

# Index

## A

- ACT. *See* Adoptive cellular therapy
- Activation-induced cytidine deaminase (AID), 38, 48, 56–57, 214, 218
- Acute myeloid leukemia (AML), 392
- ADCC. *See* Antibody-dependent cell-mediated cytotoxicity
- ADCP. *See* Antibody-dependent cellular phagocytosis
- ADE. *See* Antibody-dependent enhancement
- Adoptive cellular therapy (ACT), 122
- Affinity maturation
- antibody affinity reversion/antibody redemption, 56–57
  - antibody feedback
    - affinity maturation effects, 31–32
    - B-cell receptor–antigen interactions, 30–31
    - Epitope-spreading role, 32–34
  - antigenic seniority, 41
  - diminishing returns, 38–40
  - founder effect as limitation, 40–41
  - human immunodeficiency virus response.  
*See* Human immunodeficiency virus
  - immunoglobulin gene mutability, 41–42
  - overview, 30, 38, 54
  - pertussis booster vaccination, 342–343
  - somatic hypermutation in germinal center B cells, 54–55
  - vaccine driven V(D)J hypermutation and selection, 55–56
- AID. *See* Activation-induced cytidine deaminase
- AML. *See* Acute myeloid leukemia
- Animal models. *See also specific animals*
- biomarker development, 294
  - coinfection effect on immune response, 293–294
  - controlled variability, 294
  - discrepancies with human infection
    - improvements, 292–293
    - natural infection nonexistence, 291
    - overview, 290
    - pathophysiology differences, 291–292
  - preconditioning effect on immune response, 293–294
  - proof-of-concept studies, 260
  - selection of model, 292
  - vaccine effectiveness evaluation
    - anthrax, 261–262
    - ebola vaccine studies
    - bridging animal protection data to humans, 263–264
    - overview, 262
    - pathogen considerations, 262–263
    - surrogate markers, 263
  - human immunodeficiency virus studies in nonhuman primates
    - immune response measurement, 265
    - overview, 264–265
    - SHIV challenge models, 265–266
    - SIV challenge models, 265
    - vaccine design, 265
  - human papillomavirus, 261
  - overview of challenge models, 260–261
- Animal Rule, 261, 267
- Anthrax, vaccine studies in animals, 261–262
- Antibody affinity maturation. *See* Affinity maturation
- Antibody-dependent cell-mediated cytotoxicity (ADCC), 265
- Antibody-dependent cellular phagocytosis (ADCP), 265
- Antibody-dependent enhancement (ADE), 76, 87, 92, 104, 110
- AP-1, 2
- APRIL, 233
- ATAC-seq, 5

## B

- Bacille Calmette–Guérin (BCG), 227
- B-cell affinity maturation. *See* Affinity maturation
- BCG. *See* Bacille Calmette–Guérin
- Bcl6, 19, 24

## C

- Cancer vaccine
- historical perspective, 128
  - neoantigens
    - cancer vaccine development, 115
    - checkpoint inhibitor therapy combination, 132
    - delivery, 125
    - ideal properties of vaccine, 129–130
    - overview, 114
    - prophylactic cancer vaccines, 117–118
    - rationale for vaccines, 128–129
    - selection for vaccine, 117, 123–124

