Candida
and Candidiasis
SECOND EDITION
Candida and Candidiasis
SECOND EDITION

EDITED BY
Richard A. Calderone
Georgetown University Medical Center, Washington, DC
Cornelius J. Clancy
Department of Medicine, Infectious Diseases Division,
University of Pittsburgh, Pittsburgh, PA

WASHINGTON, DC
Cover: Candida albicans (red) and Staphylococcus aureus (green) biofilm stained with species-specific peptide nucleic acid (PNA)-FISH probes, demonstrating extensive adherence of S. aureus to the C. albicans hyphae. Courtesy Mary Ann Jabra-Rizk, University of Maryland, Baltimore.
Contents

Contributors / vii
Preface / xi

1 Candida: What Should Clinicians and Scientists Be Talking About? / 1
BRAD SPELLBERG, KIÈREN A. MARR, AND SCOTT G. FILLER

SECTION I
THE ORGANISMS, THEIR GENOMICS, AND VARIABILITY / 9

2 An Introduction to the Medically Important Candida Species / 11
GARY MORAN, DAVID COLEMAN, AND DEREK SULLIVAN

3 Comparative Genomics of Candida Species / 27
GERALDINE BUTLER

4 The Genetic Code of the Candida CTG Clade / 45
ANA CATARINA GOMES, GABRIELA R. MOURA, AND MANUEL A. S. SANTOS

5 Genome Instability and DNA Repair / 57
GERMÁN LARRIBA AND RICHARD A. CALDERONE

6 Switching and Mating / 75
DAVID R. SOLL

7 Detection and Clinical Significance of Variability among Candida Isolates / 91
LOIS L. HOYER

8 Cell Cycle and Growth Control in Candida Species / 101
CHERYL A. GALE AND JUDITH BERMAN

SECTION II
HOST-PATHOGEN INTERACTIONS (THE HOST) / 125

9 Immunology of Invasive Candidiasis / 127
LUIGINA ROMANI

10 Mucosal Immunity to Candida albicans / 137
PAUL L. FIDEL, JR., AND MAIRI C. NOVERR

11 Innate Immunity to Candida Infections / 155
MIHAI G. NETEA AND NEIL A. R. GOW

12 Vaccines and Passive Immunity against Candidiasis / 171
BRAD SPELLBERG, YUE FU, AND ASHRAF S. IBRAHIM

13 Salivary Histatins: Structure, Function, and Mechanisms of Antifungal Activity / 185
WOON SIK JANG AND MIRA EDGERTON

SECTION III
HOST-PATHOGEN INTERACTIONS (THE PATHOGEN) / 195

14 The Cell Wall: Glycoproteins, Remodeling, and Regulation / 197
CAROL MUNRO AND MATHIAS L. RICHARD
Contributors

DEEPU ALEX
Georgetown University Medical Center, Washington, DC 20057

DAVID R. ANDES
Department of Medicine, Medical Microbiology and Immunology, University of Wisconsin School of Medicine and Public Health, Madison, WI 53792

KATHERINE S. BARKER
Department of Clinical Pharmacy, College of Pharmacy, University of Tennessee Health Science Center, Children's Foundation Research Center, Le Bonheur Children's Hospital, Memphis, TN 38163

JUDITH BERMAN
Department of Genetics, Cell Biology and Development and Department of Microbiology, University of Minnesota, Minneapolis, MN 55455

ALISTAIR J. P. BROWN
School of Medical Sciences, University of Aberdeen, Institute of Medical Sciences, Foresterhill, Aberdeen AB25 2ZD, United Kingdom

GERALDINE BUTLER
School of Biomolecular and Biomedical Science, Conway Institute, University College Dublin, Belfield, Dublin 4, Ireland

RICHARD A. CALDERONE
Department of Microbiology and Epidemiology, Medical School, Georgetown University, Washington, DC 20057

YEISSA CHABRIER-ROSELLÓ
Department of Pediatrics, University of Rochester, School of Medicine and Dentistry, Box 850, 601 Elmwood Ave., Rochester, NY 14642

HUI CHEN
Georgetown University Medical Center, Washington, DC 20057

CORNELIUS J. CLANCY
Department of Medicine, University of Pittsburgh, Pittsburgh, PA 15261

DAVID COLEMAN
Microbiology Research Unit, Division of Oral Biosciences, Dublin Dental School & Hospital, Trinity College Dublin, University of Dublin, Dublin 2, Ireland

BRENDAN CORMACK
Department of Molecular Biology and Genetics, Johns Hopkins University School of Medicine, Baltimore, MD 21205

CHRISTOPHE D’ENFERT
Institut Pasteur, Unité Biologie et Pathogénicité Fongiques, Département Génomes et Génétique, and INRA, USC2019, F-75015 Paris, France

DANIEL J. DIEKEMA
Departments of Pathology and Medicine, University of Iowa Carver College of Medicine, Iowa City, IA 52242

MIRA EDGERTON
Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY 14214

PAUL L. FIDEL, JR.
Department of Oral and Craniofacial Biology, Louisiana State University Health Sciences Center, School of Dentistry, New Orleans, LA 70119

SCOTT G. FILLER
David Geffen School of Medicine at the University of California Los Angeles (UCLA), and Division of Infectious Diseases, Los Angeles Biomedical Research Institute, Harbor-UCLA Medical Center, Torrance, CA 90502

JONATHAN SEWELL FINKEL
Department of Biological Sciences, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, PA 15213
THOMAS H. FOSTER  
Department of Imaging Sciences, University of Rochester Medical Center, 601 Elmwood Ave., Box 648, Rochester, NY 14642

YUE FU  
David Geffen School of Medicine at UCLA, and Division of Infectious Diseases, Los Angeles Biomedical Research Institute, Harbor-UCLA Medical Center, Torrance, CA 90902

CHERYL A. GALE  
Department of Pediatrics and Department of Genetics, Cell Biology and Development, University of Minnesota, Minneapolis, MN 55455

FRANÇOISE GAY-ANDRIEU  
Georgetown University Medical Center, Washington, DC 20057, and Nantes Atlantique Universities, EA1155-IICiMed, Nantes, France

ANA CATARINA GOMES  
Genomics Unit, Biocant, BiocantPark–Parque Tecnologico de Cantanhede, 3060-197 Cantanhede, Portugal

