INDEX

Page references followed by t indicate material in tables.

AAAV vaccinations, 100
Acceptors, in carbohydrate synthesis, 17, 18
ACE1 gene, in yeast-based vaccine vector design, 142
Actin-polymerizing (ActA) protein, Listeria monocytogenes and, 116, 117
Activated T cells
   CD137 on, 256–257
   PD-1 expression on, 249
Activation-induced cell death (AICD). See also Apoptosis
   anti-CD137 and, 255, 260
   in cancer vaccine evaluation, 300
Active immunization, as cancer immunotherapy strategy, 230–231
Acute myeloblastic leukemia (AML), CD137L and, 254
Adaptive immune responses, in immune monitoring, 273
Adaptive immunity
carcinogenesis and, 229
coupling yeast-based cancer immunotherapy with, 131–149
CpG ODNs in stimulating, 47–49
   in immune rejection of solid tumors, 51–52
Adaptor molecules, CpG ODNs in stimulating, 47
Adenocarcinoma
   BCG versus, 36
Adenomatous polyposis coli (APC) protein, in yeast-based immunotherapy, 135, 146
Adenoviruses
   in CD137 studies, 258
   as gene therapy vehicles, 95–96
Adenovirus LIGHT-expressing vectors (Ad-LIGHT), treatment of metastases and, 235–236
ADH1 (alcohol dehydrogenase) promoter, in yeast-based vaccine vector design, 142
Adjuvants, 4–6. See also Biological adjuvants in cancer vaccines, 296
   CpG ODNs as, 47, 48, 49
   CpG ODN synergy with, 50
   human clinical trials with CpG ODNs, 50–51, 51–53
Listeria monocytogenes as, 114
   in mouse tumor models, 51
   safety of, 53–54
   yeasts as, 132
Administration route, in yeast-based immunotherapy, 143–144
Adoptive T cell immunotherapy, 3
   in immune monitoring, 272
Adoptive T cell transfer therapy, as cancer immunotherapy strategy, 217–218, 230–231
Adult T cell lymphoma/leukemia, CD25 antibodies versus, 191
Ag104A immunity, in CD137 studies, 257
Ag104L2-LIGHT tumor cell line, creating tumor lymphoid tissue and, 233–234
Age, in vaccine evaluation, 292
Allogeneic cell lines, 155
Allogeneic HSCT, 218–219
   immunotherapy and, 9
   T cell depletion and, 219–220
Allogeneic vaccines, 8
   modification to secrete cytokines, 157–159
   tumors and, 155s
   whole-cell, 153–157
Alloimmune response, 8
Allospecific response, 8

Cancer Vaccines and Tumor Immunity
Edited by Rimas Orentas, James W. Hodge, and Bryon D. Johnson
Copyright © 2008 John Wiley & Sons, Inc.

309
Alphaviruses, as cancer-therapy vaccine vectors, 96
ALVAC canarypox vector, in cancer therapy, 96–97, 98t
American Urological Association (AUA) guidelines, for BCG, 32
Amino acid sequences, flanking, 71–72
Anastrozole, in endocrine therapy, 174
Androgen ablation, in endocrine therapy, 175
Androgen signaling, 223
Angiogenesis, inside tumors, 234–235
Animal studies, of BCG in prostate cancer treatment, 36
Animal tumor models, in yeast-based immunotherapy, 135–137. See also Mice
Animal studies, of BCG in prostate cancer treatment, 36
Animal tumor models, in yeast-based immunotherapy, 135–137. See also Mice
Animal studies, of BCG in prostate cancer treatment, 36
Animal tumor models, in yeast-based immunotherapy, 135–137. See also Mice
Bacterial vaccine vectors and, 114
in CD137 studies, 257
in evaluating immune competence, 296
inside tumors, 234
vaccine activation of, xiii
Antibody-dependent cellular cytotoxicity (ADCC)
in endocrine therapy, 174
in monoclonal antibody therapy, 173
Antibody therapy, 3
immunotherapy and, 8
Antibody titers, in immune monitoring, 273
Anticancer vaccines, investigation of, xiii–xiv
See also Antitumor vaccines; Cancer vaccines; Vaccine entries
Anti-CD3 antibody
in CD137 studies, 258, 259–260
PD-1/B7-H1/B7-DC pathway and, 248
PD-1 gene and, 245
Anti-CD28 antibody
in CD137 studies, 260–261
PD-1/B7-H1/B7-DC pathway and, 247–248
Anti-CD137 antibody
CD137 and, 255, 260–261
PD-1/B7-H1/B7-DC pathway and, 253
Anti-CD137L antibody, in CD137 studies, 258
Anti-CD137 mAbs, CD137L and, 255
Anti-CTLA4 antibodies. See also Cytotoxic T lymphocyte antigen 4 (CTLA4)
PD-1/B7-H1/B7-DC pathway and, 248
Tregs and, 193
“Antigen cascade,” xiv
Antigen delivery, in yeast-based immunotherapy, 146
Anti-GITR antibodies, versus Tregs, 192–193.
See also Glucocorticoid-induced tumor necrosis factor receptor (GITR)
Anti-human papilloma virus antibody titers, in immune monitoring, 272
"Anti-TLR9" antibodies, 45
Antitumor immune response. See also Antitumor response
CD137 and, 255–256, 257–258
as goal of cancer immunotherapy, 229–230
intratumor generation of, 229–242
PD-1/B7-H1/B7-DC pathway and, 253
     tumor cells and, 171
Antitumor immunity, generation of, xiii, xvi
Antitumor response, strategies for activating, xiii–xiv. See also Antitumor immune response
Antitumor vaccines. See also Anticancer vaccines; Cancer vaccines; Vaccine entries
carbohydrate-based, 15–27
evaluation of, 291–307
Apoptosis. See also Activation-induced cell death (AICD); PD-1 (programmed death 1) gene
      breast tumor vaccines and, 171, 172
     in evaluating immune competence, 297, 304
     PD-1 gene and, 245
     Aromatase inhibitors, in endocrine therapy, 174
Artificial APC (aAPC), in CD137 studies, 260–261
Assays
in cancer vaccine evaluation, 295, 297–301
in cancer vaccine use, 10
in immune monitoring, 273–274, 284–285, 295
QA/QC program for, 301–303, 304
Assay validation, 284
quality assurance/quality control for, 303
Augustine, Matthew, ix, 243
Autoimmune disease, cancer immunity suppression and, 211
Autoimmune pathogenesis, PD-1/B7-H1/B7-DC pathway and, 246, 248
Autoimmune responses, PD-1/B7-H1/B7-DC pathway and, 246
Autoimmunity, cancer immunotherapy strategies and, 231–232
Autologous DCs, in ELISpot assay, 275
Autologous HSCT
animal models of, 206
future of, 214
immune reconstitution following, 206–210
immune regulatory cells and, 211–212, 213
immunotherapy and, 9
tumor burden and, 212–213
Bacterial CpG DNA, in adjuvants, 5–6
Bacterial lipopolysaccharide (LPS), in yeast-based immunotherapy, 134
Bacterial vaccine vectors, 114
safety concerns related to, 123
Barnett, Brian G., ix, 189
Basiliximab, versus CD25, 191
Batching
in cancer vaccine evaluation, 298
quality assurance/quality control in, 303
B7-1/CD80 costimulatory molecules, 157
B7-1 costimulatory molecule
     in combination therapies, 103
     immune-response induction and, 100, 101
     B7/CD28/CTLA4 pathway, 261–262
     costimulatory and coinhibitory molecules and, 244
B7-DC ligand
     functions of, 246, 247–248
     PD-1/B7-H1/B7-DC pathway and, 245–247, 251, 252, 253
     structure of, 246–247
B7-H1 ligand
     functions of, 246, 247, 248–249
     PD-1/B7-H1/B7-DC pathway and, 245–247, 251, 252, 253
     structure of, 245–246, 246–247
B7-H1 molecule, mDCs and, 195–196
B7-H4+ myeloid cells, 197
B16/D5 melanoma tumor, in CD137 studies, 261
Bacillus Calmette–Guérin (BCG), xiv, 8
as adjuvant, 5
allogeneic vaccines and, 156
chemotherapy versus, 32–33
combination immunotherapy using, 35
disease progression and, 34–35
in genitourinary cancer immunotherapy, 29–42
immunotherapy technique using, 31–32
improving immunotherapy using, 35
in situ bladder carcinoma treatment using, 33–34
maintenance, 34–35
mortality and, 34–35
toxicity of, 37–38
Bacteria
in antigen-specific therapy, 7, 113–129
recombinant antigen expression in, 121
Bacterial CpG DNA, in adjuvants, 5–6
Bacterial lipopolysaccharide (LPS), in yeast-based immunotherapy, 134
Bacterial vaccine vectors, 114
safety concerns related to, 123
Batching
in cancer vaccine evaluation, 298
quality assurance/quality control in, 303
B cell lymphoma, PD-1/B7-H1/B7-DC pathway and, 251
B-cell-mediated IgM response, 16. See also Immunoglobulin M (IgM)
B cells. See also B lymphocytes
CpG ODNs and, 49
PD-1/B7-H1/B7-DC pathway and, 246
PD-1 expression on, 246
in stimulating innate and adaptive immunity, 47–48
BCG antigens, 37
Becacizumab, in monoclonal antibody therapy, 174
β cells, PD-1/B7-H1/B7-DC pathway and, 248
β-glucan receptor, in yeast-based immunotherapy, 133
Bioanalytical Method Validation, 303
Biofection, with Listeria monocytogenes, 119
Biological adjuvants, for immune system activation, xiv. See also Adjuvants
Biologic vectors
in antigen-specific therapy, 7, 113–129,
131–149
safety concerns related to, 122–123
Bioluminscent imaging (BLI), in vivo imaging via, 283
Biomarkers, in cancer vaccine evaluation, 304
Biphosphonate therapy, clinical trials of, 219
Blood handling, vaccine production and, 293
B lymphocytes, CD137 mRNA in, 253–254. See also B cell entries
Bone marrow (BM)
autologous HSCT and, 206–207, 208, 209
cancer immunity suppression and, 211, 213
CD137L and, 254–255
Bone marrow transplantation, 3
immunotherapy and, 9
Boosts
for intracellular bacteria-based vaccines, 121
for poxvirus vaccines, 100
Borges, Virginia, ix, 131
Breast cancer, 169
application of polyepitope technology to, 74t, 76
globo-H-KLH conjugate and, 18–19
human clinical trials of GM-CSF-secreting vaccines in, 178
Listeria monocytogenes versus, 118
treatment of, 217
Breast cancer cells, costimulatory-molecular whole-cell vaccine modification and, 157
Breast cancer therapeutics, jump-starting tumor immunity with, 169–187
Breast cancer treatment, clinical trials of, 219
Breast cancer vaccines, 170
combined with standard cancer therapeutics, 170
Breast tumor immunity, 169–187
barriers to, 170
chemotherapy and, 170–173
diabetes therapy and, 173, 174–175
monoclonal antibody and, 173–174
new transgenic mouse model and, 175–178
novel immune-based therapies and, 178–180
Breast tumor vaccine, 8
Breuer’s yeast, in immunotherapy, 131–132, 145–147. See also Saccharomyces cerevisiae
Brumlik, Michael J., ix, 189
Bulk assays, in cancer vaccine evaluation, 297, 298
Calmette, Albert, 30
Canada, BCG treatment in, 38
Canarypox vector (ALVAC), in cancer therapy, 96–97, 98t
Cancer, 79. See also Breast cancer entries;
Carcino- entries; Melanoma entries;
Metastases; Ovarian cancer; Prostate cancer; Solid tumors; Tumor entries
Cancer–antigen–specific response, 8
Cancer immunity suppression, Tregs in, 211–212, 213
Cancer immunotherapy, 79–80. See also Antigen-specific cancer immunotherapy;
Antigen-specific therapy; Immunotherapy entries
antitumor immune response as goal of, 229–230
costimulatory molecules in, 243–268
current strategies for, 230–231
history of, 243–244
Listeria monocytogenes in, 113–129
new paradigms in, xiii–xvi
vaccines in, xiii, 95, 205–206
Cancer treatment, 224
Cancer type, in vaccine evaluation, 292
Cancer vaccines
administration of, xiv–xv
advances in immune monitoring strategies for, 271–289
in antigen-specific therapy, 6–7
as cancer immunotherapy strategy, 230–231
carbohydrate-based, 15–27
cell-based, 7–10
clinical activity of, xiv
in combination therapy, xv, xvi
defined, 4
defining effective responses to, 10–11
enhancing by stimulating TLR9, 43–66
immune evaluation of, 291–307
immune monitoring assays for, 273–274, 284–285
new paradigms in, xiii–xvi
objectives of, 295–296
poxviral vectors for, 95–111
pre-administration immune competence evaluation of, 296–297
promise of, 3–11
tools necessary to support, 292–295
tumor burden and, 212–213
Candida, yeast-based immunotherapy and, 133
Canvaxin, allogeneic vaccines and, 156
Carbohydrate-based antitumor vaccines, 15–27
future directions in, 25–26
Carbohydrates
synthesis of, 16–18
of tumor cell surfaces, 15–16
Carboxyfluorescein diacetate (CFSE), in T cell proliferation assays, 282
Carcinoembryonic antigen (CEA)
in antigen-specific therapy, 6, 97
in combination therapies, 102–103
with MVA, 104–105
in yeast-based immunotherapy, 135, 138
Carcinogenesis, genetic changes associated with, 229–230
Carcinoma in situ (CIS), BCG treatment of, 33–34
Carrier molecules, immunogenic, 16
CCL2 tumor-secreted chemokine, 194
CCR4 receptor, CCL2 chemokine and, 194
CD3, in CD137 studies, 260–261
CD3+CD8+ tetramer+ cells, in tetramer analysis, 277
CD4+CD25+ Tregs, 197–198
in immune monitoring, 272–273
inside tumors, 234
mDCs and, 196
monoclonal antibodies versus, 190–191
Ontak versus, 191–192
TAA-specific, 197, 198
in tetramer analysis, 277
CD4+Foxp3+ T cells, cancer immunity suppression and, 211, 212
CD4+ T cell responses, CpG ODNs in stimulating, 53
CD4+ T cells. See also Effector CD4+ T cells;
Helper CD4 T cells; T-regulatory (Treg) activity
in cancer vaccine evaluation, 299
CD137/CD137L in, 254, 255, 256–257
in CD137 studies, 257, 259
in chemotherapy-modulated immune tolerance, 171, 172
cytokine-secreting tumor cells and, 158
in ELISpot assay, 275
enhancing DC antigen expression via, 84, 86
in flow cytometry, 278
following syngeneic HSCT, 209, 210
GM-CSF-secreting vaccines and, 176, 177
in immune-based therapies, 179
in increasing antigen-expressing DCs, 83
inside tumors, 234
PD-1/B7-H1/B7-DC pathway and, 248, 249, 250, 251
regeneration following HSCT, 220–223
in treating HPV, 80–81
cancer vaccine activation of, xiii
whole-cell vaccines and, 154
CD4+ Tregs, 190
CD25 and, 191
CD8+ T cell responses
CpG ODNs in stimulating, 48, 51, 53
LMP polyepitopes and, 75
toll-like receptors and, 44
in yeast-based immunotherapy, 134–135, 146
CD8+ T cells. See also Effector CD8+ T cells
Ad-LIGHT administration and, 236
in cancer vaccine evaluation, 298, 299
CD137/CD137L in, 255, 256–257
in CD137 studies, 259, 261
in chemotherapy-modulated immune tolerance, 171, 172
in clinical trials of DNA-based vaccines, 87
costimulatory-molecular whole-cell vaccine modification and, 157
in cytotoxic assays, 282
in ELISpot assay, 275
in enhancing DC antigen presentation, 86
in enhancing DC–T cell interaction, 86
following syngeneic HSCT, 209, 210
CD8+ T cells (Continued)
in flow cytometry, 278
GM-CSF-secreting vaccination and monoclonal antibody therapy and,
177–178
in immune-based therapies, 179
in increasing antigen-expressing DCs, 82, 83
inside tumors, 234, 235
in microarray analysis, 280
PD-1/B7-H1/B7-DC pathway and, 249–250, 251, 252
pDC interactions with, 195
regeneration following HSCT, 221–223
in treating HPV, 80–81
vaccine activation of, xiii
whole-cell vaccines and, 154
CD8+ Tregs, 197
CD25
monoclonal antibodies versus, 190–191
Ontak versus, 191–192
CD25+ T cells, 190–191, 191–192
cancer immunity suppression and, 211, 213
CD28, CD137 and, 256, 259–260, 261
CD28 gene, PD-1/B7-H1/B7-DC pathway and, 245
CD28-independent costimulation, creating tumor lymphoid tissue and, 234
CD36 scavenger receptor, in yeast-based immunotherapy, 133
CD44hi memory T cell response, GM-CSF-secreting vaccines and, 177
CD45RA isoform phenotype, 221
CD137/CD137L pathway, 253–261, 261–262
costimulatory and coinhibitory molecules and, 244
CD137/CD137L pathway, 253–261, 261–262
costimulatory and coinhibitory molecules and, 244
CD137L pathway, 253–261, 261–262
costimulatory and coinhibitory molecules and, 244
CD137/Fc fusion protein construct, 254, 255
CD137L (CD137 ligand)
identification of, 254
structure of, 254
CD137L expression, 258–259
CD137L gene, 254
CD137 mRNA, 253–254
CD137 protein
binding partners for, 254
structure of, 253
cDNA, in microarray analysis, 280
Cell-based cancer vaccines, 7–10
Cell Genesys, Incorporated, 181
Cell-surface carbohydrate epitopes, clustered vaccines and, 21
Cell-surface carbohydrates, of tumor cells, 15–16
Cell surface glycoprotein molecules, APCs and, 244
Cellular vaccines, support for, 293
CEM cell line, CD137 mRNA in, 253
Centromeric DNA elements (CENs), yeast-based vaccine vector design and, 140
Cervical cancer, 80
as antigen-specific cancer immunotherapy model system, 79–94
application of polyepitope technology to, 74t, 76
human papillomavirus and, 80
Listeria monocytogenes versus, 117–118
Cetuximab, in monoclonal antibody therapy, 174
cGMP (current good manufacturing practices) vaccine generation, support for, 292–293
Chemistry manufacturing and controls (CMC) section, safety of yeast-based therapeutics and, 144–145
Chemokines, 194
in creating tumor lymphoid tissue, 232
Chemokine signaling, versus Tregs, 194
Chemotherapeutic drugs, antitumor immunity and, xiii
Chemotherapy, 224. See also High-dose therapy BCG versus, 32–33
breast tumor immunity and, 170–173
breast tumor vaccines and, 171
dose-intensive, 218–219
GM-CSF-secreting vaccines and, 176–177
immune-depleting, 217–218
immune tolerance modulation via, 171–172
immunotherapy and, 8, 9, 10
poxvirus vectors in combination with, 102, 103–104
tumor microenvironment and, 173
Chen, Lieping, ix, 229
Chloramphenicol transferase genes, 120
Chronic lymphocytic leukemia, fludarabine versus, 192
Chronic myelogenous leukemia (CML) patients, HSCT and, 218
Class II–associated li peptide (CLIP), in enhancing DC antigen presentation, 85, 86
Class A CpG ODNs, 46
Class B CpG ODNs, 46–47
regulatory T cells and, 48
Class C CpG ODNs, 46
Clinical responses, effective, 10–11
Clinical studies/trials, xiv, xv, xvi, 3–4
of allogeneic vaccines, 155–156
of alternatives to high-dose chemotherapy, 219–220
of bacillus Calmette–Guérin, 31, 32–33, 34–35
of breast cancer treatments, 219
INDEX

