV immunotoxins and., 207-208
- Immunotoxins (IT)
 - analysis, 18-23
 - antibody activity, 18
 - toxin activity, 18-19
 - in vitro, 19-20
 - in vivo, 20-23
 - anti-CD 19
 - quality control analysis, 22t
 - anti-HIV. *See* Anti-HIV immunotoxins
 - chemical structure, 1-23, 15t
 - Fab' fragment preparation, 4-5
 - genetic construction, 1
 - HIV-infected cells, 197, 204f
 - IgG antibody
 - chemical derivatization, 5-8
 - preparation, 4
 - preparation, 2-4, 8-17
 - SCID/Daudi mice, 21-22, 22f
 - single-chain Fv (scFv) recombinant, 217
- Impulsive initial input, 121
- Inclusion bodies
 - fusion toxins, 218, **219-220**, 224
 - recombinant RNase single-chain antibody fusion proteins
 - preparation, 79, 83-84, 89-90
 - solubilization, 79, 84, 90
- Indium-111, 99
- INF5, 260
- Infectious centers (ICs), 204
- ¹¹¹In labeling, 180-181
- Iodine, 97
- Ion exchange chromatography
 - fusion toxins, 221, 222f
- L**
- Large unilamellar liposomes (LUVs), 284
- Leukemia targeting. *See* Fusion toxins
- Lipid analysis,
 - liposome antibody conjugation methods, 59-60
- Lipid-based DNA delivery systems, 256
- Lipid-based gene transfer, 269-273
 - aggregation state, 269-270
 - carrier-membrane fusion, 271
 - DNA protection, 271-273
 - fusogenic potential, 270-271
 - particle size, 269-270
- Lipid/DNA particles, 257, 259
 - targeted gene transfer, 267-268

Lipids

- anionic, targeted gene transfer and, 262
- cationic, 256
 - DOPE, 286
 - targeted gene transfer, 261-262
- delivery
 - analysis, 276-277
 - targeted gene transfer, 274-277
- fluorescent, targeted gene transfer and, 262
- helper, 257
- PEG, 61-62
- radioactive tags, 288
- radiolabeled, 262

- Liposome/antimouse erythrocyte
 - coupling, antibody-bearing liposomes chloroquine vehicles and, 230, 233

Liposome/DNA complexes

- cationic, 257, 284
- preparation, 285
- targeted gene transfer, 267

Liposomes

- antibody-bearing. See Antibody-bearing liposome chloroquine vehicles
- antibody conjugation
 - amine modification, 55-57
 - analytical protocols, 59-61
 - carbohydrate modification, 57-59
 - disulfide modification, 59
 - indirect methods, 59
 - liposome preparation, 54-55
 - materials, 54
 - methods, 51-64
 - steric barrier molecules, 61-63
- antimycin
 - antibody, 164-165
 - cell membrane sealing, 173f
- cationic, 257
- fusion, 286
 - targeted gene transfer, 266-267

- cell survival, 183
- chloroquine estimation, antibody-bearing liposomes chloroquine vehicles and, 231
- chloroquine-laden targeted, biologic response of, 235
- in vitro binding, antibody-bearing liposomes chloroquine vehicles and, 231, 234-235
- large unilamellar, 284
- myocardial infarct targeting, 161-169, 172t
 - spontaneous accumulation, 161-164, 170f-171f
- plain, 173
- preparation, targeted gene transfer and, 262
- radiolabeling, 182
- tissue distribution, antibodybearing liposomes chloroquine vehicles and, 230-231, 234

- Localized substances, passive tumor targeting and, 97

Low receptors

- cellular expression, 103-104
- multi-agent targeting, 104
- passive tumor targeting, 103-104

Luciferase, 280

Lymphoma targeting. See Fusion toxins

M

- MAbF₁₀, antibody-bearing liposomes chloroquine vehicles and, 229-232
- MAb 2G42D7, 177
- MAb R11D10, 177
- Malaria
 - incidence, 227
 - murine, chloroquine vehicles for. See Antibody-bearing liposome chloroquine vehicles
- Maleimide groupI_gG and, 8
- Master cell blank, 224

