TUBERCULOSIS
AND THE
TUBERCLE BACILLUS
2ND EDITION
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. SCHLEISINGER

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 MCSHANE

D. HUMAN IMMUNOLOGY

11 Human Immunology of Tuberculosis / 213
   THOMAS J. SCRIBA, ANNA K. COUSSENS, AND HELEN A. FLETCHER
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>DRUG DISCOVERY AND DEVELOPMENT: STATE OF THE ART AND FUTURE DIRECTIONS</td>
<td>269</td>
</tr>
<tr>
<td>III</td>
<td>BIOMARKERS AND DIAGNOSTICS</td>
<td>361</td>
</tr>
<tr>
<td>IV</td>
<td>HOST AND STRAIN DIVERSITY</td>
<td>411</td>
</tr>
<tr>
<td>V</td>
<td>THE SIGNATURE PROBLEM OF TUBERCULOSIS PERSISTENCE</td>
<td>517</td>
</tr>
</tbody>
</table>

12 The Immune Interaction between HIV-1 Infection and *Mycobacterium tuberculosis* / 239  
Elsa du Bruyn and Robert John Wilkinson

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

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

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

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

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

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

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
30 The Minimal Unit of Infection: *Mycobacterium tuberculosis* in the Macrophage / 635
Brian C. VanderVen, Lu Huang, Kyle H. Rohde, and David G. Russell

31 Metabolic Perspectives on Persistence / 653
Travis E. Hartman, Zhe Wang, Robert S. Jansen, Susana Gardete, and Kyu Y. Rhee

32 Phenotypic Heterogeneity in *Mycobacterium tuberculosis* / 671
Neeraj Dhar, John McKinney, and Giulia Manina

33 *Mycobacterium tuberculosis* in the Face of Host-Imposed Nutrient Limitation / 699
Michael Berney and Linda Berney-Meyer

Index / 717
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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 infectious 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 fledging field expanded, para-amino salicylic acid and isoniazid were discovered to be active against the TB bacillus. Parallel studies by Salman 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
Alveolar epithelial cells (AECs), 3, 4
Alveolar macrophage (AM), 3, 4–5; see also Macrophages
M. tuberculosis infection, 215–216
Alzheimer's disease, 630
Amikacin, drug resistance, 503, 505
Amino acids, auxotrophs, 701–706
Amyloid diseases, 570–571
Anhui Zhifei Longcom Biologic Pharmacy Co. Ltd., 202
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, 279–280
mini pigs, 134
non-human primates (NHP), 132–133
primary host response to M. tuberculosis infection, 122–123
process and capacity, 135–136
rabbis, 133
rats, 133–134
Treg cell responses in experimental, 80–87
tuberculosis disease progression in, 122
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
zebrafish, 133, 685, 686
Autophagy, 8, 10
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
function of, 74, 75
Antiretroviral therapy (ART), 389
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, 855
Archivel Farma SL, 202
Arginine auxotrophs, 702
Aristotle, 413
Asparagine auxotrophs, 702
Aspartate 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
asparagines, 702
aspartate, 702
biotin (vitamin B7), 707
cobalamin (vitamin B12), 707–708
cofactor, 706–708
cysteine, 702
folic acid (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
proline, 703
purine, 708
pyridoxamine (vitamin B6), 706–707
threonine, 704
tryptophan, 704–705
valine, 704

B
Bacillus Calmette-Guérin (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
Biology
animal- and human-associated MTBC lineages, 481–482
genetic diversity of TB bacilli, 477–484
M. canettii and MTBC, 482
M. tuberculosis strains, 482–484
variations from genomes, 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

C
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
Centers for Disease Control and Prevention (CDC), 379
Chagas’ disease, 454
Chemokines
CCR (CC receptors) and ligands, 49–52
CCR1, 49–50
CCR2, 50
CCR3, 50–51
CCR5, 51–52
CXCR1, 52
CXCR2, 52
CXCR3, 52–53
CXCR5, 53
CXCR receptors and ligands, 52–53
HIV-TB coinfection, 241
M. tuberculosis infection, 49–53
positive and negative roles in TB, 36
role in adaptive response to M. tuberculosis infection, 38
role in innate response to M. tuberculosis infection, 37
Chemotherapy
latent TB infection (LTBI), 284–286
M. tuberculosis persistence, 653–658, 662
Chicago Center for Biomedical Research, 171
Chlamydia trachomatis, 609
Chlorpromazine, 299
Cholesterol, M. tuberculosis in macrophages, 645, 646
Ciprofloxacin, drug resistance, 505
Clinical testing, see Vaccine candidates
Clofazimine
animal models, 278–279
drug candidate, 272, 300
mice, 281
Chlamydia trachomatis, 521, 525
Diabetes mellitus, 222–233
Diagnostic tests 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
Cox models, cumulative risk curves, 405
Crohn’s disease, 428
Cyclophosphamide, 97
n-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, 224, 227
HIV-1 replication, 246, 247
IL-6 (interleukin-6), 40–41
IL-10, 48–49
IL-12 family, 42–45
IL-18, 42
IL-18R/IL18R/MyD88, 41
IL-22, 46
IL-23, 44
IL-23-dependent, 45–46
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