of breast cancer vaccines, 170
of cancer immunotherapy strategies, 230–231
of cancer vaccines, xv
of clustered vaccines, 21–22
of combination therapies, 102–104
with CpG ODNs, 50–51, 51–53
in DNA vaccine development, 86–87
of globo-H-KLH conjugate, 18–19
including MVA, 104–106
of Lewisy-KLH, 20
of modified cytokine-secreting whole-cell vaccines, 158–159
of Ontak, 191–192
of polyepitope vaccines, 75–77
of poxvirus vaccines, 97, 98–99t
T cell reconstitution in, 220–223
therapeutic HPV vaccine, 88–90t
in yeast-based immunotherapy, 144, 145
Clinics, for vaccine production support, 292
Cloning, 121
Clustered vaccines, 20–22
Codon optimization, enhancing DC antigen expression via, 84
Cohort inhibitory molecules, 261–262
APCs and, 244
Coley, William, 243
College of American Pathologists (CAP), 301
Colony-forming units (CFUs), 121
Colorectal cancers, immune-response induction in treating, 101
Colorectal tumor hepatic metastasis model, in CD137 studies, 259
Combination therapies
cancer vaccines in, xv, xvi
including poxvirus vectors, 102–104
using BCG and drugs, 35
Complement receptor 3 (CR3), in yeast-based immunotherapy, 133
Computed tomography (CT), in vivo imaging via, 283, 284
Concanavalin A (ConA), PD-1 gene and, 245
Conflict-of-interest policies, 181
Constitutive promoters, in yeast-based vaccine vector design, 141–142
Copenhagen rat model, allogeneic vaccines and, 155
Copier, John, ix, 153
Costimulatory molecules
APCs and, 244
in cancer immunotherapy, 243–268
modification of whole-cell vaccines with, 156–157
Coukos, George, ix, 189
CPG 7909 synthetic TLR9 agonist, 52–53
CpG (cytosine–phosphate–guanine) dinucleotides, TLR9 in detecting, 44
CpG DNA, in adjuvants, 5–6
CpG motifs, for activating TLR9, 45
CpG oligonucleotides (ODNs)
as adjuvants, 47, 48
classes of, 46–47
efficacy in mouse tumor models, 51
human clinical trials with, 50–51, 51–53
LIGHT expression and, 235
regulatory T cells and, 48
safety of, 53–54
in stimulating innate and adaptive immunity, 47–49
synergy with other adjuvants, 50
TLR9 activation and, 44–46
51Cr (chromium) isotope in cancer vaccine evaluation, 298
in cytotoxic assays, 282–283
Crispen, Ray, 38–39
“Cross-dressing,” whole-cell vaccines and, 154
Cross-presentation, 133
of exogenous yeast-associated antigens into MHC I pathway, 133–135, 146
Cross-priming, 133. See also Priming in human breast cancer therapy, 175
by whole-cell vaccines, 154
yeast-induced, 133–134
CRT (calreticulin), in enhancing DC antigen expression, 84, 85
Cryopreservation in cancer vaccine evaluation, 298
quality assurance/quality control for, 302, 304
in vaccine monitoring, 294–295
CTLA4 blockade, 190, 192. See also Cytotoxic T lymphocyte antigen 4 (CTLA4)
CTLA4 counterregulatory signaling pathway, in immune-based therapies, 179
CTLA4 gene, PD-1/B7-H1/B7-DC pathway and, 245
CTL activation, 70
CTL epitopes, 69–70
peptide-based vaccines and, 70–71
CUP1 promoter, in yeast-based vaccine vector design, 142
Curiel, Tyler J., ix, 189
Cutaneous T cell lymphoma/leukemia, Ontak versus, 191
CXCL12 chemokine ovarian cancer and, 194
pDCs and, 195
CXCR4 expression ovarian cancer and, 194
pDCs and, 195
Cycloaddition, in carbohydrate synthesis, 17
Cyclophosphamide (CY)
in chemotherapy-modulated immune tolerance, 171
clinical trials of, 219–220
GM-CSF-secreting vaccines and, 176–177, 178
poxvirus vectors in combination with, 103, 104
versus Tregs, 192
Cytokine expression, poxvirus vectors and, 101–102
Cytokine flow cytometry (CFC). See also Flow cytometry
in cancer vaccine evaluation, 298–299
in immune monitoring, 273, 274t, 278–279, 285, 304
Cytokine-induced killer (CIK) T cells, in in vivo imaging, 283–284
Cytokine responses, to allogeneic vaccines, 155–156
Cytokines
allogeneic vaccine modifications to secrete, 157–159
in antigen-specific therapy, 7
BCG immune response and, 37
in cancer vaccine evaluation, 298–299
in CD137 studies, 260
costimulatory and coinhibitory molecules and, 244
in ELISpot assay, 275–276
inside tumors, 234
in monoclonal antibody therapy, 174
PD-1/B7-H1/B7-DC pathway and, 247, 251–252
in T cell regeneration, 221–222, 223, 224
in tetramer analysis, 277
Cytokine-secreting tumor cells, 158
Cytokine secretion, in cancer vaccine evaluation, 299
Cytolytic CD8 T cells, vaccine activation of, xiii
Cytomegalovirus (CMV), 52–53
Cytoreduction, breast tumor immunity and, 170–173
Cytosine–phosphate–guanine (CpG) site. See CpG entries
Cytotoxic T lymphocyte antigen 4 (CTLA4), 244. See also CTLA4 entries
antitumor immunity and, xiii
costimulatory molecules beyond, 243–268
PD-1/B7-H1/B7-DC pathway and, 248, 250
Tregs and, 193
Cytotoxic T lymphocytes (CTLs)
Ad-LIGHT administration and, 236
allogeneic vaccines and, 155–156
in CD137 studies, 258, 259
costimulatory-molecular whole-cell vaccine modification and, 157
generation in LIGHT-mediated tumor environment, 235–236
HER2/new-specific, 176
immunosuppressive pathways and, 173
immunotherapy and, 10, 237
in monoclonal antibody therapy, 173
PD-1/B7-H1/B7-DC pathway and, 251
polyepitope vaccines and, 69–76
in yeast-based immunotherapy, 143
Cytotoxan (CY), 8
Daclizumab
in immune-based therapies, 179–180
versus CD25, 191
Dalgleish, Angus, ix, 153
Daniel, Benjamin J., ix, 189
Danishefsky, Samuel J., ix, 15
DC-based vaccines. See also Dendritic cells (DCs)
characteristics of, 82t
clinical trials of, 90t
Degradation protection, with CpG ODNs, 50
Delayed-type hypersensitivity (DTH) reactions, 4–5
to allogeneic vaccines, 155–156
in vaccine evaluation, 292, 294, 296
Dendritic-cell-based vaccines support for, 293
TLR signaling and, 193
Dendritic cell lymphocytes, cancer immunotherapy strategies and, 231–232
Dendritic cells (DCs). See also DC-based vaccines; Myeloid dendritic cells (mDCs);
Plasmacytoid dendritic cells (pDCs)
activation and maturation of, 133, 134, 172
B7-DC ligand and, 246
CD137L and, 254
in CD137 studies, 258
in chemotherapy-modulated immune tolerance, 172
in ELISpot assay, 275
LIGHT expression and, 235
DCs
Listeria monocytogenes and, 114, 115
in monoclonal antibody therapy, 174
PD-1/B7-H1/B7-DC pathway and, 249
strategies for enhancing antigen expression, processing, and presentation in, 84–86
strategies for enhancing T-cell interaction with, 86, 87
strategies for increasing, 82–83
in treating HPV, 80–81
Treg interactions with, 194–196
vascular leukocytes as, 196
whole-cell vaccines and, 154, 160
in yeast-based immunotherapy, 133–134, 135
yeast-cell phagocytosis by, 132
Denileukin diftitox (Ontak), 197, 198
in immune-based therapies, 9, 179–180, 191–192
Depot effect, with CpG ODNs, 50
Diabetes, PD-1/B7-H1/B7-DC pathway and, 246, 248–249
Dicetaxel, 160
Dihydropyrones, selective formation of, 17
Diphtheria toxin conjugate, versus CD25, 191
Direct assays, in cancer vaccine evaluation, 297
Direct cloning, 121
Disease progression, after BCG treatment, 34–35
DNA-based vaccines
in antigen-specific therapy, 6
characteristics of, 82
clinical trials of, 89–90
in enhancing DC–T cell interaction, 86
enhancing potency of, 82–87
human clinical trials of, 86–87
Listeria monocytogenes in, 119
safety of, 91
in treating HPV, 80, 81
DNA encoding apoptotic proteins, in enhancing DC–T cell interaction, 86
DNA-encoding tumor antigens, dendritic cells and, 81
DNA replication, yeast-based vaccine vector design and, 140
DNA vectors
in antigen-specific therapy, 6, 7
in polyepitope technology, 72
Docetaxel, poxvirus vectors in combination with, 104
Donor lymphocyte infusions (DLIs), 218
Donors, in carbohydrate synthesis, 17, 18
Dose-intensive chemotherapy, in cancer treatment, 218–219, 224
Dose number, in yeast-based immunotherapy, 143
Dose-response parameters, in yeast-based vaccine vector design, 143–144
Doxorubicin (DOX)
BCG versus, 32t, 33
in chemotherapy-modulated immune tolerance, 171, 172
GM-CSF-secreting vaccines and, 176, 178
poxvirus vectors in combination with, 103, 104
Draining lymph nodes (DLNs), 230
Drugs, with BCG treatment, 35
DTH skin tests, in cancer vaccine evaluation, 300–301
E6 gene, human papillomavirus and, 117, 118
E7 gene
DNA-based vaccines and, 119
human papillomavirus and, 117, 118
EBV-associated malignancies, polyepitope-based treatment of, 73–75, 76. See also Epstein–Barr virus (EBV)
Effective clinical responses, 10–11
Effector CD4+ T cells. See also CD4+ T cells
in increasing antigen-expressing DCs, 83
inside tumors, 234
Tregs and, 190, 193
Effector CD8+ T cells. See also CD8+ T cells
in evaluating immune competence, 297
in increasing antigen-expressing DCs, 83
inside tumors, 234, 235
Tregs and, 190, 193
Effector T cells. See also T cell entries
carcinogenesis and, 229
immunotherapy and, 8–9
in treating HPV, 80–81
Ehrlich, Paul, 243, 244
ELISpot (enzyme-linked immunospot) assay. See also Enzyme-linked immunosorbent assay (ELISA)
in cancer vaccine evaluation, 298, 299–300
in immune monitoring, 272, 273, 274–276, 285
quality assurance/quality control for, 303, 304
Emens, Leisha A., ix, 169
Encoded antigens, in increasing antigen-expressing DCs, 82
Endocrine therapy, breast tumor immunity and, 173, 174–175
Endoplasmic reticulum (ER)
in enhancing DC antigen expression, 85
TLR9 in, 45–46
Endosomal acidification/maturation, TLR9 in, 45–46
Endosomes, stimulating innate and adaptive immunity in, 47
Endothelial cells, PD-1/B7-H1/B7-DC pathway and, 249
Endothelial precursor cells, vascular leukocytes as, 196
Energix-B, CpG ODNs used with, 50, 51
Enhancement with CpG ODNs, 50
of tumor vaccines via chemotherapy, 170–171
ENO2 (enolase) promoter, in yeast-based vaccine vector design, 142
Enzyme-linked immunosorbent assay (ELISA), 23. See also ELISpot (enzyme-linked immunospot) assay
in immune monitoring, 273, 274t
Eosinophils, whole-cell vaccines and, 154
Epidermal growth factor receptor (EGFR) in monoclonal antibody therapy, 174
in yeast-based immunotherapy, 135, 138–139
Epirubicin, BCG versus, 32
Episomal gene expression, 121
Episomal plasmids, in yeast-based vaccine vector design, 139–140
Epitopes. See CTL epitopes; Polyepitope vaccines
“Epitope spreading.” xiv
Epstein–Barr nuclear antigens (EBNAs), in treatment of EBV-associated malignancies, 73
Epstein–Barr virus (EBV), 52–53. See also EBV-associated malignancies polypeptide technology and, 71, 72
Equine encephalitis virus, as cancer-therapy vaccine vector, 96
Eroposide, clinical trials of, 219
Escherichia coli, in constructing Listeria monocytogenes vaccine vectors, 119, 120, 121
Esophageal carcinoma (EC1), CD137L and, 254
Estrogen receptor (ER), in monoclonal antibody therapy, 174
Estrogen receptor α (ERα), 169, 180
Evaluation of cancer vaccines, 291–307
Exemestane, in endocrine therapy, 174
“Exhausted T cells.” PD-1/B7-H1/B7-DC pathway and, 250
Experimental autoimmune encephalitis (EAE), PD-1/B7-H1/B7-DC pathway and, 246, 249
Experimental vaccine development, 3
Expressed sequences tag (EST) database, in microarray analysis, 280
Extracellular receptor kinase (ERK), CpG ODNs in stimulating, 47
Extrachromosomal plasmids, in yeast-based vaccine vector design, 139–140
Ex vivo T cell analysis, 52–53
in immune monitoring, 272
Flanking amino acid sequences, in CTL epitopes, 71–72
Flow cytometry. See also Cytokine flow cytometry (CFC)
in immune monitoring, 273, 274t, 278–279, 285
in T cell proliferation assays, 282
Fludarabine (Flu)
clinical trials of, 219–220
versus Tregs, 192
Fluorescence-activated cell sorter (FACS) analysis, 19
in CD137 studies, 258
PD-1/B7-H1/B7-DC pathway and, 250
Fluorescent dye, in qRT-PCR, 279
Fms-like tyrosine kinase 3 (flt3) ligands, in increasing antigen-expressing DCs, 83
Food and Drug Administration (FDA) quality assurance/quality control by, 303
safety of yeast-based therapeutics and, 144–145
vaccine production and, 293
Foreign antigens, in yeast-based immunotherapy, 143
Fowlpox virus boosts for, 100
immune-response induction and, 101
Franzusoff, Alex, ix, 131
Frappier, Armand, 31
Freund’s adjuvant, CpG ODN coadministered with, 49
Fu, Yang-Xin, ix, 229
Fucosyl-GM1 antigen, 20
Fucosyl-GM1–KLH conjugate, 20, 21. See also Keyhole limpet hemocyanin (KLH)
Fully synthetic antitumor vaccines, carbohydrate-based, 15–27
Fulvestrant, in endocrine therapy, 174
Functional assays, in cancer vaccine evaluation, 297
FVB transgenic mice, Listeria monocytogenes in, 118
GAPDH (glyceraldehyde-3-phosphate dehydrogenase) promoter, in yeast-based vaccine vector design, 142
Gastrointestinal (GI) tract cancers, immune-response induction in treating, 101
GD3 antigen, in polyvalent vaccines, 22
INDEX

