TUBERCULOSIS

AND THE

TUBERCLE BACILLUS

2ND EDITION

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Contents

Contributors ix
Preface xiii

SECTION I
TOWARDS EDWARD JENNER’S REVENGE: DEVELOPING AN EFFECTIVE TUBERCULOSIS VACCINE / 1

A. BASIC IMMUNOLOGY
1 Innate Immune Responses to Tuberculosis / 3
JEFFREY S. SCHOREY AND LARRY S. SCHLESINGER

2 Cytokines and Chemokines in Mycobacterium tuberculosis Infection / 33
RACQUEL DOMINGO-GONZALEZ, OLIVER PRINCE, ANDREA COOPER, AND SHABAANA KHADER

3 Regulation of Immunity to Tuberculosis / 73
SUSANNA BRIGHENTI AND DIANE J. ORDWAY

4 The Memory Immune Response to Tuberculosis / 95
JOANNA R. KIRMAN, MARCELA I. HENAO-TAMAYO, AND ELSE MARIE AGGER

5 Pathology of Tuberculosis: How the Pathology of Human Tuberculosis Informs and Directs Animal Models / 117
RANDALL J. BASARABA AND ROBERT L. HUNTER

B. ANIMAL MODELS
6 Animal Models of Tuberculosis: An Overview / 131
ANN WILLIAMS AND IAN M. ORME

7 Mouse and Guinea Pig Models of Tuberculosis / 143
IAN M. ORME AND DIANE J. ORDWAY

8 Non-Human Primate Models of Tuberculosis / 163
JULIET C. PEÑA AND WEN-ZHE HO

9 Experimental Infection Models of Tuberculosis in Domestic Livestock / 177
BRYCE M. BUDDLE, H. MARTIN VORDERMEIER, AND R. GLYN HEWINSON

C. VACCINES
10 Clinical Testing of Tuberculosis Vaccine Candidates / 193
MARK HATHERILL, DERECK TAIT, AND HELEN MCSHAANE

D. HUMAN IMMUNOLOGY
11 Human Immunology of Tuberculosis / 213
THOMAS J. SCRIBA, ANNA K. COUSSENS, AND HELEN A. FLETCHER
12 The Immune Interaction between HIV-1 Infection and Mycobacterium tuberculosis / 239
   Elsa du Bruyn and Robert John Wilkinson

SECTION II

DRUG DISCOVERY AND DEVELOPMENT: STATE OF THE ART AND FUTURE DIRECTIONS / 269

13 Preclinical Efficacy Testing of New Drug Candidates / 271
   Eric L. Nuernberger

14 Oxidative Phosphorylation as a Target Space for Tuberculosis: Success, Caution, and Future Directions / 295
   Gregory M. Cook, Kiel Hards, Elyse Dunn, Adam Heikal, Yoshio Nakatani, Chris Greening, Dean C. Crick, Fabio L. Fontes, Kevin Pethe, Erik Hasenoehrl, and Michael Berney

15 Targeting Phenotypically Tolerant Mycobacterium tuberculosis / 317
   Ben Gold and Carl Nathan

SECTION III

BIOMARKERS AND DIAGNOSTICS / 361

16 Tuberculosis Diagnostics: State of the Art and Future Directions / 363
   Madhukar Pai, Mark P. Nicol, and Catharina C. Boehme

17 Latent Mycobacterium tuberculosis Infection and Interferon-Gamma Release Assays / 379
   Madhukar Pai and Marcel Behr

18 Impact of the GeneXpert MTB/RIF Technology on Tuberculosis Control / 389
   Wendy Susan Stevens, Lesley Scott, Lara Noble, Natasha Gous, and Keertan Dheda

SECTION IV

HOST AND STRAIN DIVERSITY / 411

19 The Role of Host Genetics (and Genomics) in Tuberculosis / 413
   Vivek Naranbhai

20 The Evolutionary History, Demography, and Spread of the Mycobacterium tuberculosis Complex / 453
   Maxime Barbier and Thierry Wirth

21 Impact of Genetic Diversity on the Biology of Mycobacterium tuberculosis Complex Strains / 475
   Stefan Niemann, Matthias Merker, Thomas Kohl, and Philip Supply

22 Evolution of Mycobacterium tuberculosis: New Insights into Pathogenicity and Drug Resistance / 495
   Eva C. Boritsch and Roland Brosch

SECTION V

THE SIGNATURE PROBLEM OF TUBERCULOSIS PERSISTENCE / 517

23 Acid-Fast Positive and Acid-Fast Negative Mycobacterium tuberculosis: The Koch Paradox / 519
   Catherine Vilchèze and Laurent Kremer

24 Mycobacterial Biofilms: Revisiting Tuberculosis Bacilli in Extracellular Necrotizing Lesions / 533
   Randall J. Basaraba and Anil K. Ojha

25 Killing Mycobacterium tuberculosis In Vitro: What Model Systems Can Teach Us / 541
   Tracy L. Keiser and Georgiana E. Purdy

26 Epigenetic Phosphorylation Control of Mycobacterium tuberculosis Infection and Persistence / 557
   Melissa Richard-Greenblatt and Yossef Av-Gay

27 DNA Replication in Mycobacterium tuberculosis / 581
   Zanele Ditse, Meindert H. Lamers, and Digby F. Warner

28 The Sec Pathways and Exportomes of Mycobacterium tuberculosis / 607
   Brittany K. Miller, Katelyn E. Zulauf, and Miriam Braunstein

29 The Role of ESX-1 in Mycobacterium tuberculosis Pathogenesis / 627
   Ka-Wing Wong
<table>
<thead>
<tr>
<th>30</th>
<th>The Minimal Unit of Infection: <em>Mycobacterium tuberculosis</em> in the Macrophage / 635</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Brian C. VanderVen, Lu Huang, Kyle H. Rohde, and David G. Russell</td>
</tr>
<tr>
<td>31</td>
<td>Metabolic Perspectives on Persistence / 653</td>
</tr>
<tr>
<td></td>
<td>Travis E. Hartman, Zhe Wang, Robert S. Jansen, Susana Gardete, and Kyu Y. Rhee</td>
</tr>
<tr>
<td>32</td>
<td>Phenotypic Heterogeneity in <em>Mycobacterium tuberculosis</em> / 671</td>
</tr>
<tr>
<td></td>
<td>Neeraj Dhar, John McKinney, and Giulia Manina</td>
</tr>
<tr>
<td>33</td>
<td><em>Mycobacterium tuberculosis</em> in the Face of Host-Imposed Nutrient Limitation / 699</td>
</tr>
<tr>
<td></td>
<td>Michael Berney and Linda Berney-Meyer</td>
</tr>
<tr>
<td></td>
<td>Index / 717</td>
</tr>
</tbody>
</table>
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It is the height of irony that the man who discovered the smallpox vaccine, Edward Jenner, lost both his wife and son to tuberculosis (TB). By the time smallpox was essentially eradicated, it is estimated that over 300 million people had died from this disease over the preceding century. Its eventual prevention—by a simple vaccine—clearly illustrates the power of scientific discovery and how its application can affect human health. Hundreds of millions of people have been spared death and suffering from infectious diseases because of the development of vaccines and chemotherapeutic agents in the last 100 years. Millions of lives have been saved with the use of the TB vaccine, BCG, and the development of chemotherapeutic regimens for TB. Depressingly, despite these effective interventions, TB remains one of the most challenging problems of global health, with over 9 million new cases and 1.6 million deaths each year. This crisis has been further compounded by the emergence of the HIV epidemic, as this explosive and deadly combination has dramatically increased the global spread of TB, including increasing numbers of cases of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB.