## Index

- Cancer vaccine (*Continued*)  
  T-cell response to vaccines  
    magnitude, 129–130  
    quality, 130–131  
    specificity, 131–132  
  patient selection, 124–125  
  tumor peptides, mutated versus nonmutated, 115–116
- Candida albicans*, T-cell response, 10–11, 13
- CAR T cell. *See* Chimeric antigen receptor T cell
- CCR5, 233, 280–281
- CCR6, 23, 184
- CD27, 219
- CD4 T cell  
  cell fate  
    determination, 2–3  
    fixation, 2–3  
    human studies, 12–13  
    lineage tracing, 5  
  cytokines, 10  
  Dengvaxia response, 84  
  follicular helper T cell, 200, 202–203  
  gut microbiota cross talk, 180, 191  
  heterogeneity, 10–12  
  pertussis immune response  
    infection, 332  
    vaccination  
      acellular boosting, 344–345  
      primary vaccination, 344–345
- plasticity  
  definition, 18  
  human studies, 12–13  
  intraclonal diversification, 13–15  
  phenotype heterogeneity and stability during resting memory, 22–23  
  recall and plasticity during, 23–24  
  regulation, 3–5  
  single-cell studies, 5  
  stability during  
    primary response, 18–19  
    transition from effector to memory cell, 19–22  
  subtypes, 18
- CD8 T cell  
  activating receptors, 409  
  cytokine stimulation, 408–409  
  functional overview, 298  
  memory cell protection against reinfection, 298, 410  
  subsets, 314–315  
  vaccine  
    delivery, 300  
    human immunodeficiency virus vaccine  
      cytomegalovirus-vectored vaccine, 306–309  
      prospects, 308–309  
      rationale, 304  
      vaccination studies, 304–306  
      manufacturing, 300  
      prospects, 300–301  
      rationale, 298–299  
      safety, 299  
      *Salmonella typhi* vaccines, 315–316
- CD40L, 237
- CD73, 210–211
- CD80, 210–211, 219
- CD95, 390
- CDR3, 40
- Chimeric antigen receptor (CAR) T cell, 131
- Chronic lymphocytic leukemia (CLL), 115
- CLL. *See* Chronic lymphocytic leukemia
- Clostridium difficile*, 181–182, 190
- CMV. *See* Cytomegalovirus
- c-Myc, 3
- CRISPR-Cas9, 5, 255
- CTLA-4, 122, 386
- CXCL13, 18
- CXCR3, 18, 20, 24, 184
- CXCR5, 18–20, 22–24
- CXCR6, 384–385
- Cytomegalovirus (CMV), 246, 292  
  immunogen design, 372  
  natural killer cell memory, 381–383, 390–391, 393, 399–400  
  vector for human immunodeficiency virus  
    CD8 T-cell vaccine, 306–309
- ## D
- Dengue virus  
  antibody response  
    primary infection, 71–72  
    secondary infection, 72–73, 75, 95  
  conformational quaternary epitopes, 107–109  
  epidemiology, 62, 70  
  fusion loop epitope, 107  
  immune response overview, 62–63, 71, 82–83  
  prM cleavage, 106–107  
  secondary infection, 62, 71, 104  
  serotype heterogeneity, 70–71  
  vaccines  
    challenges, 106  
    Dengvaxia, 64–65, 74, 82, 84–85, 92–97, 104–106  
    enhanced disease after vaccination, 85–87, 92–97  
    historical perspective, 104  
    immune response, 82, 84  
    live attenuated vaccine, 64, 70, 73–74  
    naïve individual vaccination, 74, 76  
    National Institutes of Health LATV enhancement, 98