NEIL A. R. GOW  
School of Medical Sciences, University of Aberdeen, Institute of Medical Sciences, Foresterhill, Aberdeen AB25 2ZD, United Kingdom

KEN HAYNES  
School of Biosciences, University of Exeter, Exeter, EX4 4QD, United Kingdom

DEBORAH A. HOGAN  
Department of Microbiology and Immunology, Dartmouth Medical School, Hanover, NH 03755

LOIS L. HOYER  
Department of Pathobiology, University of Illinois at Urbana-Champaign, Urbana, IL 61802

BERNHARD HUBE  
Department of Microbial Pathogenicity Mechanisms, Leibniz Institute for Natural Product Research and Infection Biology, Hans Knoell Institute Jena (HKI), Beutenbergstrasse 11a, D-07745 Jena, Germany

ASHRAF S. IBRAHIM  
David Geffen School of Medicine at UCLA, and Division of Infectious Diseases, Los Angeles Biomedical Research Institute, Harbor-UCLA Medical Center, Torrance, CA 90902

WOON SIK JANG  
Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY 14214

DIMITRIOS P. KONTOYIANNIS  
University of Houston College of Pharmacy and University of Texas M. D. Anderson Cancer Center, Houston, TX 77030

SUJATHA KRISHNAN  
Division of Infectious Diseases, University of Texas Medical School at Houston, Houston, TX 77030

DAMIAN KRYSAN  
Departments of Pediatrics and Microbiology/Immunology, University of Rochester, School of Medicine and Dentistry, Box 850, 601 Elmwood Ave., Rochester, NY 14642

ANUJ KUMAR  
Department of Molecular, Cellular, and Developmental Biology, Life Sciences Institute, 210 Washburn Avenue, Ann Arbor, MI 48109

GERMÁN LARRIBA  
Área Microbiología, Edificio Biológicas, F. Ciencias, Universidad de Extremadura, 06006 Badajoz, Spain

MÉLANIE LEGRAND  
Institut Pasteur, Unité Biologie et Pathogénicité Fongiques, Département Génomes et Génétique, and INRA, USC2019, F-75015 Paris, France

RUSSELL E. LEWIS  
University of Houston College of Pharmacy and University of Texas M. D. Anderson Cancer Center, Houston, TX 77030

DONGMEI LI  
Georgetown University Medical Center, Washington, DC 20057

MICHAEL C. LORENZ  
Department of Microbiology and Molecular Genetics, The University of Texas Health Science Center, 6431 Fannin St., Houston, TX 77030

KIEREN A. MARR  
Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, MD 21205

JARED MAY  
Georgetown University Medical Center, Washington, DC 20057

FRANCOIS MAYER  
Department of Microbial Pathogenicity Mechanisms, Leibniz Institute for Natural Product Research and Infection Biology, Hans Knoell Institute Jena (HKI), Beutenbergstrasse 11a, D-07745 Jena, Germany

AARON P. MITCHELL  
Department of Biological Sciences, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, PA 15213

SOUMYA MITRA  
Department of Imaging Sciences, University of Rochester Medical Center, 601 Elmwood Ave., Box 648, Rochester, NY 14642

A. BRIAN MOCHON  
Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at UCLA, 10833 Le Conte Ave., Brentwood Annex, Los Angeles, CA 90095-1732

GARY MORAN  
Microbiology Research Unit, Division of Oral Biosciences, Dublin Dental School & Hospital, Trinity College Dublin, University of Dublin, Dublin 2, Ireland
GABRIELA R. MOURA
Department of Biology and CESAM, University of Aveiro, Campus de Santiago, 3810-193 Aveiro, Portugal

CAROL MUNRO
Aberdeen Fungal Group, University of Aberdeen, School of Medical Sciences, Institute of Medical Sciences, Aberdeen, AB25 2ZD, United Kingdom

MIHAI G. NETEA
Department of Medicine and Nijmegen University Centre for Infectious Diseases, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

JENIEL E. NETT
Department of Medicine, Medical Microbiology and Immunology, University of Wisconsin School of Medicine and Public Health, Madison, WI 53792

M. HONG NGUYEN
Department of Medicine, University of Pittsburgh, Pittsburgh, PA 15261

MAIRI C. NOVERR
Department of Oral and Craniofacial Biology, Louisiana State University Health Sciences Center, School of Dentistry, New Orleans, LA 70119

LUIS OSTROSKY-ZEICHNER
Division of Infectious Diseases, University of Texas Medical School at Houston, Houston, TX 77030

MICHAEL A. PFALLER
Department of Pathology, University of Iowa Carver College of Medicine, and Department of Epidemiology, University of Iowa College of Public Health, Iowa City, IA 52242

AMY E. PIISPANEN
Department of Microbiology and Immunology, Dartmouth Medical School, Hanover, NH 03755

JANET QUINN
Institute for Cell and Molecular Biosciences, Newcastle University, Newcastle upon Tyne, NE2 4HH, United Kingdom

SANJAY G. REVANKAR
Division of Infectious Diseases, Wayne State University School of Medicine, Detroit, MI 48201

MATHIAS L. RICHARD
MICrobiologie de l’ALimentation au service de la Santé, Equipe “Virulence et Infection Fongique,” INRA UMR1319 AgroParisTech, 78850 Thiverval Grignon, France

P. DAVID ROGERS
Department of Clinical Pharmacy, College of Pharmacy, University of Tennessee Health Science Center, Children’s Foundation Research Center, Le Bonheur Children’s Hospital, Memphis, TN 38163

LUIGINA ROMANI
Microbiology Section, Department of Experimental Medicine and Biochemical Sciences, University of Perugia, Via del Giochietto, 06122 Perugia, Italy

MANUEL A. S. SANTOS
Department of Biology and CESAM, University of Aveiro, Campus de Santiago, 3810-193 Aveiro, Portugal

JACK D. SOBEL
Division of Infectious Diseases, Wayne State University School of Medicine, Detroit, MI 48201

DAVID R. SOLL
Department of Biology, The University of Iowa, Iowa City, IA 52242

BRAD SPELBERG
Division of General Internal Medicine, Los Angeles Biomedical Research Institute at Harbor-University of California Los Angeles (UCLA) Medical Center, and David Geffen School of Medicine at UCLA, Torrance, CA 90502