Historically, mycobacterial disease has long been at the forefront of scientific discovery for infectious diseases. The leprosy bacillus, *Mycobacterium leprae*, the first bacterium to be associated with human disease, was initially visualized by Gerhard Armauer Hansen in 1873. Earlier, Jean Antoine Villemin was the first person to realize that lung tubercles were infectious and not cancerous. By the 1880s, Robert Koch, aware of both of these discoveries, not only observed the tubercle bacilli in tubercles, but developed a growth medium of heated serum to cultivate the tubercle bacillus outside of humans. He went on to repeat the transfer experiment of Villemin and transferred the disease of TB to numerous animal species, establishing the experimental paradigm (“the postulates”) of how to prove that an infective agent is a cause of a disease. Koch’s findings led Albert Calmette and Camille Guérin to follow Jenner’s approach of developing an attenuated pathogen for use as a vaccine, using the bovine tubercle bacillus to develop the bacille Calmette-Guérin (BCG) vaccine that bears their names and is still used to this day.

It is noteworthy that Paul Ehrlich was sitting in the lecture hall when Robert Koch presented his work in 1882; he later went on to help Koch improve his staining techniques. By observing the selective staining of various cell types, including human cells and different bacteria, Ehrlich also developed the idea of chemotherapy—“magic bullets” that could kill microbial pathogens. He tried for years to develop a chemical that could kill the tubercle bacillus, with little success, though at the same time was far more successful in developing a treatment for syphilis. In the 1930s, his protégé Gerhard Domagk discovered the first sulfonamide to treat bacterial infections such as streptococcus, and as this fledgling field expanded, para-aminosalicylic acid and isoniazid were discovered to be active against the TB bacillus. Parallel studies by Salaman Waksman and Albert Schatz in the 1950s led to the discovery of streptomycin, the first bactericidal drug for the tubercle bacilli.

Despite these many historical advances, the TB bacillus—*Mycobacterium tuberculosis*—has proven to be a formidable adversary against numerous interventions. Nevertheless, despite the arduous challenges of
working with this dangerous pathogen, the field continues to persevere, and our continued success in the pursuit of knowledge would, we suspect, be applauded by Koch, Ehrlich, Calmette, and many others, as we strive to find and apply more effective cures for this dreadful disease. In this spirit, this textbook is a collection of state-of-the-art research aimed at understanding the TB bacillus, the way it infects its host, the mechanisms by which it persists in the face of host immunity, and current intervention and therapeutic methods. The contributors of this book believe that such continued and dedicated research efforts will eventually lead to better vaccines, better chemotherapies, and ultimately the eradication of TB—Edward Jenner’s revenge.

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Index

A
Acid-fast (AF) mycobacteria, 519, 528–529
AF-negative M. tuberculosis and cell wall alterations, 527–528
brief history of AF staining, 520–522
chemical structures of mycolic acids, 520
clinical diagnosis of TB, 522–523
importance of mycolic acids, 523–524
Koch paradox, 523
lipid accumulation, 526–527
loss of AF property, 526–527, 528
mycobacterial cell envelope, 523–526
non-mycolic acid-containing components, 524–526
process for loss of acid-fastness, 525
Acquired immunity, 35, 43
CD4 T cells in HIV-TB coinfection, 248–251
HIV-TB coinfection, 248–252
TB-immune reconstitution inflammatory syndrome (TB-IRIS), 255–256
Adjunctive therapeutic vaccination, TB disease, 196–197
Animal models, 131, 139; see also
Experimental infection models;
Guinea pigs; Mouse models
assessment of new drugs, 136–137
assessment of vaccines, 135
cattle, 134
common experimental designs, 280
efficacy testing, 277–284
ethical and husbandry issues, 138–139
guinea pigs, 132
host response and pathogenesis, 134–135
limitations of, 137–139
mechanism of protection, 136
mice, 132, 278–280
mini pigs, 134
non-human primates (NHP), 132–133
pathology of tuberculosis, 117–121
primary host response to M. tuberculosis infection, 122–123
process and capacity, 135–136
rabbits, 133
rats, 133–134
Treg cell responses in experimental, 80–87
Treg cells in guinea pig model of TB, 85–86
Treg cells in mouse models of TB, 80–85
Treg cells in non-human primate models of TB, 86–87
tuberculosis disease progression in, 122
vaccine testing protocols, 136, 137
zebrafish, 133, 685, 686
Anopheles, 17
Antibiotics, golden era of, 317
Antibiotics treatment, extracellular M. tuberculosis in, 535
Antibiotic tolerance, 596
Antibodies
BCG vaccination and, 220
M. tuberculosis infection, 219–220, 221
role in anti-M. tuberculosis infection, 219
tuberculosis, 225–226
Antigen-presenting cells (APCs)
development of memory T cells, 98
HIV, 239
HIV-TB coinfection, 250
HIV-TB immune constitution inflammatory syndrome (IRIS), 252–253, 255–256
influence on T cell responses in coinfection, 251
Apoptosis, 563
Archaebacteria, 455
Archivel Farma SL, 202
Arginine auxotrophs, 701–706
Asparagine auxotrophs, 702
Aspartate auxotrophs, 702
Aspergillus auxotrophs, 702
Association of Internal Medicine, 520
AstraZeneca, 282
ATP synthesis, 308–309
Auramine O, staining of M. tuberculosis, 522–523, 526–527
Austin, Robert, 597
Autophagy, 8, 10
Auxotrophies, 701; see also Nutrient use of pathogens
amino acid, 701–706
arginine, 702
asparagine, 702
aspartate, 702
biotin (vitamin B7), 707
cobalamin (vitamin B12), 707–708
cofactor, 706–708
cysteine, 702
folate (vitamin B9), 707
glutamate, 703–706
glutamine, 705
histidine, 703
isoleucine, 704
leucine, 704
lysine, 703–704
methionine, 702–703
nicotinamide, 706
pantothenate (vitamin B5), 706
purine, 708
pyridoxamine (vitamin B6), 706–707
threonine, 704
tryptophan, 704–705
valine, 704

Bacillus Calmette-Guerin (BCG), original vaccine, 95, 117
Bacillus subtilis, 582, 673
Bacterial cell biology, tuberculosis research, 185
Bacterial clearance, 16–17
Bacterial replisome, components of, 584–586
B cells
M. tuberculosis infection, 217, 219–220
tuberculosis (TB), 225–226
Bedaquiline
animal model, 278
drug candidate, 271, 273
mice, 279
proof-of-concept molecule, 333
Biofilms, see Mycobacterial biofilms
Biography
animal- and human-associated MTBC lineages, 481–482
genetic diversity of TB bacilli, 477–484
M. canetti and MTBC, 482
M. tuberculosis strains, 482–484
variations from genomics, 480–481
Biomarkers
classes of TB, 371
human tuberculosis (TB), 226–227
transcriptomic profiling, 226–227
treatment response, 227
Biomedical Primate Research Center (Netherlands), 165, 167
Biosynthesis, menaquinone, 302–303, 304
Biotin (vitamin B7), 707
British Medical Research Council, 654
Bronchoalveolar lavage (BAL), 215, 242