- primed individual vaccination, 76
  - prospects, 77
  - safety, 64, 76–77, 105–106
  - serotypes, 64–65, 85, 94, 96
  - TDV, 97–98
  - virus breathing, 70–71, 107
  - zika infection interactions, 108, 110
- E**
- Ebola, vaccine studies in animals
    - bridging animal protection data to humans, 263–264
    - overview, 262
    - pathogen considerations, 262–263
    - surrogate markers, 263
  - Enterotoxigenic *Escherichia coli*, 315
  - ERB-B2, 131–132
- F**
- FDC. *See* Follicular dendritic cell
  - Fecal microbiome transfer (FMT), 181
  - FMT. *See* Fecal microbiome transfer
  - Follicular dendritic cell (FDC), 31, 48, 255
  - Follicular helper T cell, 200, 202–203
  - Foxp3, 24
- G**
- GATA3, 24
  - GC. *See* Germinal center
  - GCN2, 233, 245
  - Germinal center (GC). *See also* Affinity maturation
    - antigen-specific B-cell memory, 198
    - follicular helper T cell, 200, 202–203
    - memory B cell
      - antibody suppression of cell fate, 211
      - formation, 208–209
      - functions, 209, 210
      - prospects for study, 211–212, 218–219
      - secondary germinal center formation
        - history of study, 214
        - human studies, 217–218
        - mouse studies, 214–217
        - pathogen studies, 217
        - somatic hypermutation, 218
    - memory-response germinal cell
      - reaction, 198–199
      - single-cell level programs, 199–201
      - vaccine significance, 203
  - GN2, 245
  - gp100, 128
  - gp120, 282, 362
  - Guillain–Barré syndrome, 142
  - Gut microbiota
- adaptive immunity against pathogens, 182–184
  - adjuvant applications, 175
  - immune system and infection response influence, 172, 180–182, 192
  - overview, 172, 180
  - points test for different microbial taxa, 190–193
  - political modeling
    - agitation across federal borders, 190–193
    - federalism versus sovereignty, 188–189
    - immigration control, 189–190
  - sampling, 188–189
  - systems vaccinology studies, 245
  - vaccine efficacy impact
    - dysregulation in failure, 174–175
    - microbiotal stratification to predict efficacy, 173–174
    - prospects for study, 176
- H**
- HA. *See* Hemagglutinin
  - HBV. *See* Hepatitis B virus
  - HCV. *See* Hepatitis C virus
  - Hemagglutinin (HA), 48, 138–139, 146–147, 151, 156–160, 164–169, 292
  - Hepatitis B virus (HBV), 130, 244
  - Hepatitis C virus (HCV), 130
  - HIV. *See* Human immunodeficiency virus
  - HPV. *See* Human papillomavirus
  - hTERT, 115
  - Human immunodeficiency virus (HIV)
    - antigenic variation and somatic hypermutation, 47–48
  - CD8 T-cell vaccine
    - cytomegalovirus-vectored vaccine, 306–309
    - prospects, 308–309
    - rationale, 304
    - vaccination studies, 304–306
  - epitope loss, 131
  - immune perturbations, 56
  - immunogen design, 362–364, 372–374
  - natural killer cell memory, 382–383
  - somatic hypermutation and broadly neutralizing antibody development, 46, 56, 183
  - vaccination
    - history, 222
    - nonhuman primate studies
      - immune response measurement, 265
      - overview, 264–265
      - SHIV challenge models, 265–266
      - SIV challenge models, 265
      - vaccine design, 265
      - somatic hypermutation load, 48–51
  - Human papillomavirus (HPV), 261