BRAM STYNNEN
VIB Department of Molecular Microbiology, K.U. Leuven Laboratory of Molecular Cell Biology, Institute of Botany and Microbiology, Kasteelpark Arenberg 31, Postbus 2438, B-3001 Leuven, Belgium

DEREK SULLIVAN
Microbiology Research Unit, Division of Oral Biosciences, Dublin Dental School & Hospital, Trinity College Dublin, University of Dublin, Dublin 2, Ireland

NUO SUN
Georgetown University Medical Center, Washington, DC 20057

HÉLÈNE TOURNU
VIB Department of Molecular Microbiology, K.U. Leuven Laboratory of Molecular Cell Biology, Institute of Botany and Microbiology, Kasteelpark Arenberg 31, Postbus 2438, B-3001 Leuven, Belgium

PATRICK VAN DIJCK
VIB Department of Molecular Microbiology, K.U. Leuven Laboratory of Molecular Cell Biology, Institute of Botany and Microbiology, Kasteelpark Arenberg 31, Postbus 2438, B-3001 Leuven, Belgium

SLAVENA VYLKOVA
Department of Microbiology and Molecular Genetics, The University of Texas Health Science Center, 6431 Fannin St., Houston, TX 77030

DUNCAN WILSON
Department of Microbial Pathogenicity Mechanisms, Leibniz Institute for Natural Product Research and Infection Biology, Hans Knoell Institute Jena (HKI), Beutenbergstrasse 11a, D-07745 Jena, Germany

REBECCA ZORDAN
Department of Molecular Biology and Genetics, Johns Hopkins University School of Medicine, Baltimore, MD 21205
Preface

Over the past three decades, as one of the editors himself has witnessed, the experimental approaches and desired outcomes in the study of Candida spp. and the infections they cause naturally have changed. The overwhelming focus now is in molecular biology at a number of levels of research, such as genome comparisons and assessing virulence factors and host responses, as well as the promise of translational research into new antifungal drug discovery, diagnostics, and vaccines. The Candida community has been fortunate to witness the sharing of mutant libraries, strains, techniques, vectors, and probes; collaboration among laboratories seems to be increasing, a development that will be needed to solve the increasing complexity of research that requires interdisciplinary and “systems biology” approaches. Through genomics, we can now identify similarities and differences among Candida species, other human pathogenic and nonpathogenic fungi, and nonfungal species. “Omic” studies and databases are especially useful in designing new targets for drug discovery, but their application extends beyond this goal, to showing why pathogens are pathogens. That knowledge is in many cases at our fingertips.

This is the fourth in a series of volumes on Candida and candidiasis (candidosis) and the first that is coedited to reflect a more thorough treatise of human disease, treatment, and expectations in health care delivery. Each of the preceding books emphasized different things. Candida and Candidosis (University Park Press, Baltimore, MD, 1979) and Candida and Candidosis: a Review and Bibliography, 2nd Ed. (Bailliére Tindall, Oxford, U.K., 1988), both written by Frank C. Odds, focused on the species that cause candidiasis, including their morphogenesis, virulence, and structure; the first of these books included special emphasis on the types of candidiasis. Dr. Odds gave us meaning and direction, a unification to address new problems that existed. The third book, Candida and Candidiasis, edited by Richard A. Calderone, was published in 2002 by ASM Press.

The present book, Candida and Candidiasis, 2nd Edition, is a natural extension of the previous three. In this volume are emphasized genomes and variability, host-pathogen interactions, antifungal resistance and new drug discovery, and evolving diagnostics. Variability among Candida species is described with regard to genomes, molecular adaptation to the external milieu whether in a host or in vitro, and sexuality of Candida albicans; we have learned how variability contributes to resistance to triazole drugs. Traditional areas of interest remain. For example, research in morphogenesis and the cell cycle (and, ultimately, growth) has provided new heights of understanding. Major advances in immune responses are also covered in this volume. Chapters discuss vaccine candidates in the community and how host responses may be useful in diagnosis of blood-borne candidiasis. Virulence attributes are now placed in the context of gene families. While the cell wall is critically included, it is represented more now as an entity that interacts with the innate host system. Broad representation of specific pieces of the cell is included, ultimately reflecting the current interests among like scientists. Biofilms, either mixed-species or monospecific, tell us much about the survival of the fungus in the host.

Discovery has continued, and translational research is moving toward attainable goals. But have we made a difference in increasing awareness of public health issues in candidiasis? An answer to that question is not easily discerned. Candidiasis is the third most frequent hospital-acquired infection. But who knows that fact, beyond the candidiasis community? In reality, new drug discovery features little more than remodeled old drugs. The search for that magic bullet that can kill all 100+ fungal pathogens still survives, at least partially, but this objective lacks sense and is not part of the paradigm in antibacterial drug discovery.

We must lose the notion that we cannot do better. The greatest risk for the next decade is that candidiasis research will become lost in the current economic times, at least in the United States. Emphasis on other important, nonfungal pathogens has overwhelmed the goal of controlling candidiasis, cryptococcosis, aspergillosis, the endemic mycoses, and dermatophytosis in public health. Solutions to this dilemma are not easy. To a much broader extent, we in this field must educate the public by choosing leaders among us, especially physician-scientists, who can testify to the importance of these diseases. These leaders should be called on to seize the interest of “think tanks” and other groups that influence policy makers. But also, each of us needs to remind our professional societies, the major advocates of microbiology, that this field demands equal attention with all the other pathogenic microorganisms, whether in newsletters, public education, or influence peddling.

Even within our discipline, we cannot keep up with everything. Both of us marveled at the outstanding research presented at the most recent “Candida and Candidiasis”
conference, held in Miami Beach, Florida, in March of 2010. That message should continue to be carried to the public, in a language that conveys the importance of these diseases. For this reason, just as the present volume offers the most current information in this critical field, new books on *Candida* and candidiasis should continue to present new discoveries and developments.