GD3 ganglioside, CpG ODN coadministered with, 49

Gene expression
episomal, 121
in *Listeria monocytogenes*, 119, 120

Gene expression cassettes, in yeast-based vaccine vector design, 139–140

Gene gun delivery, of DNA, 82

Genes, in microarray analysis, 280–281

Gene therapy approach, in CD137 studies, 257

Genetic changes, associated with carcinogenesis, 229–230

Genetic engineering, of *Listeria monocytogenes*, 114

Genetic manipulation, in constructing *Listeria* vaccine vectors, 121

Genitourinary cancer immunotherapy, bacillus Calmette–Guérin in, 29–42

GI-3000 yeast strains, in yeast-based immunotherapy, 138

GI-4000-01 phase I safety and immunogenicity, 145

GI-4000-02 phase II testing, 145

GI-4000 yeast strains safety of yeast-based therapeutics and, 144–145

in yeast-based immunotherapy, 135–137, 138, 139

GL261 glioma cells, in CD137 studies, 261

Glioma cell lines, PD-1/B7-H1/B7-DC pathway and, 244

Globo-H-KLH conjugate. See also Keyhole limpet hemocyanin (KLH)
clinical trials of, 18–19
in pentavalent vaccine, 24, 25
synthesis of, 18
in trivalent vaccine, 23
as vaccine, 18
β-Glucan receptor, in yeast-based immunotherapy, 133