D
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, 222–233
Diagnostics 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
looph-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, 591–592
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
persistence and resistance, 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
targeting replisome for new TB drug development, 595–596
DNA synthesis, 334–335

Domestic livestock, 177, 186
antigen mining, 184–186
bacterial cell biology, 185
cattle, 177–178
comparative genomic analysis, 185
cytometry, 186
comparative transcriptome analysis, 185
deer, 177, 179
development and evaluation of TB vaccines, 179–182
DIVA (differentiating infected from vaccinated animals) tests, 184–186
DIVA skin test development, 185–186
experimental infection models, 177–179
goats, 178–179
immune correlates of protection and disease, 182–184
tuberculosis (TB) in, 177

Dormancy
definition, 654
secretion, 610, 611, 619

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)
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, 498–499
Drug susceptibility testing (DST), 363

Drugs, 329–346
class I persisters, 321–322
class II persisters, 322–325
coexpression with CD25, 325–326
contention, 329–332
canonical and noncanonical targets of, 334

e
Ebola virus, 454
Efficacy, see Preclinical efficacy testing
Ehrlich, P., 520
Electron flow, 467

Enterococcus faecalis, 610

Erdman strain, 166, 167, 168, 170, 171–172
Escherichia coli, 12, 309, 321, 464, 467, 533, 536, 557, 583, 590, 599, 610, 638, 662, 673, 676, 701
ESX-1 (ESAT-6 secretion system-1), 627, 631–326
damage of M. tuberculosis-containing phagosome, 628–630
innate immune mechanisms, 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, 655

Evolution of MTBC
animal-related M. tuberculosis complex (MTBC) strains, 461
biogeographical structure of M. tuberculosis Beijing lineage, 463
correspondence table of strains by typing methods, 457
diagram of proposed evolutionary pathway, 456
fingerpring era, 454–455
genome-based phylogeny of MTBC, 459
global phylogeny of MTBC isolates, 465
global picture, 458–461
history and early misconceptions, 453–454
limitations, 466–467
multicuor era, 455–458
pattern for evolving populations, 466
pregenomic era, 454–458
relativity of clock, 464–467
spoligotyping, 453, 457, 461
substitution rate estimates, 464–466
taxonomic nomenclature, 464
whole-genome phylogeny of strains of MTBC, 460
zooming into lineagtes, 461–464

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

evolution of M. tuberculosis L2
Beijing and L4 strains, 499–500
L2 Beijing sublineage, 500–501
L4 sublineage, 501–502
lessons from M. canetti, 496–498
molecular key events in evolution, 497
neighbor-joining phylogeny scheme, 499
professional pathogenicity, 498–502

Expanded Program on Immunization (EPI), 203–206
World Health Organization, 193

Experimental infection models
cattle, 177–178
deer, 179
goats, 178–179

Experimental medicine
controlled human challenge models, 205
examples of, 205
potential outcomes in studies, 204–205
preclinical studies in, 205–206
product development and, 204
role in TB vaccine development, 203–206
scientific community, 206

Extensively drug-resistant (XDR) strains, 533

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)
coeexpression with CD25, 74, 75–76, 78–79
function of, 73
host defense against M. tuberculosis, 82
Francisella tularensis, 609, 699, 709
Genetic diversity
biological impact of, 480
intrapatient, 479–480
M. tuberculosis complex (MTBC), 477–484

Genetic deficiency, mycobacterial disease, 38

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 otitidis, 498
Granulocyte-macrophage colony-stimulating factor (GM-CSF), 144
Granulocytes, M. tuberculosis infection, 14–16
Granulomas
development, 680–681, 684, 687
growth, 243–244
lung of human with primary tuberculosis, 118, 120–121
morphological features of, 533
M. tuberculosis infection, 217, 636
progressive cavitating, 126
restricting M. tuberculosis movement, 35–36
term, 16
Granulomatous inflammation, 123
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