RICHARD A. CALDERONE
CORNELIUS J. CLANCY
Index

A
a/α and α/α cells, in mating, 75–84
ABC transporters, in drug resistance, 66
Abdomen, candidiasis in, 433–434
Abscess, brain, 434
Accidental infections, versus opportunistic infections, 1–2
Ace2 protein
in biofilm formation, 301, 306
in carbon metabolism, 335
in cell cycle, 117
Acetic acid, stress response to, 228–229
N-Acetylglucosamine
in chitin synthesis, 197
in switching, 81, 83
Acid stress response, 228–229
Acinetobacter baumannii,
Candida albicans interactions with, 319–320
Aco1 protein
in kidney lesions, 290
in liver lesions, 292
Acs1 protein, in kidney lesions, 290
Actin, in cell cycle, 106–107
Active immunization, 5, 175–178
Ada2 protein, in multidrug resistance, 410
Adaptive immunity
activation of, 156–157
in gastrointestinal candidiasis, 141
Adh proteins
in biofilm formation, 301, 307–308
in morphogenesis, 334
Adhesins, 243–259
in biofilms, 249–250, 303–304
in Candida albicans, 245–250
in Candida glabrata, 250–253
cell wall structure and, 243
for endothelial cell invasion, 289–290
evolution of, 254–255
functions of, 243
in Saccharomyces cerevisiae, 253–254
structure of, 243–254
types of, 270–272
Adhesion
Als protein family in, 31–32
cell-cell, in biofilm formation, 304–306
Adherence molecules, in oropharyngeal candidiasis, 139
Afbgt1 protein, in cell wall, 199
Affirm test, for mucosal candidiasis, 424
Agglutinin-like sequence genes, 15–16, 30–32
Ahp1 protein, in histatin response, 190
AI-2 protein, in fungal-bacterial interactions, 320
AIDS, see HIV/AIDS
AIRE gene, polymorphisms of, 161
Albacezole, 396
Alkylolation, reversal of, 62
O-Alkylguanine-DNA alkyltransferase II, in DNA repair, 66
Als protein family, 31–32
adherence properties of, 245–247, 270–272
amyloid formation and, 246–247
in biofilm formation, 301, 304–305
Candida albicans, 15–88, 245–247
in cell wall, 206, 208, 210
in colonization, 286
in dissemination, 289–290
evolution of, 254–255
in invasion, 288
iron acquisition and, 246
in kidney lesions, 291
in liver lesions, 293
regulation of, 247
strain variation due to, 94, 96
structures of, 200, 245–247
in vaccine development, 175–178
Alternative oxidase pathway, for respiration, 331
Ambiguous-intermediate theory, of codon reassignment, 46–48
Amino acids
formation of, in biofilm formation, 307
starvation of, 261
Aminocandin, 396
Anfotericin B
for candidemia, 30–33
for cardiovascular candidiasis, 343–345
for central nervous system candidiasis, 343
chemical structure of, 348
clinical uses of, 350–351
cochleate formulation of, 396
dosing of, 350
drug-drug interactions of, 350
for hepatosplenic candidiasis, 433
lipid formulations of, 346–348
mechanism of action of, 347
for mucosal candidiasis, 421
for osteomyelitis, 435
for peritonitis, 433–434
pharmacodynamics of, 347–348
pharmacokinetics of, 347, 350
resistance to, 310, 403
spectrum of activity of, 347, 349
toxicity of, 348, 350
Amphotericin B deoxycholate
advantages of, 346
disadvantages of, 346
for endophthalmitis, 433
fluconazole with, 3
Amso1 protein, in dissemination, 290
Amyloid formation, Als proteins and, 246–247
Anuploidy
genetic instability and, 58–60
in strain variation, 94
Angular cheilitis, 12, 420
Anidulafungin, 358–360
advantages of, 346
for candidemia, 343–345
chemical structure of, 349
disadvantages of, 346
dosing of, 351
drug-drug interactions of, 353
for mucosal candidiasis, 421
spectrum of activity of, 349
susceptibility to, 465–466, 468
Animal models
for adhesion action, 2
Candida imaging in, 501–503
for disseminated candidiasis, 2, 4, 95–96
for gastrointestinal candidiasis, 141–142
for oropharyngeal candidiasis, 138
for vulvovaginal candidiasis, 143, 145
Animals, strain variation found in, 95
Annexin, in oropharyngeal candidiasis, 139
Anp1 protein, in DNA repair, 62
Antibiotics, vulvovaginal candidiasis due to, 172, 422
Antifungal drugs, see also specific drug classes (polyenes) and individual drug names
for Candida albicans, 16
clinical characteristics of, 345
Antifungal drugs (continued)
discovery of
approaches to, 391
current developments in, 395–396
genomic approaches to, 394–395
global candidiasis incidence and,
387–388
myths about, 396–397
traditional approaches to, 391–394
treatment difficulties and, 388–391
for disseminated candidiasis, 3–5, 9
economic costs of, 390–391
historical overview of, 345
mitochondria as targets of, 335–336
pharmacodynamics of, 346–347
pharmacokinetics of, 346–347
pharmacology of, 345
preemptive, 44
susceptibility to, See Drug resistance;
Susceptibility
Antigen(s), cell surface, protein microarray
for, 489–496
Antigen-presenting cells, in innate immu-
nity, 159
Antiglucan antibodies, for vaccines,
174–175
Antihistamine antibody, 435
Antihistamine antibodies, for vaccines,
175
Antimannan antibodies as biomarkers, 445
for vaccines, 174
Antimicrobial peptides, in oropharyngeal
Antioxidants, 232–233
Antimycin (complex III), 331–336
Antimicrobial peptides, in oropharyngeal
Antigen(s), cell surface, protein microarray
infection due to, health care costs of,
390
meiosis in, 34
Aspergillus species, glycoproteins of, 214
Aspergillus nidulans
azoles for, 354
farnesol effects on, 323
gene regulatory instability in, 58
Aspergillus terreus, azoles for, 354
Atg proteins, in nutrient starvation, 268
ATP, in histatin action, 190
ATP-binding cassette transporters, in mul-
drug resistance, 404
Autoimmune, 265
Azp proteins, adhesive properties of, 253
Azoles, 352–358; see also individual drugs
chemical of, 354
clinical uses of, 357–358
drug–drug interactions of, 357
mechanism of action of, 356
monitoring of, 356
new, 396
pharmacodynamics of, 356–357
pharmacokinetics of, 354–356
resistance to
generic instability and, 65–67
multidrug, 404–412
spectrum of activity of, 354
targeting mitochondria, 335–336
toxicity of, 357
B
B6.1 antibody, for vaccines, 174
B lymphocytes, in immune response,
156–157
Bacillus subtilis
adhesins in, 270–272
AP-1 family, in stress response, 233–234
Apoptosis
in immunity modulation, 270
of macrophages, 156
Apurinic/apurinic sites, in DNA repair,
62
Arabidopsis thaliana, codon reassignment in,
46
Arf1 protein, in general stress response, 229
ARTEMIS Surveillance Program, 16,
483–487
Arthritis, septic, 435
ARTEMIS Surveillance Program, 142
Arthritus, septic, 435
Asparyl proteases, in cell wall, 202
Aspergillus
azoles for, 354
echinocandins for, 360
fluconazole for, 352
aspartyl proteases, in cell wall, 202
Aspergillus fumigatus, azoles for, 349
Aspergillus nidulans, azoles for, 354
carbohydrate-active enzymes of, 199
cell wall of, glycoproteins of, 211, 213
farnesol effects on, 323
histatin action against, 185
infections due to, health care costs of,
390
meiosis in, 34
Aspergillus glabrata, glycoproteins of, 214
Aspergillus nidulans
azoles for, 354
farnesol effects on, 323
gene regulatory instability in, 58
Aspergillus terreus, azoles for, 354
Atg proteins, in nutrient starvation, 268
ATP, in histatin action, 190
Azoles, 352–358; see also individual drugs
chemical of, 354
clinical uses of, 357–358
drug–drug interactions of, 357
mechanism of action of, 356
monitoring of, 356
new, 396
pharmacodynamics of, 356–357
pharmacokinetics of, 354–356
resistance to
generic instability and, 65–67
multidrug, 404–412
spectrum of activity of, 354
targeting mitochondria, 335–336
toxicity of, 357
azoles for, 354
polyenes for, 347
Blood cultures, disadvantages of, 2–3
Bloodstream, organism spread and escape
by, 289–290
Bone infections, 435
Brain, candidiasis of, 434
Break-induced replication, 28, 60–61
Broad Institute database, 37
Bud proteins, in cell cycle, 106–107
Bud site selection, 104, 106
Burkholderia cenocepacia, Candida albicans
interactions with, 320
Burkholderia cepacia, Candida albicans inter-