Callithrix jacchus (common marmoset), 172, 284
Canadian Tuberculosis Standards, 379
Candida albicans, 321
Canetti, Georges, 496
Capreomycin, drug resistance, 503, 505
Carbon starvation, screening, 341, 342
Carbonyl cyanide m-chlorophenyl hydrazine (CCCP), 298
Cattle
animal model, 134
experimental infection of, 177–178
as model of TB in humans, 178
new TB vaccines tested in, 181
potential correlates of protection, 183
Caulobacter crescentus, 594
Cavity formation, pathology of tuberculosis, 119, 120
CD4 T and T helper 1 (Th1) cells, memory immunity, 95–96, 102–104
CD4 T and T helper 17 (Th17) cells, memory immunity, 104–105
CD8 memory T cells, 105–106
Cellular immunity, 143
CD8 memory T cells, 105–106
Centers for Disease Control and Prevention
Collaborative Drug Discovery, 329
Comprehensive liquid culture, 364
Comparative genomic analysis, 185
Comparative transcriptome analysis, 185
Computed tomography (CT), 171
Congenic mice, 145
Consumption, 453
Cox models, cumulative risk curves, 405
Crohn’s disease, 428
Cyclophosphamide, 97
β-Cycloserine, drug resistance, 505
Cynomolgus macaques
comparing TB in humans to, 164
Golden Age of research, 163, 166
Macaca fascicularis, 163, 172
TB studies, 166–167, 168
21st century TB research, 166
Cysteine auxotrophs, 702
Cytokines
enhancing HIV-1 replication, 246, 247
HIV-1 replication, 246, 247
IL-6 (interleukin-6), 40–41
IL-10, 48–49
IL-12 family, 42–45
IL-18, 42
IL-1R1/IL18R/MyD88, 41
IL-22, 46
IL-23, 44
IL-24, 46
IL-27, 44–45
IL-35, 45
interferons, 37–40
M. tuberculosis infection, 34–49
positive and negative roles in TB, 35
proinflammatory IL-1, 41–42
regulatory, 47–49
role in adaptive response to M. tuberculosis infection, 38
role in innate response to M. tuberculosis infection, 37
transforming growth factor β (TGFβ), 48
tumor necrosis factor alpha (TNFα), 34–37
type II interferon (IFNγ), 38–39
type I IFN, 39–40
Cytomegalovirus (CMV) infection, 249, 251, 255
Damage-associated molecular pattern molecules (DAMPs), 11
Dannenberg, Arthur, 680
Dartmouth University, 202
Deer, experimental infection of, 177, 179
Dehydrogenases
NADH:menaquinone oxidoreductases, 299–300
oxidative phosphorylation, 301–302
succinate:quinone oxidoreductase, 300–301
Delamanid, drug candidate, 271, 273
Dendritic cells (DCs)
development of memory T cells, 98
HIV-TB coinfection, 241, 244
lung, 5
M. tuberculosis infection, 11–12
Diabetes mellitus, 222–223, 630
Diagnosis for TB
acid-fast (AF) staining in clinical diagnosis, 522–523
classes of TB biomarkers, 371
commercial liquid culture, 364
current, for active TB, 363–366
current, for drug-resistant TB, 366–369
line probe assays for detecting resistance, 367–368
loop-mediated amplification test, 365–366
maximizing impact of new diagnostics, 361, 373–374
pipeline of future, 369–371
rapid speciation strip tests, 364
smear microscopy, 363–364
tests impacting patient outcomes, 373
translational challenges, 371, 372
unmet needs and gaps, 369
urine lipoarabinomannan rapid test, 366
Xpert MTB/RIF, 365, 368

Diagnostics of TB, see also GeneXpert MTB/RIF technology
background, 390–391
GeneXpert technology, 391
impact of GeneXpert MTB/RIF, 399–401
Disease burden, impact of GeneXpert MTB/RIF, 400
DIVA (differentiating infected from vaccinated animals) tests, domestic livestock, 184–186

Diversity outbred mice, 146
DNA replication
bacterial, 582–583, 586
B-family DNA polymerase, 591
components of bacterial replisome, 584–586
components of mycobacterial replisome/repair, 587
coordinating, and cell division, 594–595
DnaE1 PHP domain proofreading activity coordinating, and cell division, 594–595
DnaE1 PHP domain proofreading activity in maintaining fidelity, 588–590
DnaE1 versus DnaE2, 590–591
DNA polymerases at replication fork, 591–592
mycobacterial C-family DNA polymerases, 586, 588–591
mycobacterial persistence and, 596–599
mycobacterial replication rate, 592–594
peristasis, and cell division, 597–599
PHP (polymerase and histidinol phosphatase) domain, 586, 588
replication rate, 592
structure of C-family polymerases, 589
subcomplex division of bacterial replisome, 588

Drug-targeting approaches, 95
future directions, 96

E

Ebola virus, 454
Efficacy, see Preclinical efficacy testing
Ehrlich, P., 520
Electron flow, 296
Enterococcus faecalis, 610
Erdman strain, M. tuberculosis, 166, 167, 168, 170, 171–172
Escherichia coli, 12, 309, 321, 464, 467, 535, 536, 557, 583, 590, 599, 610, 638, 662, 673, 676, 701
ESX-1 (ESAT-6 secretion system-1), 627, 631–632
damage of M. tuberculosis-containing phagosome, 628–630
innate immune mechanisms, 631
interventions by target, 631
phagosome disruption by, 628
regulations of, 630–631
role in TB pathogenesis, 630
Ethambutol
drug resistance, 502, 503, 504
tolerance of infected cells, 640
Ethical issues, animal models, 138–139
Ethionamide, drug resistance, 505
Eubacteria, 455
Evolution of MTBC
animal-related M. tuberculosis complex (MTBC) strains, 461

Drosophila melanogaster, 17
Drug development
clinical trials, 272–273
macaque models for evaluation, 170–171
targeting replisome for new, 595–596
Drug-resistant M. tuberculosis strains
evolution of, 502–508
evolution of MDR-TB, 503, 506
evolution of resistance to second-line drugs, 506–507
impact of GeneXpert MTB/RIF, 401, 402–404
microevolution during TB infection, 507–508
resistance to first-line drugs, 504
resistance to second-line drugs, 505
suggested model for genetic diversity of subpopulations, 507
Drug susceptibility testing (DST), 363
commercial liquid culture-based DST, 366–367
genotypic tests for, 367
line probe assays for resistance detection, 367–368
noncommercial methods, 367
phenotypic tests for, 366
pipeline of diagnostics, 370
Drug targets, menaquinone biosynthesis, 638, 662, 673, 676, 701
Drug-tolerant cells
class I persisters, 321–322
class II persisters, 322–325, 329–346
population of nonreplicating, 322–325, 329–346
Dual-active molecules, 331–332
canonical and noncanonical targets of, 334