- Metaiodo-benzylguanidine (MIBG), 97
 5-methyltetrahydrofolate, 70
 MLV, 63-64
 Model stimulation, standard parameters
 of, 122t
 Monoclonal antibodies (MAb), 39
 vs. folic acid, 70-71
 generation, bispecific antibody intra-
 cellular targeting and, 45-46
 HIV-infected cell targeting, 193-195
 myocardial infarct targeting, 159-
 161
^{99m}Tc, 160
 Multilamellar vesicles (MLV), 63-64
 Murine malaria, chloroquine vehicles
 and. *See* Antibody-bearing
 liposome chloroquine vehicles
 Myocardial infarction targeting, 159-
 186
 antibody-related experiments, 176-
 181
 antibody preparation, 177-178
 immunoreactivity determination,
 180
 polylysine modification, 178-180
 radiolabeling, 180-181
 cell-related experiments, 177, 183-
 184
 cell cultivation, 183
 DNA intracellular delivery, 183-
 184
 liposome-related experiments, 177,
 181-183
 antibody modification, 181
 IL preparation, 181
 liposome preparation, 181
 PEG-liposome preparation, 181-
 182
 PEG-PE synthesis, 181
 liposomes, 161-169, 172t
 immunoliposomes, 164-166
 PEG ILs, 166-169
 PEG-liposomes, 166-169
 MAbs, 159-161
 materials, 176-177
 methods, 177-184
 in vivo experiments, 177, 184-
 186
 liposome targeting, 185-186
 radiolabeled antibodies imaging,
 184-185
 Myosin, 169
 cardiac, 165
N
 NBD-PE fluorescence, 270
 NC, 173
 Necrosis, tumor vasculature and, 133-
 134
 N-glutaryl phosphatidyl ethanolamine
 (NGPA), 167-168
 NGPA, 167-168
 NHS, 56
 NHS-activated folate
 protein conjugation, 73
 synthesis, 73
 NHS-ester of folic acid (NHS-folate), 72
 protein derivatization, 73-74
 N-hydroxysuccinimide (NHS), 56
 Noncovalent conjugation, 52
 Nontumor receptors
 passive tumor targeting, 104-105
 peripheral binding site blocking,
 104-105
 targeting agent dosage, 105
 Nonviral DNA delivery systems
 carriers, 257
 characterization, 285
 examples, 258t
 plasmids, 256
 targeted gene transfer, 257-260
 targeting, 260
 Normoxic cardiocytes (NC), 173
 Nucleic acids
 HIV-infected cell targeting, 197-198
 quantitation, 203

O

Overlap extension

gene splicing, 81f, 82

P

P24, 203

Paclitaxel, 139

PAMAM, 259

Pancreatic RNase A type genes, 87

PAP, 1, 12-13

Parasitemia, 125

Passive tumor targeting, 97-106

localized substances, 97

maximizing tumor:normal tissue

concentration, radiolabel:

radiolabeling methods and, 98-99

maximizing tumor:normal tissue

concentration ratios

experimental approaches, 98-105, 98t

plasma targeting molecules, 99-101

models, 105-106

tumor accumulation, limiting factors of, 98

tumor:normal tissue uptake ratios

cellular receptor modulation, 104

immune reactions, 103

low receptor availability, 103-104

nontumor receptors, 104-105

targeting agent, 101-103

PDPH coupling protocol, carbohydrate modification and, 58-59

PE, 13-14, 17

PE35, chemical structure of, 15t

PEG, 100

lipids, 52, 61-62

PEG ILs, 166-169

PEG-liposomes, 166-169

Peptides, cationic, 259

PET vector system, 85

PHA, 200

Phytohemagglutinin (PHA), 200

Phytolacca americana, 12

Pierce Coomassie Plus assay, pure

protein characterization of, 222

PL, 173

Plain liposomes (PL), 173

Plasmapheresis, passive tumor targeting and, 103

Plasma targeting molecules, 99-101

image manipulation, 99

pretargeting, 100-101

second antibody, 99-100

small, 100

Plasmid, radiolabeled, isolation of, 275

Plasmid DNA integrity

analysis, 275-276

Plasmid pEScFv, 175

Plasmids

carrier molecules, 256

carrier systems, 288

differential separation, 283

fluorescently labeled, 272, 283-284

fusion toxins, 218, 219

gel filtration, 282-283

nonviral DNA delivery, 256

purification, 281-282

radiolabeled, 288

targeted gene transfer, 263-266

delivery, 274-277

isolation and purification, 263-

265, 264t

preparation, 261

transfected cells, quantification of, 274-275

Plasmodium *berghei*, chloroquine-susceptible, 228-229

Plug and seal, 173

4-(p-maleimidophenyl)butyric acid N-hydroxysuccinimide ester (SMPB), 56

Pokeweed antiviral protein (PAP), 1, 12-13, 16

chemical structure, 15t

- Pokeweed plant, 12
 - Polyamidoamines, 259
 - Polyethylene glycol (PEG), 100
 - lipids, 52, 61-62
 - Polylysine, 257, 259, 260, 285
 - covalent coupling, 178-179
 - DPTA, 178
 - modification, myocardial infarction
 - targeting and, 178-180
 - Polymers, cationic, 256
 - Polymixin B, 282
 - Primary cell cultures, HIV-infected cell
 - targeting and, 100
 - Protein-folate conjugate
 - characterization, 74
 - preparation, 72-74
 - purification, 74
 - Proteins
 - analysis, liposome antibody
 - conjugation methods and, 60
 - biotinylation, 247
 - pulmonary vascular endothelium
 - catalase immunotargeting, 243
 - characterization, 222-224
 - conjugation
 - EDC-activated folate, 73
 - NHS-activated folate, 73
 - derivatization, NHS-folate and, 73-74
 - immobilization, catalase
 - immunotargeting and, 244
 - radiolabeling, catalase
 - immunotargeting and, 244
 - synthesis, RFB4-SMPT-dgRTA and, 20f
- Pseudomonas exotoxin (PE), 1'215
- Pulmonary vascular endothelium catalase
 - immunotargeting, 241-253
 - materials, 242-243
 - methods, 243-246
 - β -antibody-SA/ β -catalase conjugate, 245-246
 - β -catalase- β -antibody conjugate, 245
 - β -MAB 9B9/SA/ β -catalase conjugate, 246
 - catalase activity determination, 243
 - protein biotinylation, 243
 - protein immobilization, 244
 - protein radiolabeling, 244
- Pyridyldisulfide crosslinkers, structure of, 6f
- Q**
- QELS analysis, 269
 - Qiagen purified plasmids, 87
- R**
- Radioiodination, 180
 - Radiolabeled
 - antibody-liposome, 182-183
 - antimyosin (AM), 160
 - catalase, kinetics and, 252f
 - lipids, targeted gene transfer of, 262
 - plasmid, isolation of, 275
 - targeted gene transfer, plasmids and, 265-266
 - Radiolabeling
 - ¹¹¹In labeling, 180-181
 - liposomes, 182
 - myocardial infarction targeting, 180-181
 - radioiodination, 180
 - Radiolabel: radiolabeling methods,
 - passive tumor targeting and, 98-99
 - R11D10, 160
 - Recombinant protein renaturation,
 - recombinant RNase single-chain antibody fusion proteins and, 79-80, 84, 90-91
 - Recombinant RNase single-chain
 - antibody fusion proteins, 77-93
 - inclusion bodies preparation, 79, 83-84, 89-90