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)
fractional impairment of CD4 T cells, 250–251
heritability 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 infection, 245–247

M. tuberculosis epidemic and, 389
tuberculosis resurgence, 222
HIV-TB-associated immune reconstitution inflammatory syndrome (IRIS)
acquired immunity and TB-IRIS, 255–256
hypercytokemia in TB-IRIS, 233, 251
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 mycobacteremia 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-imicking 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, 217–222
alveolar macrophages, 215–216
antibody responses, 219–220, 221
B cells, 217, 219–220
biomarkers in human TB, 226–227
granuloma, 217–227
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, 454–456
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, 120–121
in vitro expansion of mycobacteria-specific Treg cells, 76–77
novel TB vaccine candidate MVA85A, 77–78
post-primary lung reinfection, 124–125
TB disease progression, 122
Treg at site of infection, 79–80
Treg cell responses in, 74–80
Mycobacterium orygis, 460, 476, 479, 496, 498
Mycobacterium phlei, 6, 295
Mycobacterium pinnipedii, 460, 461, 476, 477, 479
Mycobacterium prototuberculosis, 458
Mycobacterium smegmatis, 10, 308–309, 535, 536, 609, 673, 675, 679, 703
replisome components, 584–586, 587
Mycobacterium suricatta, 496
Mycobacterium szulgai, 382
Mycobacterium tuberculosis, 3; see also HIV-TB coinfection
ATP synthesis by F,F F, 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, 247
HIV-1 replication at site of disease, 243–247
hypothetical states of response to infection, 214
immune system, 95
interactions with macrophages, 6–8, 10–11
interaction with granulocytes, 14–16
latent TB infection (LTBI), 217, 226, 227
macrophage receptors, 7
mouse response to infection, 146–150
mutagenesis in, 595
oxidative phosphorylation in, 295
pathology of, 117–121, 125–127, 672
physiology for nonreplicating persistence, 567–571
prevention of infection, 193–195
primary host response to infection, 122–123
protein phosphorylation in, 557, 559–560
pulmonary innate immune cells during infection, 4
replisome components, 584–586, 587
respiration overview in, 295
responses of innate immune cells to, 12
schematic of electron transfer components, 296
spectrum of infection, 379–380
targeting primary dehydrogenases in, 299–302
targeting proton motive force (PMF) in, 299–293
vaccination, 95–96
Mycobacterium tuberculosis complex (MTBC), see also Evolution of MTBC
biological differences among M. tuberculosis strains, 482–484
biological differences between animal and human MTBC lineages, 481–482
biological differences between M. canettii and, 482
biological impact of genetic diversity, 480
evidence for potential of biological variation, 480–481
global phylogenetic reconstruction of MTBC
beijing lineage population, 478
Mycobacterium 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, 640
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 methylcitrate 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 vaccae, 197

Mycolic acids
chemical structures of, 520
importance of, 523–524
loss of acid-fastness, 519, 529
Mycobacterium ulcerans, 673

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
memory, 107
M. tuberculosis infection, 12–14
Natural resistance-associated macrophage protein (Nramp), 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
extracellular M. tuberculosis in, 534–535
Neelesn, E., 520
Neisseria 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
Nicotinamide, 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, 533–534
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, macaque models, 171–172

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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 mycobacteria (NTM), 495
Nucleic acid amplification testing (NAAT), 390, 391, 392; see also GeneXpert MTB/RIF technology
Nutrient use of pathogens, see also
Auxotrophs
amino acid auxotrophies, 701–706
cofactor auxotrophies, 706–708
future perspectives, 708–710
lessons from auxotrophic strains, 701–708
lessons from metabolomics, 700–701
M. tuberculosis in host tissue, 701
M. tuberculosis in macrophages, 700–701

Offoxacin, drug resistance, 505
Oxford University, 200
Oxidative phosphorylation
growth reactivation, 301–302
M. tuberculosis, 295

P
Paabo, Svante, 467
Paleomicrobiology, 467
PAMP (pathogen-associated molecular pattern), 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, 125–127
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
drug 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, 672
physiology of M. tuberculosis, 653
predicted genes for in vivo 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, 671
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
killing 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, 277–284
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), 101–104
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), 358–359
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 morphology, 564–565, 567
Proteomics, 679, 683–684