Eubacteria

Ethical issues, animal models, 138–139
Ethambutol

Evolution of Mycobacterium tuberculosis drug-resistant strains, 502–508

F

Fatty acids, M. tuberculosis in macrophages, 644–645

Fauci, Anthony, 117
flow cytometry, 682–684, 685
Fluorescence-activated cell sorting (FACS), 683
Fluorescence recovery after photobleaching (FRAP), 678, 684
Foam cell formation, human post-primary TB, 125
Folate (vitamin B9), 707
Foxp3 (transcription factor forkhead box P3)
coexpression with CD25, 74, 75–76, 78–79
function of, 73
host defense against M. tuberculosis, 82
Francisella tularensis, 609, 699, 709
Genetics and genomics

Genetic diversity
- biological impact of, 480
- intrapatient, 479–480

M. tuberculosis complex (MTBC), 477–484

Genomics
- see Genetics and genomics

Genotype
- 671

GlaxoSmithKline, 199

Global TB epidemic, 389–390

Glutamate auxotroph, 705–706

Glutamine synthetase (GS), 705

Goats, experimental infection of, 177, 189, 427

intrapatient, 479–480

biological impact of, 480

M. tuberculosis infection in macrophages, 118, 120–121

Mendelian susceptibility to mycobacterial infection, 118, 120–121

linkage studies, 416–417

identification of genetic variants with TB, 416–417

host-pathogen coevolution, 416–417

epidemiology of TB, 428

future prospects, 427–430

epigenetic variation, 414, 429

future for, 401, 405

historical context of national implementation, 394–396

financial modeling, 398

failures in, 399

expansion in other countries, 399

cumulative risk curves, 405

expansion in other countries, 399

failures in, 399

financial modeling, 398

future for, 401, 405

historical context of national implementation, 394–396

impact on diagnostics, 399–401

impact on national programs, 396–398

innovations in South Africa, 397

nucleic acid amplification testing (NAAT) strategies, 390, 391, 392

procurement strategies, 398

South African national implementation of, 390–396

treatment outcomes, 401, 402–404

Xpert Omni, 392, 401, 405

Xpert ULTRA, 392, 395, 397, 401

GeneXpert Omni, 365

Genome-wide association studies (GWAS)
- host-genetic evidence, 417

revisiting heritability in post-GWAS era, 416

TB susceptibility, 413, 418–419, 427

Genomics, see Genetics and genomics

Genotype, 671

GlaxoSmithKline, 199

Global TB epidemic, 389–390

Glutamate auxotroph, 705–706

Glutamine synthetase (GS), 705

Goats, experimental infection of, 177, 178–179

Gordonia oitidis, 498

Granulocyte-macrophage colony-stimulating factor (GM-CSF), 144

Granulocytes, M. tuberculosis infection, 14–16

Granulomas
- development, 680–681, 684, 687

Guinea pigs, 150–153; see also Animal models

animal model, 132

anti-TB treatment, 86

BCG vaccination, 86

devices for aerosol exposure, 147

gating host cells from lung, 153

granulomas in lungs, 118, 124, 126

human-to-guinea pig transmission, 153

immunopathology of, 152

magnetic resonance imaging of infected lungs, 155

preclinical efficacy models, 282

response to infection, 123, 124, 154

TB disease progression, 122

Treg cells in, 80, 85–86

vaccines, 153–154

H

H37Rv strain of Mycobacterium tuberculosis, 166, 167, 168, 170, 172, 215

Harvard School of Public Health, 467

Helicobacter pylori, 462, 464, 594

Heritability, see Genetics and genomics

Heterogeneity, see Phenotypic heterogeneity

Histidine auxotroph, 703

HIV-1 (human immunodeficiency virus type 1)
- functional impairment of CD4 T cells, 250–251

heterogeneity at site of M. tuberculosis disease, 247

immunity to TB, 50

infected people, 239

interferons and, 39

mediating immunosuppression, 239–241

M. tuberculosis infection risk, 172, 475

replication at site of M. tuberculosis disease, 245–247

tuberculosis epidemic and, 389

tuberculosis resurgence, 222

HIV-TB-associated immune reconstitution inflammatory syndrome (IRIS)

acquired immunity and TB-IRIS, 255–256

hypercytokinemia in TB-IRIS, 233, 253

innate immunity and TB-IRIS, 252–253

model of innate receptor signaling in TB-IRIS, 254

HIV-TB coinfection

acquired immunity, 248–252

CD4 T cells in, 248–251

cytotoxic lymphocytes in, 251–252

dendritic cells in, 244

dissemination and mycobacteria in, 248

immune activation in, 247–248

immune reconstitution inflammatory syndrome (IRIS), 252–256

macrophages in, 241–243

natural killer (NK) cells in, 244–245

neutrophils in, 243–244

spectrum of disease in, 240

Hollow fiber systems

diagram, 276

tuberculosis (TB) model, 275–277

Homeostatic regulation, 73

Homo sapiens

M. tuberculosis, 653

tuberculosis in, 453–454, 458, 460–462, 467

Host genetic studies, tuberculosis, 429

Host-mimicking platforms, 685–686

Host-pathogen coevolution, 428

Host response, application of animal models, 134–135

Human immunology of tuberculosis acquisition of M. tuberculosis infection, 213, 215–221

adaptive responses and spectrum of infection, 217–220

alveolar macrophages, 215–216

antibody responses, 219–220, 221

B cells, 217, 219–220

biomarkers in human TB, 226–227

granuloma, 2178

immunity to M. tuberculosis, 213

innate T cells, 216–217

neutrophils, 216

progression from infection to TB disease, 222–226

spectrum of pulmonary TB lesions, 218

stages of response to infection, 214

T cells, 217–218

Human models

challenge models, 205

in vitro, 345–346

Human tuberculosis (TB)