Glucocorticoid-induced tumor necrosis factor receptor (GITR), in immune-based therapies, 180. See also Anti-GITR antibodies

Glycals, in carbohydrate synthesis, 17, 18

Glycoconjugates, as adjuvants, 5

Glycoprotein molecules, APCs and, 244

Glycoproteins with cell-surface carbohydrates, 15, 16
clastered vaccines and, 21

Glycosphinoglipids, cell-surface, 15

GM2 antigen
in hexavalent vaccine, 24
in pentavalent vaccine, 25

GM-CSF-secreting vaccines. See also Granulocyte–macrophage colony stimulating factor (GM-CSF) chemotherapy and, 176–177
human clinical trials of, 178
monoclonal antibody therapy and, 177–178
*neu* transgenic mouse model and, 175–176

Golgi zone, in cancer vaccine evaluation, 299

Good laboratory practice (GLP)
in cancer vaccine use, 10
in vaccine monitoring, 302t, 304

gp100 melanoma antigen, 96
in tetramer analysis, 277

Granulocyte–macrophage colony stimulating factor (GM-CSF). See also GM-CSF-secreting vaccines
in antigen-specific therapy, 7
BCG immune response and, 37
in combination therapies, 103
cytokine-secreting tumor cells and, 158–159, 159–160
in ELISpot assay, 276
in enhancing DC–T cell interaction, 86
immunotherapy and, 8
in mouse tumor models, 51
poxvirus vectors and, 101–102
in yeast-based immunotherapy, 134

Green fluorescent protein (GFP) gene, in in vivo imaging, 283

Gress, Ronald, x, 217

Guérin, Camille, 30

Guinea pigs, intracellular bacteria-based vaccines in, 122

Guo, Zhimin, x, 131

Heaf gun, 32

Heatshock proteins, following syngeneic HSCT, 210

Helper CD4 T cells. See also CD4+ T cells
GM-CSF-secreting vaccines and, 176, 177
vaccine activation of, xiii

Helper T cells, BCG immune response and, 37. See also T cell entries

Hematopoietic stem cell transplantation (HSCT)
cancer immunity suppression and, 211, 212, 213
following high-dose therapy, 205–206
future of, 214
high-dose chemotherapy and, 219–220
immunotherapy and, 9
T cell reconstitution following, 220–223
tumor burden and, 212–213
tumor mass and, 218–219
Hematopoetic stem cell transplantation (HSCT), (Continued)
vaccines and, 217–228
window of survival following, 219
Hematuria, during BCG treatment, 38
Hepatic metastasis model, in CD137 studies, 259
Hepatitis B, application of polyepitope technology to, 74t
Hepatitis B surface antigen (HBsAg), CpG ODN coadministered with, 49, 51
Hepatitis C, application of polyepitope technology to, 74t
HER2 epitopes, clinical studies of, 77
HER2/neu-negative breast cancers, 178
HER2/neu-positive breast cancers, 178
HER2/neu-positive tumors, 176
HER2/neu protooncogene, 175. See also neu transgenic mouse model
HER2/neu-specific CTLs, 176, 177–178
HER2/neu-specific monoclonal antibody, 169–170, 173, 174
HER2/neu-specific T cells, 176
in immune-based therapies, 179
HER2/neu tyrosine kinase expression, breast cancer and, 118, 124, 169
Herpes simplex virus type I (HSV-1), in increasing antigen-expressing DCs, 82
Herpesvirus entry mediator (HVEM), in creating tumor lymphoid tissue, 232–233, 235
Heterologous proteins, in yeast-based vaccine vector design, 141–142
Hexamer CpG motif, in activating TLR9, 45
Hexavalent vaccines, evaluation of, 24, 25
High-dose therapy. See also Chemotherapy alternatives to, 219–220
followed by autologous hematopoetic stem cell transplantation, 205–206
High-dose vitamin administration, with BCG treatment, 35
HLA-A2 epitopes, clinical studies of, 76, 77. See also Human leukocyte antigen (HLA) types
HLA genotypes, in yeast-based immunotherapy, 146
HLA-restricted peptide epitopes, in immune monitoring, 271
HLA transgenic mice, LMP polyepitopes and, 74
Hodge, James W., x, 3
Hodgkin’s lymphoma (HL), polyepitope technology and, 72, 74t
treatment of EBV-associated malignancies and, 73, 75
Homeostatic cytokines, in T cell regeneration, 223
Homogeneous carbohydrates, synthesis of, 16–17
HPV-associated cervical cancer, as antigen-specific cancer immunotherapy model system, 79–94. See also Human papillomavirus (HPV)
HPV vaccines characteristics of, 82t
clinical trials of, 88–90t
H-Ras protein, in yeast-based immunotherapy, 135–137
Human cancer cells, costimulatory-molecular whole-cell vaccine modification and, 157
Human clinical trials. See also Clinical trials with CpG ODNs, 50–51, 51–53
in DNA vaccine development, 86–87
of GM-CSF-secreting vaccines with standard breast cancer therapy, 178
Human cytomegalovirus (HCMV), polyepitope technology and, 72
Human diseases peptide-based vaccines for treating, 70–71
polyepitope technology applications to, 74t, 76
Human glioma cell lines, PD-1/B7-H1/B7-DC pathway and, 251–252
Human immunodeficiency virus (HIV)
application of polyepitope technology to, 74t, 76
PD-1/B7-H1/B7-DC pathway and, 250
polyepitope technology and, 72
Human leukocyte antigen (HLA) types. See also HLA entries
in immune monitoring, 271
LMP polyepitopes and, 74, 75
peptide-based vaccines and, 70–71
in tetramer analysis, 277
in vaccine monitoring, 294
Human papillomavirus (HPV). See also HPV entries
application of polyepitope technology to, 74t, 77
in CD137 studies, 258
in immune monitoring, 272
Listeria monocytogenes versus, 117–118
types of, 80
Human papillomavirus–based vaccine, xv–xvi
Humans Listeria monocytogenes cancer immunotherapy
in, 116, 117–122, 122–123, 123–124
safety of CpG ODN in, 53
Human specimens, vaccine production and, 293–294. See also Specimen collection
Human T cell leukemia, CD137 and, 253
Hung, Chien-Fu, x, 79
Hypothesis-driven preclinical studies, of cancer vaccines, xiii
ICOS gene, PD-1/B7-H1/B7-DC pathway and, 245
IgG antibodies, clustered vaccines and, 21–22
IgM antibodies, clustered vaccines and, 21–22.
See also Immunoglobulin M (IgM)
Immature myeloid cells, 197
tumors and, 234–235
Immune assays, in cancer vaccine use, 10
Immune-based therapies, novel, 178–180
Immune cell phenotype changes, in vaccine monitoring, 294
Immune cells, in evaluating immune competence, 297
Immune competence, evaluation of, 296–297
Immune costimulatory molecules,
immunotherapy and, 10
Immune-depleting chemotherapy, in cancer treatment, 217–218
Immune evaluation, of cancer vaccines, 291–307
Immune monitoring
assay validation in, 284
of cancer vaccines and immunotherapy, 271–289
current tumor immunotherapy approaches to, 272–284
need for, 271–272
in vaccine evaluation, 292
Immune monitoring assays, 273–274, 284–285
Immune reconstitution, following autologous HSCT, 206–210
Immune response
to BCG, 37
cancer therapy and, 205–206
as cancer vaccine objective, 295
CD137 and, 255–256, 257–258
in immune monitoring, 273
intratumor generation of antitumor, 229–242
monitoring of, 303–304
PD-1/B7-H1/B7-DC pathway and, 253
Th1-like, 43, 44
toll-like receptors and, 43–44
to tumor-associated antigens, 189–190
tumor cells and, 171
in yeast-based immunotherapy, 143–144, 146
Immune screen, 296
Immune status, in evaluating immune competence, 297
Immune stimulatory CpG ODNs, classes of, 46–47
Immune suppression, tumor-induced, 218, 219
Immune surveillance, in vaccine evaluation, 291
Immune system
adjuvant stimulation of, 4–6
cancer and, 4
in cancer treatment, 217
theories of, 243–244
tumors and, 3
vaccine activation of, xiii, xv
versus tumor cells, 15–16
Immune tolerance, chemotherapy-modulated, 171–172
Immunity. See Adaptive immunity; Innate immunity
Immunization, as cancer immunotherapy strategy, 230–231
Immunization routes, for intracellular
bacteria-based vaccines, 122
Immunodeficiencies, cancer and, 4
Immunogenic carrier molecules, 16
Immunogenicity, allogeneic vaccines and, 155
Immunoglobulin G (IgG), clustered vaccines and, 21–22
Immunoglobulin M (IgM). See also
B-cell-mediated IgM response
clustered vaccines and, 21–22
fucosyl-GM1–KLH conjugate and, 20
Immunoglobulins (Igs)
in cancer vaccine evaluation, 301
in CD137 studies, 254–255, 258
in evaluating immune competence, 296
Immunologic checkpoints, manipulation of, 178–180
Immunologic memory, in vaccine evaluation, 292
Immunophrophylaxis, history of, 243–244
Immunoreceptor tyrosine-based inhibiting motif (ITIM), PD-1/B7-H1/B7-DC pathway and, 245, 246
Immunoreceptor tyrosine-based switch motif (ITSM), PD-1/B7-H1/B7-DC pathway and, 245, 246
Immunostimulatory complexes (ISCOMs)
CTL activation and, 70
polypeptide technology and, 72
Immunosuppression, in BCG treatment, 34
Immunosuppressive entities, xiii, xvi
Immunosuppressive pathways, 173
Immunotherapy, 224. See also Antigen-specific cancer immunotherapy; Cancer immunotherapy; Yeast-based immunotherapy
advances in immune monitoring strategies for, 271–289
bacillus Calmette–Guérin, 29–42
cancer vaccines and, 4
in immune monitoring, 273
improving BCG, 35
tumor cells in, 7–10
Immunotherapy trials, immune monitoring of, 272
Indirect assays, in cancer vaccine evaluation, 297
Inducible promoters, in yeast-based vaccine vector design, 141–142
Infectious agents, polyepitope technology and, 72
Infectious disease vaccines, CpG ODNs as adjuvants for, 49
Innate immunity
bacterial vaccine vectors and, 114
coupling yeast-based cancer immunotherapy with, 131–149
CpG ODNs in stimulating, 47–49
Interassay variability, in cancer vaccine evaluation, 298
Intercellular adhesion molecule I (ICAM-I)
BCG immune response and, 37
in combination therapies, 102, 103
immune-response induction and, 101
Interferon (IFN)
in BCG combination immunotherapy, 35
CpG ODNs in stimulating, 47
Interferon alpha (IFNα)
CpG ODN classes and, 46
in pDC contamination, 45
Interferon gamma (IFNγ)
BCG immune response and, 37
in CD137 studies, 258, 260
in ELISpot assay, 276
in flow cytometry, 278
following syngeneic HSCT, 209
LIGHT expression and, 235
Listeria monocytogenes and, 115
PD-1/B7-H1/B7-DC pathway and, 247–248, 249, 250, 251, 252
in T cell activation, 53
in yeast-based immunotherapy, 146
Interleukin 1 (IL-1), BCG immune response and, 37
Interleukin 1 receptor-associated kinase (IRAK-1), CpG ODNs in stimulating, 47
Interleukin 2 (IL-2), xiv, 96
in BCG combination immunotherapy, 35
BCG immune response and, 37
CD4+CD25+ Tregs and, 191–192
CD25 and, 190
CD137L and, 255
in combination therapies, 103
cytokine-secreting tumor cells and, 158
in immune-based therapies, 179–180
PD-1/B7-H1/B7-DC pathway and, 249, 251, 252
poxvirus vectors and, 101
Interleukin 6 (IL-6), BCG immune response and, 37
Interleukin 7 (IL-7), in T cell regeneration, 221–222, 223
Interleukin 8 (IL-8), BCG immune response and, 37
Interleukin 10 (IL-10)
BCG immune response and, 37
inside tumors, 234
mDCs and, 195–196
PD-1/B7-H1/B7-DC pathway and, 247, 252
vascular leukocytes and, 196
Interleukin 12 (IL-12)
BCG immune response and, 37
in CD137 studies, 259
Listeria monocytogenes and, 115
in stimulating innate and adaptive immunity, 47
Interleukin 15 (IL-15), in T cell regeneration, 223
Interleukins (ILs)
cytokine-secreting tumor cells and, 158, 159
in ELISpot assay, 276
in flow cytometry, 278
Intracellular bacteria, as vaccine vectors, 114
Intracellular cytokine flow cytometry (CFC), in immune monitoring, 273, 274, 278–279
Intradermal (ID) administration, of bacillus Calmette–Guérin, 31–32
Intravesical administration, of bacillus Calmette–Guérin, 31–32
Investigational new drug (IND) applications, safety of yeast-based therapeutics and, 144
Investigator-initiated drug (IND) application, 293
In vitro assays, in immune monitoring, 273
In vitro sensitization (IVS), in cancer vaccine evaluation, 301
In vitro stimulation (IVS), in ELISpot assay, 275
In vivo assays, in immune monitoring, 273
In vivo imaging, advances in, 283–284
Jenner, Edward, 243
Jing, Weiqing, x, 205
Johns Hopkins University, 181
Johnson, Bryon D., x, 3, 205
Jurkat cell line, CD137 mRNA in, 253
Kaufman, Howard L., x, 271
Kelley, Victoria, x, 131
Keratinocyte growth factor (KGF), 223
Keyhole limpet hemocyanin (KLH), 5. See also Fucosyl-GM1–KLH conjugate; Globo-H-KLH conjugate; KLH carrier
INDEX