actions with, 319–320
CaAda2 protein, in multidrug resistance, 410
Cables, in cell cycle, 106–107
CaCrm1 protein, in multidrug resistance,
410
CaCzr1 protein, in multidrug resistance,
410–411
Cadherins, in oropharyngeal candidiasis,
139
Cadmium, stress response to, 229
CaFcr proteins, in multidrug resistance, 411
Cag1 protein in mating, 79, 84, 85
in reproduction, 75
Calcineurin
in immunity modulation, 270
in cell wall, 198
CaN Crz1 protein, in multidrug resistance,
404
Benzoic acid, stress response to, 228–229
Beta glucan test, 3
Bifidobacterium, in gastrointestinal tract,
142
Bifidobacterium infantis, in, 142
Bifidobacterium animalis, in, 140
Bifidobacterium infantis, in, 142
Bifidobacterium animalis, in, 140
Candida
imaging of, in animals, 501–503
number of species in, 11
phylogeny of, 27
stress response in, 225–242
taxonomy of, 11
Candida africana, 92–93
Candida albicans, 14–16
adaptive immune response to, 156–157
adhesins of, 245–250, 270–272
adjuvant immunotherapy for, 162–163
antifungal susceptibility of, 16, 161–163,
349–350, 465–469
azoles for, 354
in bacteria-fungi populations
disseminated infections due to, 318–319
drug resistance and, 317–318
farnesol effects on, 324
gram-negative bacteria and, 319–320
gram-positive bacteria and, 320–321
in oral environment, 319
in biofilms, 249–250, 299–315, 317–318
versus C. dubliniensis, 33
cell cycle in
checkpoints of, 119–120
perturbation of, 119
stationary phase of, 119
cell wall of, 157–158
glycoproteins of, 200–214
Candida holmsii
- antifungal susceptibility of, 466
- distribution of, 453
Candida humicola
- antifungal susceptibility of, 465, 466
- distribution of, 453
Candida inconspicua, 18
- antifungal susceptibility of, 465–467
- distribution of, 453, 461
Candida intermedia
- antifungal susceptibility of, 466–467
- distribution of, 453
Candida kefyr, 18
- antifungal susceptibility of, 466–469
- distribution of, 453
- resistance in, 375
Candida krusei
- antifungal susceptibility of, 349–350,
  465–469
- description of, 18
- distribution of, 453–460
- echinocandins for, 359
- flucytosine for, 352
- infections due to, see Candida krusei
  infections
- MLST methods for, 94
- polyenes for, 347
- quorum sensing in, 322
- related to CTG clade, 11
- resistance in, 373, 375–376, 379, 389, 403
  - vaccines for, 175
Candida krusei infections, 18
- animal models for, 2
- candidemia, 431–432
- invasive, 127, 131–132
- mucosal, 425
- oropharyngeal, 419
Candida lambica
- antifungal susceptibility of, 465–467
- distribution of, 453
Candida lipolytica, 18
- antifungal susceptibility of, 466–467,
  469
- distribution of, 453
- meiosis in, 34–35
- mitochondria of, 331
Candida longiseta, 11
- antifungal susceptibility of, 349–350,
  465–469
- azoles for, 354
- cell wall of, glycoproteins of, 203–208
  in CTG clade, 10
- description of, 18
- distribution of, 453–455, 458, 461
- flucytosine for, 352
- gene families of, 31–32
- genome of, 27, 31–32, 34–35, 37
- horizontal gene transfer to, 37
- infections due to, 18
- mating type-like locus of, 34
- mitochondria of, 338
- phylogeny of, 27
- repetitive DNA elements in, 29–30
- resistance in, 375, 377, 389
Candida marinum
- antifungal susceptibility of, 465, 466
  in biofilms, 299, 304
- azoles for, 354
- cell wall of, glycoproteins of, 203–208
  in CTG clade, 11
- description of, 17
- distribution of, 17, 453–460
- echinocandins for, 359
- flucytosine for, 352
- gene families of, 31–33
- genome of, 27, 29–34, 36–37
- groups of, 92
- horizontal gene transfer to, 36–37
- immunity modulation and, 270
- infections due to, see Candida parapsilosis
  infections
- mating type-like locus of, 34
- mitochondria of, 331–333, 335, 338
- phylogeny of, 31–32
- polyenes for, 347
- quorum sensing in, 322
- repetitive DNA elements in, 30
- resistance in, 375–376, 378, 389
- single nucleotide polymorphisms of, 27
- strains of, 17
- vaccines for, 175
- virulence of, 17
Candida parapsilosis infections, 17
- candidemia, 431–432
- incidence of, 388
- oropharyngeal, 419
Candida selaii
- antifungal susceptibility of, 466
- distribution of, 453
- mitochondria of, 331
Candida subhominis
- antifungal susceptibility of, 465–468
- azoles for, 354
- echinocandins for, 359
- flucytosine for, 352
- gene families of, 31–33
- genome of, 27, 29–31, 37
- horizontal gene transfer to, 37
- immunity modulation and, 270
- infections due to, see Candida tropicalis
  infections
- mating type-like locus of, 34
- mitochondria of, 331
- resistance in, 375–376, 378, 384–405
- single nucleotide polymorphisms of, 27
- switching in, 77–78
- vaccines for, 175, 176
Candida tropicalis infections, 17–18
- candidemia, 431–432
- incidence of, 388
- oropharyngeal, 419
Candida utilis
- antifungal susceptibility of, 465–468
- azoles for, 354
- in biofilms, 299, 304
- cell wall of, glycoproteins of, 203–208
  in CTG clade, 11
- description of, 17
- distribution of, 17, 453–460
- echinocandins for, 359
- flucytosine for, 352
- gene families of, 31–33
- genome of, 27, 29–34, 36–37
- groups of, 92
- horizontal gene transfer to, 36–37
- immunity modulation and, 270
- infections due to, see Candida parapsilosis
  infections
- mating type-like locus of, 34
- mitochondria of, 331–333, 335, 338
- phylogeny of, 31–32
- polyenes for, 347
- quorum sensing in, 322
- repetitive DNA elements in, 30
- resistance in, 375–376, 378, 389
- single nucleotide polymorphisms of, 27
- strains of, 17
- vaccines for, 175
- virulence of, 17
Candida valida
- antifungal susceptibility of, 466
- distribution of, 453
- mitochondria of, 331
Candida valida
- antifungal susceptibility of, 466
- distribution of, 453
- mitochondria of, 331
Candida subhominis
- antifungal susceptibility of, 465–468
- azoles for, 354
- echinocandins for, 359
- flucytosine for, 352
- gene families of, 31–33
- genome of, 27, 29–31, 37
- horizontal gene transfer to, 37
- immunity modulation and, 270
- infections due to, see Candida tropicalis
  infections
- mating type-like locus of, 34
- mitochondria of, 331
- resistance in, 375–376, 378, 384–405
- single nucleotide polymorphisms of, 27
- switching in, 77–78
- vaccines for, 175, 176
Candida tropicalis infections, 17–18
- candidemia, 431–432
- incidence of, 388
- oropharyngeal, 419
Index
CsA proteins
in biofilm formation, 301, 305
in cell wall, 202, 205–206, 210
in liver lesions, 293
CsbE protein
in biofilm formation, 301
in mating, 84
CTA2 gene family, 33
Cta proteins
in general stress response, 230
in heavy metal stress response, 229
in kidney lesions, 291
in oxidative stress response, 277, 278
in stress response, 234–235
Ctrl protein, in carbon starvation, 268
CTG clade
CUG codon reassignment in, 46–48
genetic code of, 45–55
genomes of, 27–43
members of, 11, 27; see also specific members
CtsI protein, in liver lesions, 293
Cys3 protein, in heavy metal stress re-
Cyr1 protein, in cell cycle, 107
Cyclin(s), 109–119
Cyanide and azide (complex IV), in respi-
CUN codons, reassignment of, 48
Candida albicans
ambiguity of, 49, 51
Candida albicans, 49–54
reassignment of, 46–48
usage of, 51–54
CUN codons, reassignment of, 48
Cyanide and azide (complex IV), in respi-
Cyclin(s), 109–119
G, 110, 117
genes for, 111
hypha-specific, 117–118
mitotic, 111, 116–117
Pcl, 118–119
regulation of, 117–118
Cyclin-dependent kinases, in cell cycle, 101
Cyr1 protein, in cell cycle, 107
Cys3 protein, in heavy metal stress re-
Cystic fibrosis, polymicrobial infections in,
Cytokines
in gastrointestinal candidiasis, 141
in immune response, 156–157
in oropharyngeal candidiasis, 139
in resistance, 128
Cytokinesis, in cell cycle, 108–109
Cytoskeletal cables, in cell cycle, 106–107
Ctf1 protein
in biofilm formation, 301, 306, 309
in mating, 80
in switching, 82–83