balance of Treg activity, 77

cavity formation in lungs, 119, 120

CD3+ Treg cell subsets in, 77–78

granuloma in lungs, 118, 124, 126

human-to-guinea pig transmission, 153

immunopathology of, 152

magnetic resonance imaging of infected lungs, 155

preclinical efficacy models, 282

response to infection, 123, 124, 154

TB disease progression, 122

Treg cells in, 80, 85–86

vaccines, 153–154

Index
Macrophages (Continued)
mycobacterial growth and HIV-1 viral replication, 243
non-human primate in vitro models, 544–545
Magnetic resonance imaging (MRI), infected rhinoceros pig lungs, 155
Major histocompatibility complex (MHC), 38, 39, 49, 74, 97
Malnutrition, 223–224
Marmosets (Callithrix jacchus), 172, 284
McMaster (Ad5Ag85A), 201
Memory immune response
against tuberculosis (TB), 96–97
alternative mediators of memory immunity, 105–107
CD4T and Th17 cells, 104–105
CD4T and T helper (Th) 1 cells, 95–96, 102–104
CD8 T cells, 105–106
development after TB infection or vaccination, 98
γδ T cells, 106
generation of memory T cells, 97–99
innate memory, 106–107
memory T cell heterogeneity, 99–102
models of T cell fate, 98–99
natural killer (NK) cell memory, 107
novel TB vaccines, 107–108
resident memory T cells, 101–102
stem cell-like memory T cells, 102
T cell memory and TB vaccination, 107–108
T cell memory phenotypes, 100
trained immunity in monocytes, 107
Memory T cells, 95
CD8, 105–106
development after infection or vaccination, 98
enzyme-linked immunospot (ELISPOT) method, 182
generation of, 97–99
heterogeneity, 99–102
models of fate, 98–99
phenotypes, 100
proposed models of differentiation, 99
resident, 101–102
stem cell-like, 102
TB vaccination and, 107–108
vaccine efficacy, 182
Menquinoine biosynthesis, 302–303, 304
Mendelian susceptibility to mycobacterial disease (MSMD), 413, 415, 416, 417
Merck Research Laboratories, 596
Metabolomics, 683–684, 700–701
Methionine auxotrophs, 702–703
Methyl citrate cycle, M. tuberculosis in macrophages, 644, 645–647
Metronidazole, 278
hypoxia and activity of, 318
mice, 279, 286
non-human primates, 283
proof-of-concept molecule, 333
rabbits, 283
Microbiology, exploitative tools and methodologies, 682–686
Micrococcus luteus, 611
Microfluidics, 684–685
MicroRNAs (miRNAs), 10
Microscopy, time-lapse, 684–685
Millennium Development Goals, 389
Minimal unit of infection, 635, 648
Mini pigs, animal model, 134
Modified Henderson apparatus, 167, 173
Monocytes
trained immunity in, 107
tuberculosis, 224–225
Moorella, 458
Morbidity, impact of GeneXpert MTB/RIF, 400
Mortality, impact of GeneXpert MTB/RIF, 400–401
Mouse models, 143–150, 278–280; see also Animal models
animal model, 132, 137
anti-TB treatment, 85
C3HeB/FeJ mice, 280–281
clinical M. tuberculosis strains, 83
common experimental designs, 280
Cornell model, 284–286
devices for aerosol exposure, 147
experimental infection of mice, 279–280
gene-disrupted mice, 144–145
genetic studies in mice, 145–146
immunodeficient, transgenic and congenic mice, 145
innate immunity, 145
in vitro, 542–544
latent TB infection (LTBI), 285
low-dose aerosol exposure to M. tuberculosis, 148
lung inflammatory response, 149
mouse response to infection, 146–150
obstructive alveolar pneumonia, 126
persistence in M. tuberculosis infection, 654–655, 657–659
preclinical efficacy models, 278–281
proposed regulation T cell suppression, 84
TB disease progression, 122
Treg cells and TB vaccination, 83–84
Treg cells in early TB infection, 81–82
Treg cells in chronic TB infection, 82–83
Treg cells in M. tuberculosis infection, 654–655, 657–659
preclinical model, 281
proposed regulation T cell suppression, 84
TB disease progression, 122
Treg cells and TB vaccination, 83–84
Treg cells in, 80–85
Treg cells in chronic TB infection, 82–83
Treg cells in early TB infection, 81–82
Moxifloxacin
animal model, 279
drug candidate, 272, 331
drug resistance, 305
guinea pigs, 282
proof-of-concept molecule, 333
Mucosal associated invariant T (MAIT) cells, 5
M. tuberculosis infection, 216–217, 549
Multidrug-resistant (MDR) strains, 533
Mutagenesis, M. tuberculosis, 595
MVA85A (modified vaccinia Ankara virus expressing antigen 85A)
testing protocols, 136
trial in South Africa, 137–138, 153–154
Mycobacteria
C-family DNA polymerases, 586, 588–591
DNA synthesis, 334–335, 336
evaluating bacteacidial action against nonreplicating, 329
fluoroquinolones, 339
folate synthesis, 338
high-throughput screens targeting phenotypically tolerant, 322–323, 325
4-hydroxyquinolines, 338, 339
8-hydroxyquinolines, 338, 339
lipid synthesis, 332–334, 336
membrane depolarizers, 343–346
metabolism and respiration, 309–310
oxidative phosphorylation, 295
peptidoglycan synthesis, 335, 337, 338
persistence and resistance, 597–599
population heterogeneity as function of applied stress, 598
protein synthesis, 335, 337
protoxideysis/proteostasis pathway, 339–341
quinolines, 338–339
replication machinery, 383, 386
respiration, 309–310
RNA synthesis, 335, 336
screening, 341–343
strategies for evaluating nonreplicating, 323
targeting oxygen reduction in, 303, 305–308
Mycobacterial biofilms, 533, 535, 536
extracellular M. tuberculosis in necrotizing lesions, 535–536
formation, 535, 536, 537
Mycobacterial replisome, working model of, 582
Mycobacteria oryngis, 460
Mycobacteria other than tuberculosis (MOTT), 495
Mycobacteriology, 460, 467
Mycobacterium africanum, 453, 455–460, 477
Mycobacterium avium, 13, 52, 679
Mycobacterium bovis, 476, 477
bovine tuberculosis (TB), 177
Ravene strain, 133
Mycobacterium bovis bacille Calmette–Guérin (BCG), 6, 12, 13, 15, 703
BCG vaccine-induced protection, 43, 46
C3HeB/FeJ mice, 281
cattle model, 134
day, 134
expansions of Treg cells, 76
responses of innate immune cells to, 12
vaccine, 95, 117, 179–180, 627
Mycobacterium canettii, 456, 458, 460, 476, 477, 479, 481–483, 485
drug resistance, 502
lessons to learn from, 496–498
Mycobacterium caprae, 460, 461, 476, 477, 479, 496
Mycobacterium flavesens, 382
Mycobacterium haemophilum, 495
Mycobacterium kansasi, 382, 495
Mycobacterium leprae, 382, 428, 495, 709
replication components, 584–586, 587
Mycobacterium leprosulosis, 495
Mycobacterium marinum, 14, 382, 495, 679
mycolic acids, 523
virulence, 610
zebrafish model, 36, 133, 699
Mycobacterium mungi, 461, 496
**Mycobacterium orygis**, 460, 476, 479, 496, 498

**Mycobacterium phlei**, 6, 295

**Mycobacterium pinnipedi**, 460, 461, 476, 477, 479

**Mycobacterium prototuberculosis**, 458

**Mycobacterium smegmatis**

**Mycobacterium prototuberculosis**, 3; see also HIV-TB coinfection

ATP synthesis by F$_{1}$F$_{0}$ ATP synthase, 308–309

chemokines and cytokines in adaptive response to, 38

chemokines and cytokines in innate response to, 37

chemokines in, infection, 49–53

cytokines in, infection, 34–49

emerging strains inducing regulatory T cells in lungs, 150

Erdman strain, 166, 167, 168, 170, 171–172

fate upon macrophage infection, 9

H37Rv strain, 166, 167, 168, 170, 172

HIV-1 heterogeneity at site of disease, 547–548

HIV-1 replication at site of infection, 38

HIV-TB coinfection, 243–244

memory, 107

M. tuberculosis infection, see also Protein phosphorylation

apoptosis, 563

cell wall remodeling, 569–570

defense against host-generated reactive oxygen and nitrogen species, 563–564

growth arrest, 567–569

Ser/Thr protein kinases (STPKs)