protein; Lewisy-KLH, TF(c)-KLH clusters; Tn(c)-KLH clusters
in BCG combination immunotherapy, 35
Khanna, Rajiv, x, 69
Kim-Schulze, Seunghee, x, 271
King, Thomas H., x, 131
KLH carrier protein. See also Keyhole limpet hemocyanin (KLH)
in pentavalent vaccine, 24, 25
in polyvalent vaccines, 22
in trivalent vaccine, 23
K-Ras protein, in yeast-based immunotherapy, 135–137
Krieg, Arthur M., x, 43
Kryczek, Ilona, x, 189
Kupffer cells, PD-1/B7-H1/B7-DC pathway and, 249
Laboratories, for vaccine production support, 292
Laboratory assays, in cancer vaccine use, 10
Lamm, Donald L., x, 29
Latent membrane protein (LMP) antigens/polyepitopes, treatment of EBV-associated malignancies and, 73–75
Late-stage cancer, treatment of, 79
LCMV (lymphocytic choriomeningitis virus) infection, PD-1/B7-H1/B7-DC pathway and, 250
Lethal total body irradiation, conditioning with, 206, 207, 208, 209
Letrozole, in endocrine therapy, 174
leu2d mutation, yeast-based vaccine vector design and, 140–141
Leukemia, fludarabine versus, 192
Leukocyte function-associated antigen 3 (LFA-3) in combination therapies, 103
immune-response induction and, 101
Lewisy-KLH. See also Keyhole limpet hemocyanin (KLH)
clinical trials of, 20
in pentavalent vaccine, 24–25
in polyvalent vaccines, 22
in trivalent vaccine, 23
Lewisy pentasaccharide, 20
LIGHT expression in cell interactions, 235
in creating tumor lymphoid tissue, 232–234
immunotherapy and, 10
treatment of metastases and, 235–236
LIGHT-mediated tumor environment, CTL generation in, 235–236
Lipopolysaccharide (LPS), in yeast-based immunotherapy, 134
Lipopolysaccharide-like structures, as adjuvants, 5
Listeria monocytogenes (LM) in antigen-specific therapy, 7, 113–129
as breast cancer vaccine, 118
as cervical cancer vaccine, 117–118
constructing vectors from, 119–122
as DNA carrier vaccine, 119
infection with, 115
safety concerns related to, 122–123
as vaccine vector, 114–117
Listeriosis, 123
Live recombinant vaccine vectors, 114–122
Live vectors, safety concerns related to, 122–123
Live vector vaccines with antigen-presenting cells, 81
characteristics of, 82t
clinical trials of, 88t
LLO (listeriolysin O) hemolytic protein Listeria monocytogenes and, 116, 117, 118
safety concerns related to, 123
LLO-E7 fusion gene, in Listeria monocytogenes, 119, 120
LM-ActA-E7 vaccine, human papillomavirus and, 117–118
LM-LLO-E7 vaccine, human papillomavirus and, 117–118, 123–124
Lncap allogeneic cell line, 156
Lobund–Wistar model of prostate cancer, allogeneic vaccines and, 155
“Low copy” plasmids, yeast-based vaccine vector design and, 140
LTβR receptor, in creating tumor lymphoid tissue, 232, 233
Lu, Yingnian, x, 131
Luciferase (Luc) gene, in in vivo imaging, 283
Lung tumor model, in yeast-based immunotherapy, 135–136
Lupus erythematosus, PD-1/B7-H1/B7-DC pathway and, 246
LyD9 cells, PD-1 gene and, 245
Lymph nodes, PD-1/B7-H1/B7-DC pathway and, 252
Lymph node sensitization, in CD137 studies, 261
Lymphoblastoid cell lines (LCLs), treatment of EBV-associated malignancies and, 73, 75
Lymphocyte-associated globulin 3 (LAG-3), in immune-based therapies, 180
Lymphocyte homeostasis, in evaluating immune competence, 297
Lymphocytes. See also T lymphocytes
See also T lymphocytes cancer and, 4
carcinogenesis and, 229
Lymphocytic leukemia, fludarabine versus, 192
Lymphoid tissue reconstitution, following syngeneic HSCT, 207, 209
Lymphoma cells, in CD137 studies, 259
Lymphopenia
breast tumor vaccines and, 170, 171
following HSCT, 206–210
Lymphotoxin α (LTα)
in creating tumor lymphoid tissue, 232
PD-1/B7-H1/B7-DC pathway and, 250
Lymphotoxin α1β2 (LTαβ2), in creating tumor lymphoid tissue, 232
Lymphotoxin β (LTβ), in creating tumor lymphoid tissue, 232
Lysosome-associated membrane protein 1 (LAMP-1), in enhancing DC antigen expression, 84, 85
Macrophages (Mφ)
antitumor immunity and, xiii
Listeria monocytogenes and, 114, 115
whole-cell vaccines and, 154
yeast-cell phagocytosis by, 132
Magnetic resonance imaging (MRI), in vivo imaging via, 283, 284
Maintenance immunotherapy, after BCG treatment, 34–35
Major histocompatibility complex (MHC), xv.
See also MHC entries; Peptide–MHC complex
in antigen-specific therapy, 7
clinical studies of, 76
costimulatory-molecular whole-cell vaccine modification and, 157
cytotoxic T lymphocytes and, 69, 70
immune-response induction and, 100
peptide-based vaccines and, 70–71
whole-cell vaccines and, 154
Malaria
application of polyepitope technology to, 74t, 76
polyepitope technology and, 72
Mannose receptor, in yeast-based immunotherapy, 133
Marek’s disease virus type 1 (MDV-1), in increasing antigen-expressing DCs, 82
MART1 melanoma antigen, 96
in tetramer analysis, 277
yeast-expressed, 138t, 139
MCA26 tumor cells, in CD137 studies, 259
MCA205 sarcoma cells, in CD137 studies, 261
McCullough, David, 31
MCF-7 cell lines, globo-H antigen and, 18
Mediastinal B cell lymphoma,
PD-1/B7-H1/B7-DC pathway and, 251
Melan-A human tumor antigen, T cell vaccination with, 52
Melanoma
allogeneic whole-cell vaccines versus, 153, 155, 156, 160
application of polyepitope technology to, 74t, 76, 77
in CD137 studies, 261
cytokines versus, 157–158
Melanoma antigens, 96
in yeast-based immunotherapy, 135
Melphalan, clinical trials of, 219
Memorial Sloan Kettering (MSK), bacillus Calmette–Guérin trials at, 31
Mesothelin, in yeast-based immunotherapy, 135
Metastases, CTL and LIGHT in treating, 235–236
Metastatic cancer, GI-4000–01 phase I safety and immunogenicity in, 145
Metastatic tumors, treatment of, 217
Metronomic chemotherapy, 173
MHC class I pathway. See also Major histocompatibility complex (MHC) bacterial vaccine vectors and, 114
in CD137 studies, 257
in combination therapies, 102, 103–104
cross-presentation of exogenous yeast-associated antigens into, 133–135
enhancing DC antigen expression via, 84, 85
Listeria monocytogenes and, 115
in monoclonal antibody therapy, 173
PD-1/B7-H1/B7-DC pathway and, 248, 250
whole-cell vaccines and, 154
yeast-based immunotherapy and, 132, 133, 146
MHC class II-invariant chain (Ii), in enhancing DC antigen presentation, 85
MHC class II pathway
bacterial vaccine vectors and, 114
CD137L and, 257
in enhancing DC antigen expression, 84, 85–86
Listeria monocytogenes and, 115
whole-cell vaccines and, 154
yeast-based immunotherapy and, 132, 133, 146
MHC class II+ antigen-presenting cells, in creating tumor lymphoid tissue, 232
Mice. See also Mouse tumor models; neu transgenic mouse model
Ad-LIGHT administration to, 236
autologous HSCT models in, 206, 207, 208, 209, 210
CD137-deficient, 254–255, 256
CD137L studies in, 257–258
CD137 mRNA expression in, 254. See also mRNA
CD137 protein in, 253
intracellular bacteria-based vaccine boosts in, 121
in vivo imaging in, 283
Listeria monocytogenes cancer immunotherapy in, 116–117, 118
PD-1/B7-H1/B7-DC pathway studies in, 248–249, 251, 252–253
PD-1-deficient, 246
safety of CpG ODN in, 53–54
TLR9 in, 44–45
Microarray analysis, in immune monitoring, 274t, 280–281
Microtiter plate, in ELISpot assay, 275
Minimal residual disease (MRD) in evaluating immune competence, 297
in vaccine evaluation, 292
Mitomycin C, BCG versus, 32–33, 34–35
MMTV mammary-specific promoter, 175
Model systems, HPV-associated cervical cancer as, 79–94. See also Mouse tumor models; neu transgenic mouse model
Modified vaccinia Ankara (MVA) vaccines, 104
clinical trials of, 88t, 99t, 104–106
Monitoring, of vaccine administration, 294, 296
Monitoring strategies, for cancer vaccines and immunotherapy, 271–289
Monoclonal antibodies in flow cytometry, 278
versus CD25, 190–191
Monoclonal antibody therapy, GM-CSF-secreting vaccines and, 177–178
Monoclonal T cells, in tetramer analysis, 276, 277
Monovalent vaccines, unimolecular, 18–20
Montanide in cancer vaccines, 296
CpG ODNs used with, 50
Mortality, after BCG treatment 34–35
Mouse tumor models, 135–137. See also Mice; neu transgenic mouse model
CpG ODNs in, 51
mRNA, in microarray analysis, 280, 281. See also CD137 mRNA
MUC1 antigen
CpG ODN coadministered with, 49
HCST and, 218
in combination therapies, 102
in polyvalent vaccines, 22
poxviruses vectors and, 101
yeast-expressed, 138–139
MUC2 antigen, in polyvalent vaccines, 22
Mucin polypeptide core molecules, in polyvalent vaccines, 22
Macins, clustered vaccines and, 21
Multiantigen products, in yeast-based vaccine vector design, 142
Multimer binding, 304
Multiplex arrays, in cancer vaccine evaluation, 304
Multiplex assays, in cancer vaccine evaluation, 297–298, 304
Multivalent vaccines, unimolecular, 23–25
Monson, Sibyl, x, 131
Mutated Ras proteins, in yeast-based immunotherapy, 135–137
Mutations, in yeast-based vaccine vector design, 139–141
Mycobacteria as adjuvants, 4–5
as bacterial vaccine vectors, 114
in tuberculosis, 30
Mycobacterium tuberculosis hsp (heat shock protein), 70
in clinical trials of DNA-based vaccines, 87
in enhancing DC antigen expression, 84
MyD88 adaptor molecule, CpG ODNs in stimulating, 47
Myeloablative chemotherapy, breast tumor vaccines and, 171
Myelodysplastic syndrome (MDS), CD137L and, 254
Myeloid cells immature, 197
tumors and, 234–235
Myeloid dendritic cells (mDCs)
PD-1/B7-H1/B7-DC pathway and, 252
in T cell activation, 53
Treg interactions with, 194, 195–196
Myeloid progenitors, CD137L and, 254
Nasopharyngeal carcinoma (NPC)
application of polyepitope technology to, 74t
polyepitope technology and, 72
treatment of EBV-associated malignancies and, 73, 75
Natural killer (NK) cells
in CD137 studies, 257, 258, 259
CpG ODNs in stimulating, 47, 53
following syngeneic HSCT, 210
LIGHT expression and, 235
Natural killer (NK) cells (Continued)