D
Danish Center for Biological Sequence
Analysis, glycoprotein data in, 201–202, 208
Databases, genome, 36–38
Daughter cells
in mating, 76–77
polarized, 107
DC-SIGN
in immune response, 156, 157, 160
in invasive candidiasis, 129–130
Dcw1 protein, in cell wall, 203
Ddr48 protein, in histatin response, 190
Deharyomyces harseii, 27
codon reassignment in, 46
gene families of, 31
genome of, 30–31, 34, 36–37
horizontal gene transfer to, 36–37
matting type-like locus of, 34
mitochondria of, 338
replicative DNA elements in, 30
Debridement, for osteomyelitis, 435
Dectin(s)
gene polymorphisms in, 162
in immune response, 156, 158–162
in invasive candidiasis, 129–130
Dectin-1 defects
as candidiasis risk factor, 2
in vulvovaginal candidiasis, 145
Deep-organ infections, 432–436
structural, 433
organ infections with, 290–294
for gastrointestinal, 433–434
hepatosplenic, 433
intra-abdominal, 433–434
kidney, 291–294
liver, 291–294
osteomyelitis, 345
pneumonia, 436
septic arthritis, 435
urinary tract, 435–436
“De-escalation” antifungal therapy, for dis-
seminated candidiasis, 3
Defensins, in oropharyngeal candidiasis,
Dendritic cells
“De-escalation” antifungal therapy, for dis-
seminated candidiasis, 3
Dimension, Candida albicans, 14–15
Diplloid sequence type, in genetic instabil-
ity, 57–58
Disseminated candidiasis
animal models for, 2, 4, 95–96
antifungal agents for, 3–4
Candida tropicalis, 17–18
chronic, 128, 433
diagnostic tests for, 2–3
epidemiology of, 171–172
gene expression in, 289–294
gene polymorphisms in, 161–162
inflammatory response in, 128
in kidney lesions, 291
in liver lesions, 293
in prenatal candidiasis, 140
organ infections with, 290–294
origin of, 5
polymerizable, 318–319
risk factors for, 1–2, 171–172
strain variation in, 85
DNA, extracellular, in biofilm formation, 308
DNA damage
repair of, 60–65, 111–113
reversal of, 62–65
DNA elements, repetitive, 29–30
DNA repair
genes for, 111–113
genetic instability and, 60–65
Dose fractionation, 346–347
Dot proteins, in oxidative stress response, 278
Double-strand break repair, 63–64
Drug resistance, 373–375; see also individual
Drugs, resistance to acquired, 378
in biofilms, 309–310, 317–318
drug discovery and, 388–389
genetic instability in, 65–67
intrinsic, 376–378
invasive candidiasis mortality and, 129–130
invasive candidiasis, 129–130
multi-, see Multidrug resistance
pathogen virulence and, 375–376
strain variation in, 96–97
susceptibility testing and, 378–379
temporal trends in, 376–378
treatment failure due to, 378
Dur1 protein, in nutrient starvation, 268
Dur3 protein, in histatin transport, 188
DYRK kinase, in biofilm formation, 306