coordinating physiology of, 567–571

slowing central metabolism, 570–571

STPK cell signaling network, 568

subversion of innate immune response, 560–564

Mycobacterium tuberculosis in macrophage bottleneck response, 637

chemical genetics of infection, 643–644

cholesterol, 645, 646

construction of reporter strains, 638–639

drug sensitivity of, 641

environmental cues and responses, 638

fatty acids, 644–645

flow cytometry gating strategy, 642

flow sorting strategy, 641

guilt-by-association analysis, 637

life and death dynamics, 637

lipid acquisition from host cell, 647

lipid utilization by, 644

manipulating host cell for nutritional purposes, 647–648

minimal unit of infection, 635, 648

phagocytosis, 636

replication clock plasmid, 637

response of M. tuberculosis to intracellular environment, 636–638

role of isocitrate lyase (Icl) and methyl citrate cycle (MCC), 645–647

single-cell suspension, 639–642

Mycobacterium tuberculosis-macrophage biology

downstream proinflammatory signaling, 547–548

innate immune sensing, 547–548

modulation of cell death pathways, 547

phagosome maturation arrest, 546

principles of, 546–548

survival in the face of host antimycobacterial molecules, 546–547

Mycobacterium tuberculosis sensu stricto, 454, 476, 477

Mycobacterium ulcerans, 495

Mycobacterium avium, 197

Mycolic acids

chemical structures of, 520

importance of, 523–524

loss of acid-fastness, 519, 529

Mycobacterium tuberculosis, 453–536

characteristic of active pulmonary TB, 533–534

extracellular environment, 533–534

N

NADH:menaquinone oxidoreductases, 299–300

National Institute for Health and Care Excellence (UK), 379

National Institute of Allergy and Infectious Diseases, 117

National Primate Research Centers (NPRCs), 164, 165, 166, 170, 171, 172

National TB Costing Model, 395, 398

Natural killer (NK) cells

HIV-TB coinfection, 244–245

Necrotizing lesions

biofilms as perspective of extracellular M. tuberculosis in, 533–536

characteristic of active pulmonary TB, 533–534

experiments, 533–534

macaque models for study of TB

N. meningitidis, 197

Neutrophils

HIV-TB coinfection, 243–244

lung, 5

M. tuberculosis infection, 12, 39, 216, 548

response to M. tuberculosis, 125

Niclosamide, 343–344, 346

Nitric oxide, 706

Nigericin, 297, 298

Nile red stain, 526–527

Nitro-containing compounds, dual- and nonreplicating active, 343, 344

3-Nitropropionate, 300, 301

Nocardia farcinica, 13

Nongrowing but metabolically active bacteria (NGMA), 676

identification of, 678, 681, 683

Non-human primate models, see also Animal models

animal model, 132–133

comparison of rhesus and cynomolgus macaque models, 165–167

cynomolgus macaques, 166–167, 169

future research strategies, 172

historical use of macaque models, 163–165

in vitro, 544–545

macaque models for study of TB

pathogenesis, 171

macaque models for TB drug evaluation, 170–171

macaque models for TB vaccine evaluation, 167, 170

M. tuberculosis/simian immunodeficiency virus coinfection, 171–172

NADH:menaquinone oxidoreductases, 299–300

National Institute for Health and Care Excellence (UK), 379

National Institute of Allergy and Infectious Diseases, 117

National Primate Research Centers (NPRCs), 164, 165, 166, 170, 171, 172

National TB Costing Model, 395, 398

Natural killer (NK) cells

HIV-TB coinfection, 244–245

memory, 107

M. tuberculosis infection, 12–14

Natural resistance-associated macophagy protein (Nremap), 146

Neanderthals, 467

Necrosis-associated extracellular clusters (NECs), 151, 153

Necrotizing lesions

biofilms as perspective of extracellular M. tuberculosis in, 533–536

characteristic of active pulmonary TB, 533–534

experiments, 533–534

macaque models for study of TB

N. meningitidis, 197

Neutrophils

HIV-TB coinfection, 243–244

lung, 5

M. tuberculosis infection, 12, 39, 216, 548

response to M. tuberculosis, 125

Niclosamide, 343–344, 346

Nitric oxide, 706

Nigericin, 297, 298

Nile red stain, 526–527

Nitro-containing compounds, dual- and nonreplicating active, 343, 344

3-Nitropropionate, 300, 301

Nocardia farcinica, 13

Nongrowing but metabolically active bacteria (NGMA), 676

identification of, 678, 681, 683

Non-human primate models, see also Animal models

animal model, 132–133

comparison of rhesus and cynomolgus macaque models, 165–167

cynomolgus macaques, 166–167, 169

future research strategies, 172

historical use of macaque models, 163–165

in vitro, 544–545

macaque models for study of TB

pathogenesis, 171

macaque models for TB drug evaluation, 170–171

macaque models for TB vaccine evaluation, 167, 170

M. tuberculosis/simian immunodeficiency virus coinfection, 171–172
Non-human primate models (Continued)
preclinical efficacy models, 283–284
rhesus macaques, 165, 166, 168
Treg cells in, 80, 86–87
validation of macaques in TB research, 163
Nonreplicating (NR) models, selecting and designing, 323, 324
Nonreplicating persistence (NRP)
M. tuberculosis physiology for, 567–571
sensing when to exit NRP, 571–572
Nonreplication, diversity in, 319–321
Nonreplicating (NR) models, selecting and designing, 323, 324
PAMP (pathogen-associated molecular patterns), 145
Paleomicrobiology, 467
Oxford University, 200
Ofloxacin, drug resistance, 505
Oxidative phosphorylation, 277–278
M. tuberculosis, 295
P
Pago, Svante, 467
Paleomicrobiology, 467
PAMP (pathogen-associated molecular pattern), 461
M. tuberculosis-derived, 246
Pantothenate (vitamin B₅), 706
Paradigm, 121
Parkinson diseases, 630
Pathogenesis
application of animal models, 134–135
macaque models for studying TB, 171
persisting, 672
Pathogens, see Nutrient use of pathogens
Pathology of tuberculosis, 117–121
alveolar pneumonia, 126
cavity formation, 119, 120
disease progression in animal models, 122
granuloma within the lung, 118
hypersensitivity of pathogenesis of post-primary TB, 123–125
intrapulmonary spread of mixed inflammatory cells, 121
lipid pneumonia, 121, 125
obstructive lobular pneumonia, 121, 123
post-primary lung reinfection, 124–125
primary host response to M. tuberculosis infection, 122–123
Pattern recognition, 145
Penicillin, 317–318
Peripheral blood mononuclear cells (PBMCs), 4
Peroxisome proliferator-associated receptor gamma (PPARγ), 4, 10
Persistence definition, 654
drug-induced, 662
gene deletion studies, 659–661
host-induced, 657–662
measurements, 656–662
messages, 662–663
methods, 656
models, 654–656
pathogenicity of M. tuberculosis, 653
physiology of M. tuberculosis, 653