## Index

### I

- IFN- $\alpha$ . *See* Interferon  $\alpha$
  - IFN- $\gamma$ . *See* Interferon  $\gamma$
  - IL-1. *See* Interleukin 1
  - IL-2. *See* Interleukin 2
  - IL-4. *See* Interleukin 4
  - IL-5. *See* Interleukin 5
  - IL-6. *See* Interleukin 6
  - IL-7. *See* Interleukin 7
  - IL-8. *See* Interleukin 8
  - IL-9. *See* Interleukin 9
  - IL-10. *See* Interleukin 10
  - IL-12. *See* Interleukin 12
  - IL-13. *See* Interleukin 13
  - IL-15. *See* Interleukin 15
  - IL-17. *See* Interleukin 17
  - IL-18. *See* Interleukin 18
  - IL-21. *See* Interleukin 21
  - IL-22. *See* Interleukin 22
  - ILC. *See* Innate lymphoid cell
  - Immunogen design
    - cytomegalovirus, 372
    - design
      - immunization strategy, 373–374
      - shape selection, 371–373
    - human immunodeficiency virus, 362–364, 372–374
    - influenza virus, 361–362
    - overview, 370–371
    - prospects, 364–366
    - respiratory syncytial virus, 360–361, 372
  - Immunological memory, overview, 398–399
  - Influenza virus
    - epidemiology, 138
    - hemagglutinin stem
      - antibody response, 156–158, 164
      - epitope vaccine design from antibodies of vaccinated individuals, 158
    - monoclonal antibody therapy
      - clinical trials, 165–166
      - enhanced disease risks, 167–168
      - immunogenicity in natural infection, 166–167
      - prospects, 168–169
    - multidonor class antibody induction by universal vaccine, 158–160
    - neutralization mechanisms, 164–165
    - next-generation universal vaccine design, 160
  - immunodominance
    - antigenic drift driving, 148–149
    - outflanking strategies, 149–150
    - overview of virus humoral immunity, 147–148
  - immunogen design, 361–362
  - memory B-cell studies in mice, 217
  - memory natural killer cells, 382–383
  - neutralizing antibodies, 146
    - original antigenic sin, 146–147, 150
    - strains, 156, 164
    - systems vaccinology studies, 224–227
    - vaccination
      - challenges, 146, 150–151
      - conserved antigens as targets, 138–139
      - gut microbiota and efficacy, 174
      - universal vaccine development
        - costs, 142–143
        - factors to consider, 140–143
        - prospects, 151
        - rationale, 139–140
        - safety, 142
- Innate lymphoid cell (ILC)
  - immune memory role, 394–395
  - origins, 390–391
  - prospects for study, 395
  - vaccination role, 394–395
- Interferon  $\alpha$  (IFN- $\alpha$ ), 390
- Interferon  $\gamma$  (IFN- $\gamma$ ), 10–12, 18, 82, 182, 315–316, 390–391, 406, 408
- Interleukin 1 (IL-1), 10
- Interleukin 2 (IL-2), 391
- Interleukin 4 (IL-4), 10, 12, 18, 20, 237
- Interleukin 5 (IL-5), 10, 18, 22, 394
- Interleukin 6 (IL-6), 82, 233
- Interleukin 7 (IL-7), 174
- Interleukin 8 (IL-8), 82
- Interleukin 9 (IL-9), 11
- Interleukin 10 (IL-10), 18
- Interleukin 12 (IL-12), 12–13, 379, 391–394, 408
- Interleukin 13 (IL-13), 18, 22, 394
- Interleukin 15 (IL-15), 174, 379, 391–394
- Interleukin 17 (IL-17), 10, 22, 394
- Interleukin 18 (IL-18), 379, 390–394
- Interleukin 21 (IL-21), 18, 237
- Interleukin 22 (IL-22), 10, 394
- IRF4, 2
- IRF7, 232
- ### J
- JUNB, 2
- ### K
- KLF2, 381
  - Klf4, 3
  - KLRC2*, 400
- ### L
- LCMV. *See* Lymphocytic choriomeningitis virus
  - Listeria monocytogenes*, 276
  - Lymphocytic choriomeningitis virus (LCMV), 19, 129, 131, 408

## M

- Malaria, memory B-cell studies in mice, 217
- Marburg virus, 262–263
- MART-1, 132
- Memory. *See* Immunological memory; *specific cells*
- Memory B cell. *See* Germinal center
- Meningitis B vaccine, 371
- Microbiota. *See* Gut microbiota
- MMRN. *See* Multiscale multifactorial response network
- Mouse models
  - dirty versus clean mouse studies, 275–276
  - human immune system comparison, 272–273
  - memory B-cell studies, 214–217
  - previous microbial exposure impact on immune response, 273–274
  - specific pathogen-free mice, 275–276
- mTOR, 245
- MUC1, 115, 117
- Multiscale multifactorial response network (MMRN), 237

## N

- NA. *See* Neuraminidase
- Narcolepsy, 142
- Natural killer (NK) cell
  - activation states and cell maintenance, 409
  - cytokine stimulation, 408–409
  - functional overview, 378
  - memory
    - antigen-nonspecific memory-like natural killer cells, 379, 381–382
    - antigen-specific memory of highly diverse antigens, 382–383
    - bystander responses, 401
    - cancer targeting, 401
    - cytomegalovirus, 381–382, 390–391, 393, 399–400
    - experimental evidence, 380–381
    - forms of memory, 390–392
    - human immunodeficiency virus, 382–383
    - immunological memory, 378–379, 399–400
    - prospects for study, 384–386, 395, 409–411
    - subset expansion and functional memory, 407–408
    - vaccination role, 392–394, 400
    - vaccine utilization, 383–384
  - origins, 390–391
  - receptors in activation, 406–407
  - subsets, 378, 407–408
- Neoantigen. *See* Cancer vaccine
- Neuraminidase (NA), 138–139, 146, 151, 164
- NF- $\kappa$ B. *See* Nuclear factor  $\kappa$ B
- NK cell. *See* Natural killer cell
- NKG2C, 378, 390–391, 400, 407