E
Eap1 protein
adhesive properties of, 248–249
in biofilms, 249–250, 301, 305
in cell wall, 210
in mating, 84
structure of, 248–249
Ecf1 protein
in biofilm formation, 301
in cell cycle, 119
in colonization, 284
in invasion, 288
in kidney lesions, 291
in mating, 79
Ece proteins, in mating, 80
Echinocandins, 358–360; see also individual
new, 396
resistance to, 65–67, 376–378
Ecm proteins, in cell wall, 202, 203
Economic costs, of candidiasis, 390–391
EFG1 gene, Candida albicans, 14
Efgl protein
in Abs regulation, 247
in biofilm formation, 301, 304, 306
in cell cycle, 117–118
in colonization, 284
in switching, 82–83
Efg proteins, in cell cycle, 119
Efh proteins, in colonization, 284
Efungimab, 3, 175
Electron transport chain complexes, 331
Empirical therapy, for disseminated candidi-
Era proteins, in kidney lesions, 291
Endocarditis, 434–435
Endocytosis, 272
Endonucleases, in DNA repair, 63
Endophalmonics, 432–433
Endothelial cells
adhesion to, 289
Als protein adhesion to, 245–246
Candida interactions with, 262, 289–290
dissemination through, 289–290
Epa adhesion to, 251
Enterococcus faecalis, Candida albicans inter-
actions with, 318
Enterococcus faecalis, Candida albicans inter-