- inclusion bodies solubilization, 79, 84, 90
- materials, 78-80
 - methods, 80-85
 - recombinant protein renaturation, 79-80, 84, 90-91
 - refolded recombinant protein
 - chromatography, 80, 84-85, 91-93
 - RNase-sFv gene construction, 78-79, 80-82, 85-88
 - RNase-sFv gene expression, 79, 83, 89
 - RNase-sFv protein expression
 - analysis, 79, 82-83, 88-89.
 - RNase-sFv recombinant protein
 - growth, 79, 83, 89
- Recombinant toxins, 215
 - purification, 217-218, 217f
 - schematic diagram, 216-217, 216f
- Refolded recombinant protein
 - chromatography, recombinant RNase single-chain antibody fusion proteins and, 80, 84-85, 91-93
- Reporter genes, transfection of, 278-280
- Resonance energy transfer (RET), 270
- RFB4, chemical structure of, 15t
- RFB4(Fab'), chemical structure of, 15t
- RFB4-SMPT-dgRTA, protein synthesis and, 20f
- Ribonuclease-antibody conjugates
 - selective cytotoxicity construction, 27-34
- Ribonuclease-antibody conjugates
 - construction, 27-34
 - disulfide linkage antibody
 - derivatization, 28, 29, 30-31
- RNase-antibody purification, 28, 30, 33-34
- RNase conjugation via disulfide linkage, 28, 30, 32-33
- RNase conjugation via thioether linkage, 28, 30, 32-33
- RNase derivatization, 27-29
 - thioether linkage antibody
 - derivatization, 28, 29-30
- Ribosome inactivating proteins (RIPs), 12
- Ribozyme, HIV-infected cell targeting and, 197-198
- Ricin, 39
- Ricin A chain (RTA), 1, 9-12
- Ricin toxin (RT), 1
 - preparation, 9-12
 - flow diagram, IOF
- RNase-antibody purification,
 - ribonuclease- antibody conjugates construction and, 28, 30, 33-34
- RNaseA superfamily, host defense activities of, 77
- RNase A type genes, pancreatic, 87
- RNase conjugation
 - via disulfide linkage, ribonuclease-antibody conjugates
 - construction and, 28, 30, 32-33
 - via thioether linkage, ribonuclease-antibody conjugates
 - construction and, 28, 30, 32, 33
- RNase derivatization, ribonuclease-antibody conjugates construction and, 27-29, 31
- RNase fusion proteins, sterilization of, 93
- RNase-sFv gene
 - construction, and recombinant RNase single-chain antibody fusion proteins, 78-79, 80-82, 85-88
 - expression, and recombinant RNase single-chain antibody fusion proteins, 79, 83, 89
- RNase-sFv protein, expression analysis of, and recombinant RNase single-chain antibody fusion proteins, 79, 82, 83, 88-89