- NLRP3, 382
- Nuclear factor  $\kappa$ B (NF- $\kappa$ B), 2

## O

- Oct4, 3
- Original antigenic sin, 40–41, 146–147, 150, 353

## P

- p53, 117
- PAP. *See* Prostatic acid phosphatase
- Parkinson's disease (PD), 124
- PD. *See* Parkinson's disease
- PD-1, 386
- PD-L2, 210–211, 219
- Pertussis
  - Bordetella pertussis* evolution, 332–333
  - protection by natural infection, 324–325
  - vaccines
    - acellular versus whole vaccine, 327, 342
    - animal models, 329, 332
    - antigen composition of acellular vaccine, 342
    - booster vaccination and affinity maturation, 342–343
    - herd immunity, 332
    - historical perspective, 325
    - IgG4 response, 343–344
    - immune memory skewing by primary and booster vaccination, 345–346
    - immune responses, 327–331, 342–344
    - immunoglobulin class switching, 343–344
    - improvement of acellular vaccine, 333–335
    - overview, 324
    - priming failure by acellular vaccines
      - original antigenic sin, 353
      - overview, 350–353
      - postexposure immune memory reactivation failure, 353–354
    - prospects, 354–355
    - T-cell responses
      - acellular boosting, 344–345
      - primary vaccination, 344–345
      - waning immunity, 325–327
- Plaque-reduction neutralization test (PRNT), 84, 87
- Polio vaccine, gut microbiota and efficacy, 174
- PRNT. *See* Plaque-reduction neutralization test
- Proof-of-concept studies, 260
- Prostatic acid phosphatase (PAP), 128

## R

- RAG, 378, 392, 399
- Rel, 2

## Index

- Relb, 2  
Respiratory syncytial virus (RSV), immunogen design, 360–361, 372  
RSV. *See* Respiratory syncytial virus
- S**
- Salmonella typhi*, CD8 T-cell vaccine, 315–316  
SHIV. *See* Human immunodeficiency virus; Simian immunodeficiency virus  
SHM. *See* Somatic hypermutation  
Simian immunodeficiency virus (SIV)  
    CD8 T-cell vaccine, 304–305, 307–308  
    human immunodeficiency virus studies in nonhuman primates  
        SHIV challenge models, 265–266  
        SIV challenge models, 265  
    humoral immunity, 32  
    natural killer cell memory, 400  
    rhesus macaque challenge studies, 280–286  
    T-cell response, 19  
SIV. *See* Simian immunodeficiency virus  
SLE. *See* Systemic lupus erythematosus  
Somatic hypermutation (SHM), 46–51, 54–56, 183, 214, 216, 218  
Sox2, 3  
Specific pathogen-free (SPF) mice, 275–276  
SPF mice. *See* Specific pathogen-free mice  
SREBP-1, 237  
STAT1, 232  
STAT4, 408  
Systemic lupus erythematosus (SLE), 56  
Systems vaccinology  
    adjuvant profiling in animals, 242–243  
    age effects, 243–244  
    cell phenotyping, 226  
    challenges, 255–256  
    chronic infection studies, 246  
    correlates of infection, 246–247  
    cytokine studies, 222, 225–226  
    examples, 227  
    functional assays, 226  
    gut microbiota effect studies, 245  
    history of human studies, 243–244  
    immune response predictors  
        identification, 234, 236–237  
        robustness, 237–238  
    influenza studies, 224–227  
    lymphocyte repertoire analysis, 226  
    metabolomics, 245  
    misunderstandings, 252–255  
    overview, 222–223, 232, 242, 252–253  
    prospects, 227–228, 238  
    techniques, 222–226  
    transcriptomics, 222, 237  
    vaccine efficacy signatures, 232–234
- T**
- T helper cell. *See* CD4 T cell  
TLR4, 243  
TLR5, 233, 245  
TLR9, 243  
TNF- $\alpha$ . *See* Tumor necrosis factor  $\alpha$   
Tuberculosis, T-cell response, 11  
Tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), 82, 316
- V**
- Vesicular stomatitis virus (VSV), natural killer cell memory, 382–383, 392  
VSV. *See* Vesicular stomatitis virus
- Z**
- Zika virus  
    dengue infection interactions, 108, 110  
    nonhuman primate challenge studies, 285