Listeria monocytogenes and, 115
in stimulating innate and adaptive immunity, 47
TLR9 expression in, 45
vaccine activation of, xiii
whole-cell vaccines and, 154

Neoantigens
associated with carcinogenesis, 229
in yeast-based immunotherapy, 135

Nephrectomy, BCG versus, 36

Neuroblastoma, 208, 209, 210

neu transgenic mouse model. See also HER2/neu entries
breast tumor immunity and, 175–178
combining GM-CSF-secreting vaccination and chemotherapy in, 176–177
GM-CSF-secreting vaccination and monoclonal antibody therapy in, 177–178
GM-CSF-secreting vaccines and, 175–176
human clinical trials and, 178

Neutrophils
Listeria monocytogenes and, 114, 115
yeast-cell phagocytosis by, 132
Newcastle disease virus (NDV), as cancer-therapy vaccine vectors, 96
NOD mice, PD-1/B7-H1/B7-DC pathway studies in, 248–249
Non-Hodgkin’s lymphoma (NHL), CD137L and, 254
Nonmyeloablative chemotherapy, immunotherapy and, 9
Nonspecific assays, in cancer vaccine evaluation, 297
North America, BCG treatment in, 38
N-Ras protein, in yeast-based immunotherapy, 135–137

Nucleic acid vaccines. See also DNA-based vaccines
with antigen-presenting cells, 81
characteristics of, 82t

ODN backbone, in activating TLR9, 45
ODN uptake, 45
Oligodeoxynucleotide motifs, in BCG, 37
Oligodeoxynucleotides (ODNs)
in adjuvants, 5–6
CpG-specific responses to, 44
Oligosaccharides
synthesis of, 17
tumor-associated, 16
Oncogenes, 4
Oncology, historical background of, 4

Onk, 197, 198
in immune-based therapies, 9, 179–180, 191–192
OnyCap23 allogeneic cell line, 156
Open reading frames (ORFs), 119
Orentas, Rimas J., x, 3
Origin of replication, yeast-based vaccine vector design and, 140
Ornstein, Moshe, x, 271
Ovarian ablation, in endocrine therapy, 174–175
Ovarian cancer
CXCL12 chemokine and, 194
Lewis<sup>+</sup>-KLH and, 20
vascular leukocytes and, 196
OVCAR-3 cells, Lewis<sup>+</sup>-KLH and, 20
OX40 pathway, in immune-based therapies, 179
P4E6 allogeneic cell line, 156
p80-dal in trans complementation system, 120
P815 cells
in CD137 studies, 258, 260
PD-1/B7-H1/B7-DC pathway and, 251
Paclitaxel (PTX), 8
breast tumor vaccines and, 171
in chemotherapy-modulated immune tolerance, 171–172
clinical trials of, 219
GM-CSF-secreting vaccines and, 176, 177
in monoclonal antibody therapy, 174
poxvirus vectors in combination with, 103, 104
PADRE (pan HLA-DR binding epitope), in enhancing DC antigen presentation, 85–86
pAM401 shuttle plasmid, 120–121
Pancreatic cancer, GI-4000-02 phase II testing in, 145
Pancreatic cell lines, cytokine-secreting, 159
Pancreatic islet β cells, PD-1/B7-H1/B7-DC pathway and, 248
Paracrine secretion, of GM-CSF, 175
Paramyxoviruses, as cancer-therapy vaccine vectors, 96
Parker, Joanne, x, 131
Particle-associated molecular patterns (PAMPs), in yeast-based immunotherapy, 132
Passenger antigens, with vaccine vectors, 114
Paterson, Yvonne, x, 113
PC61 monoclonal antibody, versus CD25, 190–191
PD-1 (programmed death 1) gene. See also Apoptosis
discovery and functions of, 245
expression of, 246
PD-1/B7-H1/B7-DC pathway and, 245–247  
structure of, 245
PD-1/B7-H1/B7-DC pathway, 245–253  
costimulatory and coinhibitory molecules and,  
244, 247
PD-1-deficient mice, 246
PD-E7/D16E7 vaccines, clinical trials of, 89t
PD-L1 ligand, PD-1/B7-H1/B7-DC pathway and,  
245
PD-L2 ligand, PD-1/B7-H1/B7-DC pathway and,  
245
Pentavalent vaccines, evaluation of, 24, 25
Peptide antigens, in antigen-specific therapy, 6–7
Peptide-based vaccines, 69–71  
with antigen-presenting cells, 81  
characteristics of, 82t
clinical trials of, 88–89t
CTL peptide target identification and, 69–70
for treatment of human diseases, 70–71
vehicles for delivery of, 70
Peptide–MHC complex  
immune-response induction and, 100
interactions with T cell receptors, 244
Peptide motifs, in antigen-specific therapy, 6
Perforin, in ELISpot assay, 276
Peripheral blood mononuclear cells (PBMCs)  
in ELISpot assay, 276
in flow cytometry, 278
PD-1 gene and, 245
in polyepitope technology, 71
in tetramer analysis, 277
PEST (proline, glutamic acid, serine, threonine)-like domains, 117
Phagocytes, Listeria monocytogenes and,  
114–116
Phagocytic receptors, in yeast-based immunotherapy, 132, 133
Phagocytosis  
in BCG treatment, 37
of yeast cells, 132, 133
Phase II trials, xiv
Phase III trials, xiv, xv
Phenotype changes, in vaccine monitoring, 294
Phenotypic assays, in cancer vaccine evaluation, 297
Phorbolest mistate acetate (PMA), CD137 and,  
253–254
Phosphorothioate (PS) ODN, CpG-specific responses to, 44
Phytohemagglutinin (PHA), CD137 and, 253
Plasmacytoid dendritic cells (pDCs)  
contamination by, 45