predicted genes for in vitro survival of M. tuberculosis, 661
terms, 653–654
Persisters, 317
class I, 321–322
class II, 322–325, 329–346
diversity in nonreplicating cells, 319–321
killing class II persisters, 329, 331–341
Phagocytosis, 636
Phagosome maturation, 8, 9
Phenotype definitions, 429
Phenotypically tolerant M. tuberculosis, 317–319
class I persisters, 321–322
class II persisters, 322–325, 329–346
compound transformation during screening and secondary assays, 325, 329
conditions for replication rates of, 326
designing high-throughput screens to target, 322–325
diversity in nonreplication, 319–321
evaluating bactericidal action against nonreplicating mycobacteria, 329
fluoroquinolones, 339
future studies, 347–348
high-throughput screening (HTS), 341–343
key observations, 319
key recommendations, 348
class II persisters, 329, 331–341
membrane depolarizers, 343–346
modelling hypoxia and metronidazole activity relationship, 318
molecules persisting nonreplicating mycobacteria, 346, 347
nitro-containing compounds, 343
postscreening assays, 327, 328
proof-of-concept molecules, 331–332
proteolysis/proeostasis pathway, 339–341
quinolones and derivatives, 338–339
screening assays, 325, 329, 330
selecting and designing nonreplicating models, 324
strategies for evaluating viability of nonreplicating, 323
Phenotypic drug resistance, 317
Phenotypic heterogeneity, 671–672
asymmetric cell division and cell aging, 676–679
causes and consequences of, 673
flow cytometry and omics, 682–684
fluorescence recovery after photobleaching (FRAP), 678, 684
growth phase, 674–675
growth rate, 675–676
host microenvironment, 679–682
host-mimicking platforms, 683–686
in vivo investigation, 685–686
stochastic processes, 672–674
stress conditions enhancing, 677
time-lapse microscopy and microfluidics, 684–685
tools and methodology, 682–686
Phenotypic tolerance, 317
Phosphorylation, see Protein phosphorylation
Pneumonia, tuberculosis as obstructive lobular, 121, 123
Positron emission tomography/computed tomography (PET/CT), 171, 213, 283, 680–681, 686
Post-primary tuberculosis, 124–125
Preclinical efficacy testing, 271, 274
animal infection models of active TB, 277–278
drug candidates, 272–273
dynamic drug concentration models, 275–277
goals of, 274–275
guinea pigs, 282
hollow fiber system model of TB, 275–277
in vitro models, 275–277
mice, 278–281
modeling chemotherapy of latent TB infection (LTBI), 284–286
non-human primates, 283–284
rabbits, 283
rats, 281–282
static drug concentration models, 275
Preclinical studies, role in experimental medicine studies, 205–206
Pretomanid
drug candidate, 273
guinea pigs, 282
mice, 279
Prime, vaccine development, 197
Prime-boost, vaccine development, 197
Programmed cell death protein-1 (PD-1), 101–102
Proline auxotroph, 703
Proof-of-concept molecules
dual actives with in vivo efficacy, 331–332
nonreplicating actives with in vivo efficacy, 332
nonreplicating activity, 333
selective nonreplicating activity, 331
Protein-adjuvant TB vaccines, 198–200
Protein kinase activity, 557
Protein phosphorylation, see also Mycobacterium tuberculosis infection apoptosis, 563
biochemically verified substrates of M. tuberculosis serine/threonine protein kinases (STPKs), 538–539
effect on M. tuberculosis STPKs, 566
growth and persistence phenotypes of M. tuberculosis STPKs, 562
hierarchy of M. tuberculosis STPK activation, 561
inhibition of phagosomal-lysosome fusion, 561, 563
M. tuberculosis, 557, 559–560
STPKs coordinating M. tuberculosis physiology, 567–571
STPKs regulating M. tuberculosis morpholology, 564–565, 567
Proteomics, 679, 683–684
Proton motive force (PMF), 297
mechanisms, 297
targeting, in *M. tuberculosis*, 295–299
traditional inhibitors of PMF
generation, 298
*Pseudomonas*, 673
*Pseudomonas aeruginosa*, 13, 321, 467, 536,
591, 594
*Pseudomonas putida*, 591
*Pseudomoccardia dioxanivorans*, 498
PubChem, 329
Pyridoxamine (vitamin B6), 706–707
Pyrazinamide, 528, 681
Purine auxotroph, 708
Pyrizinamide, 86
Regulatory cytokines
β (TGFβ), 48
IL-4, IL-5, and IL-13, 47–48
interleukin IL-10, 48–49
transforming growth factor β (TGFβ), 48
Replication rate, 592; see also DNA replication
mycobacterial, 592–594
Research Institute of Influenza
(St. Petersburg, Russia), 202
Respiration, *M. tuberculosis*, 295
Restriction fragment length polymorphism
(RFLP) method, 454–455, 583
Retroviral family, 239
Rhesus macaques, 163; see also Macaque models
comparing TB in humans to, 164
“Golden Age” of TB research using,
163, 166
Macaque mulatta, 163, 173
TB studies, 166, 167, 168
21st century TB research, 166
*Rhizobiump. leguminosarum*, 613
Rifampin, 86, 527–528
animal models, 279–280
drug candidate, 272, 274, 278, 331
drug resistance, 503, 504, 674
guinea pigs, 282
latent TB infection, 285–286
line probe assays for detecting resistance,
367–368
non-human primates, 283
proof-of-concept molecule, 333
tolerance of infected cells, 639–641
Xpert MTB/RIF for resistance to, 368
Rifapentine
drug candidate, 272
guinea pigs, 282
latent TB infection (LTBI), 285–286
Salmonella
*Salmonella* biflexa, 527
*Salmonella enterica serovar Typhi*, 462
*Salmonella typhi*, 462
*Salmonella enterica serovar Typhi*, 462
*Salmonella enterica serovar Typhimurium*, 537
Sanofi Pasteur, 199
Scavenger receptors (SRs), 8
SciFinder, 329
Screening
acidic pH, 341, 342
biofilms, 341, 343
hypoxia, 341, 342
multiple physiological stresses, 341, 342
Screening assays
compound transformation during, 330
designing high-throughput screens for
phenotypically tolerant mycobacteria,
322–323, 325
post-, 327, 328
potential compound transformation
during, 325, 329
Secretion (SecA1) pathway
cell wall synthesis and remodeling
factors, 609
conserved, 607–608
conserved SecA1 exportome, 608–611
entering dormancy, 610
exported virulence factors, 610
lipoproteins, 609–610
models of SecA1 export, 608
reactivation/resuscitation from
dormancy, 611
Secretion (SecA2) pathway
dormancy, 619
features of SecA2-dependent
substrates, 613
identification, 611–612
immunomodulation and, 618–619
inhibition of apoptosis, 618
KatB (catalase-peroxidase), 616
Mce transporters, 614–615
mechanism, 612–613
models of SecA2 export, 608
multiple components of Mce
transporters, 615
phagosome maturation arrest, 617
PknG (eukaryotic-like serine-threonine
kinase), 616
protein export pathway, 611–613
reactive radicals and, 619
SBPs (solute binding proteins), 613–614
*secA2* mutant as vaccine candidate,
619–620
SecA2 and DosR regulon, 616–617
SecA2 exportome, 613–616
SodA (Fe-superoxide dismutase), 615–616