- RNase-sFv recombinant protein, growth
of, and recombinant RNase
single-chain antibody fusion
proteins, 79, 83, 89
- RTB, 9-12
- S**
- S-acetylthioglycolic acid N-
hydroxysuccinimide ester
(SATA), 56
- IgG, 8
- ScFv, transfected cardiocytes and, 176t
- SCID/Daudi mice, IT and, 21-22, 22f
- Selective cytotoxicity construction,
ribonuclease-antibody conjugates
and, 27-34
- Sensitivity analysis, 122
- Sephacryl S200 column, 225
- Serotonin, 135-136, 136f
- Serum stability, DNA protection and,
273
- Single-chain Fv (scFv) recombinant
immunotoxins, 217
- Sizing chromatography, fusion toxins
and, 219, 221
- SMCC
- IgG, 9f
- structure, 9f
- ³⁵S-methionine, 201
- SMPB, 56
- SPDP, 268
- coupling protocol, amine
modification of, 57
- modified human IgG, coupling
efficiency and, 62f
- Stabilized immunoliposomes (SIL), 260
- Starburst dendrimers (PAMAM), 259
- Steric barrier molecules, liposome
antibody conjugation methods
and, 60-63
- Stiff system, 121
- Streptavidin, 241, 247, 248
- Streptavidin-biotin crosslinker, 241
modification, 247
- Streptokinase, 162-163
- Succinimidyl 3-(2-pyridyldithio)
propionate (SPDP), 268
- coupling protocol
amine modification, 57
- modified human IgG
coupling efficiency, 62f
- Suicide genes
HIV-infected cell targeting, 198
- Sulthydryl analysis
liposome antibody conjugation
methods, 60
- Sulfide group
IgG antibody, 6-8
- Supernatural binding, 127
- Superoxide dismutase (SOD), 163
- T**
- Targeted agents
HIV-infected cell targeting, 198
- Targeted gene transfer, 255-290
- materials, 261-262
- anionic lipids, 262
- cationic lipids, 261-262
- DNA analysis, 262
- fluorescent lipids, 262
- liposome preparation, 262
- plasmid preparation, 261
- radiolabeled lipids, 262
- methods, 263-281
- active components, 263-269
- cell delivery analysis, 273-281
- lipid-based gene transfer
formulations, 269-273
- nonviral DNA delivery systems,
257-260
- Targeting
- antibody. See Antibody targeting
- HIV-infected cell. See HIV-infected
cell targeting
- intracellular
- bispecific antibodies, 37-48
- leukemia. See Fusion toxins

- lymphoma. See Fusion toxins
 - myocardial infarction. See
 - Myocardial infarction targeting
 - passive tumor. See Passive tumor targeting
 - Targeting agents
 - abnormal tumor microenvironment, 102-103
 - dose, 101-102
 - fragments, 102
 - regional administration, 101
 - tumor:normal tissue uptake ratios, 101-103
 - Technetium-99m, 99
 - Thioether bonds, 1
 - Thioether linkage antibody
 - derivatization, ribonuclease-antibody conjugates construction and, 28, 29-30, 32
 - Thiolation reagents, structure of, 7f
 - Thiol-maleimide links, 53, 54f
 - Toxin, IT and, analysis of, 18-19
 - Tracer
 - uptake, 142-144
 - washout, 144-147
 - Transfected cardiocytes, ScFv and, 176t
 - Transfection, reporter genes and, 278-280
 - Transferrin, 260
 - Transgene, expression of, 277-278
 - Triton X-1 14, 282
 - T7 RNA polymerase genes, 87
 - TSK G3000SW column, 225
 - Tumor
 - microenvironment, targeting agent and, 102-103
 - vasculature
 - blood flow inhibition, 133-135
 - hypoxia and necrosis, 133-134
 - Tumor blood flow inhibition, 133-149
 - cancer therapy, 134-135
 - drug-induced, 140-148
 - fluorescent perfusion markers, 146f
 - indirect methods, 147-148
 - per technetate washout method, 148f
 - selective inhibitors, 135-140
 - tumor vasculature, 133-135
 - Tumor content (TC), 120-126
 - Tumor marker, folate receptor and, 69-70
 - Tumor:normal tissue permeability ratios
 - antibody dose, 11 8t
 - experimentally determined, 117t
 - Tumor:normal tissue uptake ratios, targeting agent and, 101-103
 - Type- α folate receptor, 69-70
 - Type- β folate receptor, 69-70
 - Tyrocidine, 259, 268
- U**
- Uptake ratio (UR), 120-126
 - increasing dose, 127
 - optimal dose effect, 126
- V**
- Vimentin, 169
 - Vinblastine, 139
 - Vinca alkaloids, 136f, 139-140
 - Vincristine, 139
 - Viruses
 - gene therapy vectors, 255-256
 - HIV-infected cell targeting, 198
 - FIA, 204-205
 - nucleic acid quantitation, 203
 - virus product measurement, 203
- X**
- Xanthone analogs, FAA and, 136f, 139
 - ^{133}Xe , 145-147
 - XL1/Blue, 176
- Y**
- ^{90}Y trium, 99