CpG ODNs in stimulating, 47–48, 53
Treg interactions with, 194, 195
Plasmid copy number, in yeast-based vaccine vector design, 139–141
Plasmid DNA, in treating HPV, 80
Plasmid DNA vectors, in antigen-specific therapy, 6
Plasmid release, Listeria monocytogenes and,  
119–121
Pluripotential transcription factor (PrfA), Listeria monocytogenes and, 116, 119–120
Polyepitope vaccines, 69–78  
in antigen-specific therapy, 6
clinical studies of, 75–77
peptide-based, 69–71
technology of, 71–72, 74t, 76
in treatment of EBV-associated malignancies,  
73–75, 76
PolyG motifs/sequences  
in activating TLR9, 45
in immune stimulatory CpG ODNs, 46
Polymerase chain reactions (PCRs), 121, 279
“Polyvalent” approach, whole-tumor cells in, 153, 154
Polyvalent vaccines, 22–23, 160
Positron emission tomography (PET), in vivo imaging via, 283, 284
Posttransplant lymphoproliferative disease (PTLD), treatment of EBV-associated malignancies and, 73
Poxvirus vectors, 95–111  
in combination therapies, 102–104
cytokine expression and, 101–102
history of cancer-therapy viral vectors and,  
95–97, 106
modified vaccinia Ankara, 104–106
tumor-associated antigens and, 97–101
Preclinical services, for vaccine production support, 293t
Preclinical studies  
of cancer vaccines, xiii, xv
of yeast-based immunotherapeutics, 144–145
Prime-boost vaccines  
clinical trials of, 90t
strategies for, xv
Primed T cell transfer, in cancer treatment, 218
Priming. See also Cross-priming
CD137 and, 255, 256
of poxvirus vaccines, 100
of tumor-specific T cells, 230, 233
Progesterone receptor (PR), in monoclonal antibody therapy, 174
Promoters, in yeast-based vaccine vector design, 139, 141–142
Prostate cancer
  allogeneic vaccines and, 155, 160
  allogeneic whole-cell vaccines versus, 153
  bacillus Calmette–Guérin in treatment of, 36–37
  in endocrine therapy, 175
glubo-H-KLH conjugate and, 18–19
Prostate-specific antigen (PSA), 96
  in antigen-specific therapy, 6, 97
  in combination therapies, 103, 104
glubo-H-KLH conjugate and, 19
Protein antigens, in antigen-specific therapy, 6–7
Protein-based vaccines
  with antigen-presenting cells, 81
  clinical trials of, 89t
Proteins
  in enhancing DC–T cell interaction, 86
  in increasing antigen-expressing DCs, 82
Proteomics analysis, in immune monitoring, 274t, 281
PSA marker, allogeneic vaccines and, 156
Pseudomonas aeruginosa exotoxin A, in
  enhancing DC antigen expression, 84, 85
PSMA proteins, in yeast-based immunotherapy, 135
Purified protein derivative (PPD) skin test, bacillus Calmette–Guérin and, 32
Q61L mutation, yeast-based immunotherapy and, 136–137, 138
Q61R mutation, yeast-based immunotherapy and, 136–137, 138
QA/QC (quality assurance/quality control) program, assay quality and, 293t, 295, 301–303, 304
Quantitative reverse transcriptase [real time]
  polymerase chain reaction (qRT-PCR), in
  immune monitoring, 273, 274t, 279–280
Radiation therapy (radiotherapy)
  immunotherapy and, 9, 10
  poxvirus vectors in combination with, 102–103
RA-HPV vaccine, clinical trials of, 90t
Raloxifene, in endocrine therapy, 174
Randomized trials, xiv–xv
Ras proteins, in yeast-based immunotherapy, 135–137
RastaFAR GI-4000 yeast strain, 138
Rat prostate cancer, allogeneic vaccines and, 155
Rb-binding protein, human papillomavirus and, 117
RECIST (response evaluation criteria in solid
tumors) criteria, xi–xv
Recombinant antigen expression, in bacteria, 121
Recombinant cytokines, 158
Recombinant fowlpox virus expressing CEA
  (rF-CEA)
  immune-response induction and, 101
  with MVA, 104–105
Recombinant fowlpox virus expressing PSA
  (rF-PSA), in combination therapies, 103
Recombinant nonpathogenic brewer’s yeast, in
  immunotherapy, 131–132, 145–147. See also Saccharomyces cerevisiae
Recombinant vaccine vectors, 114–122
Recombinant vaccinia virus expressing CEA
  (rV-CEA)
  boosts for, 100
  in clinical trials, 97, 98t
  in combination therapies, 102–103
  immune-response induction and, 101
  with MVA, 104–105
  poxvirus vectors and, 102
Recombinant vaccinia virus expressing PSA
  (rV-PSA)
  in clinical trials, 97, 99t
  in combination therapies, 103
Recombinase activating gene (BAG),
  PD-1/B7-H1/B7-DC pathway and, 246
Regulation, of vaccine production, 293–294
Regulatory T cells (Tregs). See also Regulatory
  T lymphocytes; T-regulatory (Treg) activity;
  T-regulatory cells (Tregs)
  antitumor immunity and, xiii
  in cancer immunity suppression, 211–212, 213
  in cancer vaccine objectives, 295
  in chemotherapy-modulated immune tolerance, 171–172
  CpG ODNs and TLR9 in stimulating, 48–49
  GM-CSF-secreting vaccines and, 177
  in immune-based therapies, 179–180
  in immune monitoring, 272–273
Regulatory T lymphocytes, 190
Renal cancer, bacillus Calmette–Guérin in
treatment of, 36
Renal cell carcinoma (RCC)
  bacillus Calmette–Guérin in treatment of, 36
cytokines versus, 157–158
  TroVax and MVA versus, 106
Repressible promoters, in yeast-based vaccine
  vector design, 141, 142
Reverse signaling, PD-1/B7-H1/B7-DC pathway
  and, 248
Rheostatic promoters, in yeast-based vaccine vector design, 141, 142
RNA, in qRT-PCR, 280. See also mRNA
RNA-based vaccines, characteristics of, 82t
RNA viruses, as cancer-therapy vaccine vectors, 96
Route of administration, in yeast-based immunotherapy, 143–144
Rüter, Jens, xi, 189
Saccharides, as adjuvants, 5
Saccharomyces cerevisiae, in antigen-specific therapy, 7, 131–149
Safety factors
CpG ODN, 53–54
of DNA-based vaccines, 91
of vaccine vectors, 114, 122–123
in yeast-based immunotherapy, 144–145
Salmonella, as bacterial vaccine vector, 114, 116
Scavenger receptors, in activating TLR9, 45
Schom, Jeffrey, xi, xiii
Secondary lymphoid structure, organogenesis of, 232
Secondary lymphoid tissue chemokine (SLC, CCL21), in creating tumor lymphoid tissue, 252
L-Selectin+ naive T cells, in creating tumor lymphoid tissue, 232
Selective estrogen receptor destroyers (SERDs), breast tumor immunity and, 174
Selective estrogen receptor modulators (SERMs), breast tumor immunity and, 174
Self-antigens
polyepitope technology and, 72
in yeast-based immunotherapy, 135, 143
Self-proteins, in yeast-based immunotherapy, 135
Semliki forest virus, as cancer-therapy vaccine vector, 96
Serial monitoring, of vaccine administration, 294, 296
Serial specimens, quality assurance/quality control for, 302
Services, for vaccine production support, 292, 293t
SGN-00101 vaccine, clinical trials of, 89t
Sheep, safety of CpG ODN in, 53
Shigella, as bacterial vaccine vector, 114, 116
Short interfering RNA (siRNA), in enhancing DC–T cell interaction, 86
SHP-2 cytoplasmic tyrosine phosphatase, PD-1/B7-H1/B7-DC pathway and, 245
Shuttle plasmids, 120–121
Simulect, versus CD25, 191
Sindbis virus, as cancer-therapy vaccine vector, 96
Single-cell assays, in cancer vaccine evaluation, 297, 298, 300
Single-chain trimer (SCT) technology, enhancing DC antigen expression via, 84
SKBR3 cell line, 178
Skin tests, in cancer vaccine evaluation, 300–301
Small cell lung cancer (SCLC) cells, fucosyl-GM1–KLH conjugate and, 20
Small peptide epitopes, CTL peptide target identification and, 69–70
Smallpox, 243
eradication of, 97
Smith, Corey, xi, 69
Solid tumors, 169. See also Cancer entries;
Tumor entries
adaptive immune rejection of, 51–52
structure of, 230
treatment of, 217
Souders, Nicholas C., xi, 113
Southwest Oncology study, of BCG, 33
Species-specific TLR9 expression, 44–45
Specific assays, in cancer vaccine evaluation, 297
Specimen batching, in cancer vaccine evaluation, 298
Specimen collection, in vaccine monitoring, 294.
See also Human specimens
Speiser, Daniel E., xi, 43
Spleen
cancer immunity suppression and, 211, 212
in constructing Listeria vaccine vectors, 121
syngeneic HSCT and, 207, 208
Splenic Gr1+ immature myeloid cells, tumors and, 234–235
Splenic T cells, CD137 and, 255
Splenocytes
cancer immunity suppression and, 211, 212, 213
in CD137 studies, 257
syngeneic HSCT and, 207, 208, 209, 210
Splenomegaly, 234–235
Sportes, Claude, xi, 217
Spot-forming units (SFUs), in ELISpot assay, 275
Squamous cell carcinoma of the head and neck (SCCHN), in tetramer analysis, 277
Standard-dose chemotherapy, breast tumor vaccines and, 171
Standardization
of assays, 284–285
quality assurance/quality control for, 302–303
in vaccine evaluation, 292
Standard operating procedure (SOP) quality assurance/quality control in, 303 vaccine production and, 294
Staphylococcal enterotoxin A (SEA), CD137 and, 255
Stem cells. See Hematopoietic stem cell transplantation (HSCT)
Stereocenters, oligosaccharide synthesis and, 17
Stimulation index (SI), in T cell proliferation assays, 282
STn antigen, in pentavalent vaccine, 24, 25
Strategies, for activating antitumor response, xiii–xiv, xv, xvi. See also Monitoring strategies
Stroma, as immunologic barrier, 230, 231
Stroma-derived factor 1 (SDF1), ovarian cancer and, 194
Stromal cells, in creating tumor lymphoid tissue, 232–234
Suppressor cells, antitumor immunity and, xiii
Surface antigens, in pDC depletion, 195
Synergistic effects in breast cancer treatment, 170 with CpG ODNs, 50
Syngeneic HSCT, 206–210
cancer immunity suppression and, 211
Synthetic antitumor vaccines, carbohydrate-based, 15–27
Synthetic phosphorothioate (PS) ODN, CpG-specific responses to, 44
T47D cell line, 178
TAA-reactive Tregs, 190
TAA-specific immunity, 190. See also Tumor-associated antigens (TAAs)
TAA-specific Tregs, tumor vaccines versus, 196–197, 198
TA-CIN vaccine, clinical trials of, 90t
TA-HPV vaccine, clinical trials of, 88t
Tamoxifen, 169
in endocrine therapy, 174
Target antigens, tolerance and, 223–224
Targeted assays, in cancer vaccine evaluation, 297, 304
Tarmogens™ (targeted molecular immunogens), in immunotherapy, 131–132, 139, 145–147. See also Saccharomyces cerevisiae
T cell assays, 273–274, 282–283
T-cell-depleting nonmyeloablative chemotherapy, immunotherapy and, 9
T cell depletion, outside high-dose chemotherapy, 219–220
T-cell-independent humoral response, 16
T cell leukemia, CD137 and, 253
T cell proliferation assay, in immune monitoring, 282
T-cell receptor recognition, in cancer vaccine evaluation, 298, 299
T cell receptors (TCRs), MHC–peptide complex and, 244
T cell reconstitution following autologous HSCT, 206–210 following HSCT, 220–223 Optimizing, 223
T cell responses cancer vaccines and, 43, 44
to whole-cell vaccines, 154
in yeast-based immunotherapy, 143–144, 146
T cells. See also Activated T cells; Effector T cells; T lymphocytes; Tumor-specific T cells in adaptive-immune solid-tumor rejection, 51–52 in antigen-specific cancer immunotherapy, 79–80, 81 bacterial vaccine vectors and, 114 breast tumor vaccines and, 171 cancer immunotherapy strategies and, 231–232 in cancer treatment, 218 in cancer vaccine evaluation, 298–299, 300, 304 in cancer vaccine objectives, 295 carcinogenesis and, 229
CD137 in, 255–256, 256–257
CD137 mRNA in, 253–254 in CD137 studies, 260 in chemotherapy-modulated immune tolerance, 171–172 in combination therapies, 103, 104 costimulatory and coinhibitory molecules and, 244
Listeria monocytogenes and, 115
LMP polyepitopes and, 74, 75, 76
PD-1/B7-H1/B7-DC pathway and, 246, 247, 248, 250, 251
PD-1 expression on, 246