virulence and, 617–619
Secretion system, see also ESX-1 (ESAT-6
secretion system–1)
ESAT-6 (ESX-1), 627, 631–632
Shuman, Stewart, 591
Simian immunodeficiency virus (SIV),
*M. tuberculosis* and, coinfection
macaque models, 171–172
Smea microscopy, diagnostics for active TB,
363–364
Solute carrier, 146
South Africa
challenges and opportunities of
implementation, 394, 396
GeneXpert implementation, 397
GeneXpert placement, 394
national implementation of Xpert NTB/
RIF assay, 393–394
tuberculosis in, 391, 393
South African Tuberculosis Vaccine Initiative
(SATVI), 104, 105
Spectroscopy, 683–684, 701
Spoligotyping, 455, 457, 461
*Staphylococcus aureus*, 609, 611
Streptomycin, drug resistance, 502, 505
Streptomycetes coelicolor, 591
Streptomyces coelicolor, 591
Streptomyces parasanguinis, 611
Streptomyces pneumoniae, 197, 536
Swedish Institute of Infectious Disease
Control, 167
Systems biology, tuberculosis, 429
T
TB-associated immune reconstitution
inflammatory syndrome (TB-IRIS), 76
T cells, see also Memory T cells
cytotoxic, in TB-immune reconstitution
inflammatory syndrome (TB-IRIS),
255–256
*M. tuberculosis* infection, 217–219,
548–549
responses to tuberculosis (TB), 225
Technical Expert Group, 365
*Thioalkalivibrio*, 458
*Thiorhodovibrio*, 458
Thioridazine, 297, 299
Threonine auxotroph, 704
Time-lapse microscopy, 684–685
Tissue remodeling, tuberculosis (TB), 225
Toll-like receptor 9 (TLR9), 4
Toll-like receptors (TLRs), 7–8, 39, 145
Trained immunity, 13, 17, 107
Transcriptional profiling, M. tuberculosis in macrophages, 636–638
Transcriptome studies, 674, 683–684
Transcriptomic profiling, biomarkers, 226–227
Transforming growth factor β (TGFβ), 48
Transgenic mice, 145
TranSH screening method, 704
Treatment outcomes, impact of GeneXpert MTB/RIF, 401, 402–404
Trifluoperazine, 299, 300
Trudeau, E. L., 131
Tryptophan auxotroph, 704–705
Tuberculin skin testing (TST), 213, 214, 215, 220, 221, 225
administering and reading TST, 381
latent TB infection, 380
purified protein derivative (PPD)-based TST, 381
Tuberculosis (TB), see also Animal models; HIV-TB co-infection; Human tuberculosis (TB); Vaccine candidates
adjunctive therapeutic vaccination, 196–197
anti-TB vaccine design, 39
biomarkers in human, 226–227
diabetes mellitus, 222–223
diversity, 680
global epidemic, 389–390
HIV-1 heterogeneity at site of disease, 247
HIV-1 replication at site of disease, 245–247
HIV and, 172, 222
lung, 3–6
malnutrition, 223–224
necrotizing lesions in active pulmonary, 533–534
positive and negative roles of chemokines in, 36
positive and negative roles of cytokines in, 35
post-primary, 119–121, 123–127
preventing recurrent TB, 196–197
prevention of disease, 193–196
progression from infection to disease, 222–226
proposed framework for spectrum of infection, 380
protective memory against, 96–97
risk factors for, 222
systems biology of, 429
targeting replisome for new drug development, 595–596
Treg cell responses in human, 74–80
vaccine, 40, 43, 45, 46, 49
vaccine development strategies, 197–198
vitamin D deficiency, 223
Tuberculosis (TB) vaccination animal models, 80
guinea pig model, 86
mouse models, 83–84
Tumor necrosis factor alpha (TNFa), 34–37
roles in TB, 35
Type I interferons (IFN-γ), tuberculosis, 224
University of Pittsburgh, 166–167, 171
University of Zaragoza and Biofabri, 202
Urine lipoarabinomannan rapid test, 366
U.S. Food and Drug Administration (FDA), 382
Vaccine, vaccine candidate, 197, 198, 202
Vaccination adjunctive therapeutic vaccination, 196–197
BCG and disease protection, 194
clinical trials of TB candidates, 197–203
M. tuberculosis, 95–96
prevention of M. tuberculosis infection, 193–195
prevention of recurrent TB disease, 196–197
prevention of TB disease, 195–196
Vaccine candidates, 198
Ad5Ag85A, 201
Cruclell Ad35, 201
DAR-901, 202
development strategies, 197–198
experimental medicine role in development, 203–206
global clinical pipeline of, 198
H11C31 and H11-CAF01, 198
H44J31, 199
H56J31, 198–199
ID93+GLA-SE, 199
inactivated whole-cell and fragmented TB vaccines, 202
M72/AS01E, 199–200
MTBVAC, 202–203
MVA85A, 200–201
Protein-adjuvant TB vaccines, 198–200
recombinant mycobacterial vaccines, 202–203
RUTI, 202
secA2 mutant as, 619–620
TB/Flu-04L, 202
Vaccae, 202
VAP 1002, 203
viral-vectored vaccines, 200–202
VPM 1002, 203
Vaccines, see also Vaccine candidates
Ad85A (human adenovirus 5 expressing Ag85A), 181–182
animal models and testing protocols, 136, 137
animal models for assessment of, 135
antibody-inducing, 220
BCG protection, 40, 43, 45, 46, 49, 220
BCG vaccination in animals, 100
BCG vaccination in guinea pigs, 86
BCG vaccination in humans, 76, 100
BCG vaccination in mice, 83–84
biomarkers correlating disease severity, 184
biomarkers predicting efficacy, 182
guinea pig model, 153–154
macaque models of evaluating TB vaccine, 167, 170
mechanism of protection, 136
memory immunity by novel TB, 107–108
Mycobacterium bovis bacillus Calmette-Guérin (BCG), 95, 117, 179–180
new-generation TB, 180–182
predictivity of animal models, 137–138
proof of concept for, 194, 196, 203–206
role of experimental medicine in vaccine development, 203–206
schedules of BCG and virally vectored, 183–184
types of new, tested in cattle, 181
Vakzine Projekt Management GmbH, 203
Valine auxotroph, 704
Valinomycin, 297, 298
Vertex Pharmaceuticals, 643
Vibrio cholerae, 465
Viral-vectored vaccines, 200–202
Vitamin B1 (thiamin), 706
Vitamin B2 (riboflavin), 707
Vitamin B5 (pantothenate), 706
Vitamin B6 (pyridoxamine), 706–707
Vitamin B9 (folate), 707
Vitamin B12 (cobalamin), 707–708
Vitamin D deficiency, 223
Wayne model, hypoxia, 318, 323, 325
Whole-genome sequencing (WGS) emergence of, 495
M. tuberculosis L2 Beijing sublineage, 500
resistant strains, 502, 506–507
World Health Organization (WHO), 193, 226, 239
global TB epidemic, 389–390;line probe assay recommendations, 368–369
TB disease control, 379, 533
TB screening, 363, 364
X
XLAAD (X-linked autoimmunity allergic dysregulation syndrome), 73
Xpert MTB/RIF, see also GeneXpert MTB/RIF technology background of, 391
diagnostics for TB, 365, 368
maximizing impact of new diagnostics, 371, 373–374
timeline of availability, 374
Y
Yersinia pseudotuberculosis, 674
Z
Zebras, 215
Zebral fish animal models, 133, 685, 686
granuloma formation, 135
in vitro model, 530
M. marinum, 36, 133, 699
Ziehl, F., 520
ZN (Ziehl-Neelsen) stain, 519; see also AF (acid-fast) mycobacteria
clinical diagnosis of TB, 522–523
history of acid-fast (AF) staining, 520–522
M. tuberculosis, 521, 528