in poxvirus clinical trials, 97
as sensitive immune stimulation detectors, 52
strategies for increasing DC interaction with,
along with TLR signaling, 244
in tetramer analysis, 276–277
yeast-based immunotherapy and, 132, 134
T cell signaling, 244
T cell vaccination, 52
Technology, of polyepitope vaccines, 71–72, 74t, 76
TEF1 (translation elongation factor 1) promoter,
in yeast-based vaccine vector design, 142
TEF2 (translation elongation factor 2) promoter,
in yeast-based vaccine vector design, 142
Temperature control, quality assurance/quality control for, 302
Tertiary lymphoid structure (TLS)
cancer immunotherapy strategies and,
formation of, 232, 233
Tetramer analysis
in cancer vaccine evaluation, 298, 299
in immune monitoring, 273, 274t, 276–278
Tetramers, 276
TF(c)-KLH clusters. See also Keyhole limpet hemocyanin (KLH)
cancer immunotherapy strategies and,
clustered vaccines and, 21–22
in pentavalent vaccine, 24, 25
Th1-like immune response, 43, 44
CpG ODNs in stimulating, 47
innate immune system and, 49
in mouse tumor models, 51
in yeast-based immunotherapy, 146
Th2-like immune response, 44
innate immune system and, 49
in BCG treatment, 37
CpG ODNs in stimulating, 47
in stimulating innate and adaptive immunity, 47
TNF-secreting CTLs, 177
TNF/TNFR (tumor necrosis factor/receptor) protein superfamily, 253
Tolerance, target antigens and, 223–224
Tolerogenic dendritic cells, 196
Toll-like receptor 8 (TLR8), regulatory T cells and, 48
Toll-like receptor 9 (TLR9), 43–66
activation and expression of, 44–46
history of, 43–44
safety of CpG ODN and, 54
Toll-like receptor ligands, in adjuvants, 5–6
Toll-like receptors (TLRs), 43–44
versus Tregs, 193
in yeast-based immunotherapy, 132, 133
Total-body irradiation (TBI), conditioning with, 206, 207, 208, 209
Toxicity, of BCG, 37–38. See also Cytotoxic entries; Lymphotoxin entries
Transferrin receptor (TIR), in enhancing DC antigen expression, 85
in qRT-PCR, 279–280
vaccine activation of, 133
Thymus
Thymopoiesis, in T cell regeneration, 221
cancer immunity suppression and, 211
PD-1 gene and, 245
syngeneic HSCT and, 206, 207
in T cell regeneration, 221
Tissue handling, vaccine production and, 293
Tissue samples, quality assurance/quality control for, 302
TLR9 agonists, 52–53
safety of CpG ODN and, 54
TLR ligation, 193
TLR signaling, versus Tregs, 193. See also Toll-like receptor entries
T lymphocyte activity, antitumor, 218
T lymphocytes. See also T cell entries
cancer immunotherapy strategies and,
in cancer vaccine evaluation, 299
immunotherapy and, 10
in tetramer analysis, 276
Tn(c)-KLH clusters. See also Keyhole limpet hemocyanin (KLH)
cancer immunotherapy strategies and,
clustered vaccines and, 21–22
in pentavalent vaccine, 24, 25
in trivalent vaccine, 23
TNFR1 receptor, in creating tumor lymphoid tissue, 232
TNF-related apoptosis-inducing ligand (TRAIL). See also Tumor necrosis factor entries
in BCG treatment, 37
CpG ODNs in stimulating, 47
in stimulating innate and adaptive immunity, 47
in yeast-based immunotherapy, 146
Thymic apoptosis, PD-1 gene and, 245. See also Apoptosis
Thymic reconstitution,
effector, 223, 224
following autologous HSCT, 206–207
Thymus
Transforming growth factor β1 (TGFβ1), inside tumors, 234
Transgenic mice, CD137L studies in, 257
Transplantation. See Bone marrow transplantation; Hematopoetic stem cell transplantation (HSCT)
Trafiramab
breast cancer treatment with, 169–170
in monoclonal antibody therapy, 173–174
Treg blockade, in immune monitoring, 273
Treg trafficking blockade, 194
T-regulatory (Treg) activity
immunotherapy and, 8–9, 159
in tumor immunotherapy, 189–204
T-regulatory cells (Tregs), 190. See also
Regulatory T cells (Tregs)
anti-CTLA4 antibodies and, 193
chemokine signaling versus, 194
depletion of, 190–192
functional blockade of, 192–194
interactions with other cells, 194–196
manipulation of, 189–204
suppressing functions of, 190
suppression of effector CD4+ and CD8+ T cells by, 190
tumor vaccines versus, 196–197
vascular leukocytes versus, 196
Trials. See Clinical trials
TRICOM (triad of costimulatory molecules)
vectors. See also B7–1 costimulatory molecule; Intercellular adhesion molecule I (ICAM-I): Leukocyte function-associated antigen 3 (LFA-3)
in antigen-specific therapy, 6–7, 98t, 100–101
in combination therapies, 102–103, 104
with MVA, 104–105
poxvirus vectors and, 102
Trivalent vaccines, evaluation of, 23
TroVax, with MVA, 105–106
Tsen, Shaw-Wei D., xi, 79
Tuberculosis, bacillus Calmette–Guérin in treatment of, 29, 30
Tumor antigen exposure, in cancer treatment, 218
Tumor antigens
allogeneic whole-cell vaccines and, 153
in immune monitoring, 271
in yeast-based immunotherapy, 135, 138–139
Tumor-associated antigens (TAAs), xv
adenovirus-encoding, 95–96
in cancer vaccine objectives, 295–296
in CD137 studies, 258
in combination therapies, 102, 103
immune response to, 189–190
in polyvalent vaccines, 22
poxvirus vectors and, 97–101
vaccine production and, 293
Tumor-associated carbohydrate antigens, 16
Tumor-associated macrophages (TAMs), tumors and, 235
Tumor-associated oligosaccharides, 16
Tumor burden
in cancer treatment, 218
cancer vaccines and, 212–213
HCST and, 218–219
Tumor cell antigen escape variants, xiv
Tumor-cell-based vaccines, characteristics of, 82t
Tumor cells
in cancer immunotherapy, 7–10
CD137L on, 254
cytokine-secreting, 158
immune system versus, 15–16
Listeria monocytogenes versus, 116
modified whole-cell vaccines and, 156–157
surface carbohydrates of, 15–16
Tumor cell-surface expression, heterogeneity of, 22, 23
Tumor challenge models, in yeast-based immunotherapy, 134–135
Tumor development, 4
Tumor-draining lymph node (TDLN) T cells, in CD137 studies, 260, 261
Tumor elimination
as cancer vaccine objective, 295
in vaccine evaluation, 291
Tumor immunity
in breast cancer treatment, 170–173
jump-starting with breast cancer therapeutics, 169–187
Tumor immunology, in antigen-specific cancer immunotherapy, 79
Tumor immunosurveillance, 4
Tumor immunotherapy, 189–190
T-regulatory cell manipulation in, 189–204
Tumor-infiltrating lymphocytes (TILs)
breast tumor vaccines and, 171
in cancer immunotherapy strategies, 231
Tumor microenvironment, chemotherapy and, 173
Tumor microenvironmental Tregs, 190
Tumor necrosis factor alpha (TNFα)
BCG immune response and, 37
in flow cytometry, 278
Listeria monocytogenes and, 115, 116
PD-1/B7-H1/B7-DC pathway and, 248, 250
in T cell activation, 53
in yeast-based immunotherapy, 146
Tumor necrosis factors (TNFs), in creating tumor lymphoid tissue, 232
Tumor recurrence, after BCG treatment 34–35
Tumor regression, antigen-specific T cells and, 231
Tumor rejection, in vaccine evaluation, 291–292
Tumor removal, immunotherapy and, 9–10
Tumors. See also Cancer entries; Solid tumors
adaptive immune rejection of, 51–52
allogeneic vaccines and, 155
antigenic heterogeneity of, xiv
changing environment inside, 235, 237
costimulatory and coinhibitory molecules and, 244
immune system and, 3, 4
immunosuppressive environment inside, 234–235
internal environment of, 232–236
Listeria monocytogenes versus, 116
tumor immunotherapy versus, 189–190
Tumor size, in clinical activity valuation, xiv
Tumor-specific T cells
carcinogenesis and, 229
priming of, 230
Tumor-specific vaccines, in cancer treatment, 217–218
Tumor survival, in vaccine evaluation, 291
Tumor vaccines
breast cancer chemotherapy and, 171
breast cancer treatment with, 170
versus Tregs, 196–197
Unimolecular monovalent vaccines, 18–20
Unimolecular multivalent vaccines, 23–25
United States, BCG treatment in, 38. See also
American Urological Association (AUA) guidelines; College of American Pathologists (CAP); Food and Drug Administration (FDA)
Unmethylated CpG dinucleotides, TLR9 in
detecting, 44
Urethane-induced tumors
yeast-based immunotherapy and, 136–137
yeast-based vaccine vector design and, 139
VAAA vaccinations, 100
Vaccination. See also Vaccine entries
enhancing by stimulating TLR9, 43–66
following HSCT, 206
history of, 243–244
Vaccination therapies, tools necessary to support, 292–295
Vaccine efficacy, in yeast-based immunotherapy, 146–147
Vaccine monitoring, 293t
quality assurance/quality control for, 302–303
Vaccine preparation, 293t
Vaccine production, regulation of, 293–294
Vaccines. See also Bacillus Calmette–Guérin (BCG); Breast cancer vaccines; Cancer vaccines; Experimental vaccine development; Peptide-based vaccines; Polyepitope vaccines; Tumor vaccines; Viral vector-based vaccines; Whole-cell vaccines
clustered, 20–22
CpG ODNs as adjuvants for, 49
hematopoietic stem cell transplantation and, 217–228
in cancer therapy, xiii, 95, 205–206
polyepitope, 69–78
polyvalent, 22–23, 160
strategies for, 223–224
unimolecular monovalent, 18–20
unimolecular multivalent, 23–25
using Listeria monocytogenes, 113–129
Vaccine vectors. See also Vaccinia virus (VV) vectors; Viral vector-based vaccines
constructing from Listeria monocytogenes, 119–122
live recombinant, 114–122
safety of, 114, 122–123
Vaccinia virus (VV) vectors
in antigen-specific therapy, 6–7
applications of, 97–106
in polyepitope technology, 71, 72
Vascular endothelial growth factor (VEGF), in
monoclonal antibody therapy, 174
Vascular leukocytes, versus Tregs, 196
VaxImmune™, CpG ODNs used with, 50
Venezuelan equine encephalitis virus, as
cancer-therapy vaccine vector, 96
Verch, Thorsten, xi, 113
Viral vector-based vaccines. See also Poxviral vectors; Vaccinia virus (VV) vectors
clinical trials of, 87
safety concerns related to, 123
Virulence factors, Listeria monocytogenes and, 116
Viruses, as vaccine vectors, 114
Virus-like particle (VLP) vaccines, in immune
monitoring, 272
Vitamins, with BCG treatment, 35
VP22 viral proteins, in increasing
antigen-expressing DCs, 82
Wansley, Elizabeth K, xi, 95
Whiteside, Theresa L., xi, 291
Whole-body imaging, 283–284
Whole-cell vaccines
advantages of, 154–155
Whole-cell vaccines (Continued)
  allogeneic, 153–157
  effectiveness of, 155–156
  future research in, 159–160
  modification to secrete cytokines, 157–159
  modification with costimulatory molecules, 156–157
  T cell responses elicited by, 154
Wild-type (WT) K1736 tumor, in CD137 studies, 257
Wilson, Rebecca M., xi, 15
Wu, T.-C., xi, 79
Xenogeneic APCs, in ELISpot assay, 275
Yeast-based immunotherapy
  clinical trials in, 144, 145
  coupling innate and adaptive immunity with, 131–149
  dose-response parameters in, 143–144
  molecular mechanisms of action in, 132–135
  mutated Ras and therapeutic animal models for, 135–137
  preclinical safety studies in, 144–145
  yeast-based vaccine vector design in, 139–144
  yeast-expressed tumor-antigens in, 138–139
  Yeast “cocktail,” 132, 146
  Yeast-delivering tumor antigens, 132
  Yeast-expressed tumor antigens, 138–139
  Yeast expressing chicken ovalbumin (OVAX), in yeast-based immunotherapy, 133–134, 134–135
  Yeast lacking foreign antigens (YVEC), in yeast-based immunotherapy, 133–134, 135
  Yeast number, in yeast-based immunotherapy, 143
  Yu, Ping, xi, 229
  Zenapax, versus CD25, 191
  Zeta-chain expression, in tetramer analysis, 277
Zou, Weiping, xi, 189
ZYC-101 microencapsulated DNA-based
  vaccines, human clinical trials of, 86–87, 89t