Epa proteins
adherence properties of, 270–272
binding specificities of, 251
in biofilm formation, 303
of Candida glabrata, 16, 250–253
functions of, 250–251
regulation of, 251–252
structures of, 244, 250–251
Epithelial cells
Als protein adhesion to, 245–246
Candida interactions with, 262
Epa adhesion to, 251
invasion of, 288–289
oral, colonization of, 285–287
in oropharyngeal candidiasis, 139
vaginal, colonization of, 287
in vulvovaginal candidiasis, 144
Erg proteins
in dissemination, 290
in resistance, 65–67, 309, 405, 408
in strain variation, 97
Erythematous oropharyngeal candidiasis, 139
Erg proteins
in carbon metabolism, 336
Erg proteins
in mating, 80, 85
in biofilm formation, 304–306
in multidrug resistance, 411
in biofilm formation, 308
in invasion, 288
Fbp1 protein, in carbon metabolism, 336
Efp proteins
in liver lesions, 293
Efp proteins
in carbon starvation, 268
in invasion, 288
Fps1 protein, in osmotic stress response, 227
Fracactin, in respiration, 334
Fre proteins
in kidney lesions, 291
in liver lesions, 293
Frg23 protein, in mating, 80
Fro proteins, in cell wall, 293
in drug resistance, 376
Flo proteins
adhesive properties of, 253–254
in biofilm formation, 301
evolution of, 254–255
Flu1 protein, in multidrug resistance, 404
Flucytosine
advantages of, 346
for Candida albicans, 16
for candidemia, 431–432
for cardiovascular candidiasis, 434–435
for central nervous system candidiasis, 434
chemical structure of, 348
clinical uses of, 357–358
disadvantages of, 346
for disseminated candidiasis, 394
for endophthalmitis, 433
for HIV, 378
for hepatitis, 337
for invasive candidiasis, 388–389
for mucosal candidiasis, 421
for osteomyelitis, 435
for peritonitis, 433–434
pharmacodynamics of, 356
pharmacokinetics of, 355
resistance to, 336–337, 375–378,
888–389, 404–412
spectrum of activity of, 349, 354
susceptibility to, 465–468
for vulvovaginal candidiasis, 424
Fluconazole-amphotericin B deoxycholate,
advantages of, 346
for central nervous system candidiasis, 349
for endophthalmitis, 433
for HIV, 378
for hepatitis, 337
for invasive candidiasis, 388–389
for mucosal candidiasis, 421
for osteomyelitis, 435
for peritonitis, 433–434
pharmacodynamics of, 356
pharmacokinetics of, 355
resistance to, 336–337, 375–378,
888–389, 404–412
spectrum of activity of, 349, 354
susceptibility to, 465–468
for vulvovaginal candidiasis, 424
Fluconazole-ampicillin B deoxycholate,
advantages of, 346
for central nervous system candidiasis, 349
for endophthalmitis, 433
for HIV, 378
for hepatitis, 337
for invasive candidiasis, 388–389
for mucosal candidiasis, 421
for osteomyelitis, 435
for peritonitis, 433–434
pharmacodynamics of, 356
pharmacokinetics of, 355
resistance to, 336–337, 375–378,
888–389, 404–412
spectrum of activity of, 349, 354
susceptibility to, 465–468
for vulvovaginal candidiasis, 424
Fluconazole-ampicillin B deoxycholate,
advantages of, 346
for central nervous system candidiasis, 349
for endophthalmitis, 433
for HIV, 378
for hepatitis, 337
for invasive candidiasis, 388–389
for mucosal candidiasis, 421
for osteomyelitis, 435
for peritonitis, 433–434
pharmacodynamics of, 356
pharmacokinetics of, 355
resistance to, 336–337, 375–378,
888–389, 404–412
spectrum of activity of, 349, 354
susceptibility to, 465–468
for vulvovaginal candidiasis, 424
Galectin(s)
in immune response, 160
invasive candidiasis, 129–130
Galectin-3 receptor, in immune response, 157
Gas proteins, in cell wall, 202, 206, 211, 215
Gastrointestinal candidiasis, 433–434
dissemination of, 141
immunity to, 140–142
Gastrointestinal tract
Candida in, 12
commensalism in, 283–285
surgery on, as candidiasis risk factor, 1–2
Gca proteins, in biofilm formation, 301,
307–308
Gen4 protein, in biofilm formation, 307
Gene families, 30–33
Gene Ontology, in drug development, 393
Gene transfer, horizontal, 35–37
General stress response, 227–230
Gene families
in multidrug resistance, 410
Extracellular DNA, in biofilm formation, 308
Extracellular matrix, in biofilm formation, 306–308
Eye, candidiasis of, 432–433
F
Far proteins, in mating, 79–80
Farneos
as biofilm inhibitor, 302
in cell cycle inhibition, 119
in quorum sensing, 308–309, 322–324
Fbp1 protein, in carbon metabolism, 336
Fcr proteins
in biofilm formation, 308
in multidrug resistance, 411
Ferritin, 293
Fet proteins, in liver lesions, 293
Filamentation, 323
in biofilm formation, 304–306
in mating, 80, 85
mitochondria and, 334
Filaments, 334
Fingerprinting, for Candida strain variation, 92, 94
Fitness test, in drug development, 394–395
Fkh2 protein
in cell cycle, 119
in colonization, 286
Fks proteins
in cell wall, 199
in drug resistance, 376
Flavohemoproteins, in nitrosative stress re-
sponse, 228
Glycerol-3-phosphatase, in osmotic stress response, 227
Glycerol-3-phosphate dehydrogenase, in osmotic stress response, 227
Glycolases, in DNA repair, 62
Glycolysis
mitochondria in, 336–337
in morphogenesis, 334
Glycoproteins, cell wall, 200–214
anchoring processes of, 200
functions of, 214
glucosyltransferases in, 211
GPI-anchored, 200–201, 203–208
Plb family in, 213
Pir group, 201
Plb family in, 213
Sap family in, 213
Sod family in, 213
soluble, 200
structural variations in, 201–202, 208
study methods for, 213–214
subgroups of, 200
surface, 210–211
tandem repeats in, 208–210
transglycosylases in, 211–213
Glycoside hydrolases, in cell wall, 202
Glycosylphosphatidylinositol-anchored proteins, 200–202, 204–206
Glyoxalate cycle, carbon starvation and, 268
Gmc proteins, in biofilm formation, 301
Gnp proteins, in invasion, 288
Goa proteins
in morphology, 334
in respiration, 336–339
Gpd proteins, in stress response general, 230
osmotic, 227
Gpm proteins
in morphology, 334
in oxidative stress response, 278
Gpp1 protein, in osmotic stress response, 227
Gpx1 protein, in oxidative stress response, 277
GRACE approach, to drug discovery, 394
Green fluorescent protein yeast, in
Helicases, in innate immunity, 228
Hda1 protein, in switching, 81
Haploinsufficiency, in genetic screening, 497–498
Haploinsufficiency, in genetic screening, 497–498
Haptoglobin, in switching, 82
Heart, candidiasis of, 434–435
Heat shock, response to, 226–227
Heat shock protein antibodies, for vaccines, 175
Heavy metal stress response, 229
Helicases, in immune response, 158
Hepatosplenic candidiasis, 433
Hepatitis, viral, 117–119
HIC genes, for histatin, 185–194
Histatins, 185–194
binding to Candida, 187–188
Candida response to, 190
family-specific expression of, 185
fungicidal activity of, 187–190
interaction with membranes, 187
intracellular effects of, 190
levels in saliva, 186
in ophthalmalgeal candidiasis, 140
overview of, 185
resistance to, 190
secretion of, 186–188
structure of, 186–188
targeting mitochondria, 335
uptake of, 185
Histoplasma capsulatum
antifungal drugs for, 349
azoles for, 354
polymyxins for, 347
Hit compounds, in drug development, 393
HIV/AIDS
Candidiasis incidence in, 387–388
colonization in, 286
histatin levels in, 186
mucosal candidiasis in, 137
oropharyngeal candidiasis in, 12, 172, 419–420
vaccinations in, 172–173
vulvovaginal candidiasis in, 424
Hkr1 protein
in cell wall, 199
in stress response, 232
Hmx proteins, in liver lesions, 293
Hnt1 protein, in oxidative stress response, 278
Hog1 protein
in general stress response, 229
in histatin response, 190
in respiration, 338
in stress response, 230–233, 266
Hemolongous recombination in DNA repair, 63–64
in genetic instability, 57–58
Horizontal gene transfer, 35–37
Horizontal gene transfer, 35–37
Hormone replacement therapy, vulvovaginal candidiasis in, 422
Host, environment of, in colonization, 286
in histatin response, 191
in kidney lesions, 291
in oxidative stress response, 278
Hypfungipen, 396
Ifa proteins, 33
Ifd proteins, in biofilm formation, 301, 307, 308
Iff proteins, in invasion, 308
Iff proteins, adherence properties of, 272
in cell wall, 201, 207, 210–211
Iff proteins, in heavy metal stress response, 229
Imidazoles, 354
Immunocompromised patients, 135
Immunocompromised patients, 135
Immunocompromised patients, 135
Hyperimmunoglobulin E syndrome
autosomal dominant, 132
gene polymorphisms in, 161
Hypermutable cell populations, 67–68
Hyperosmotic stress response, 227
Hyperplasia, in colon, 249
Hyphane, morphology of, 101–103, 299–300
Hyr proteins
adherence properties of, 272
in biofilm formation, 306
in cell wall, 207
in colonization, 286
in kidney lesions, 291
Hyp/lf1 protein family, 32–33
I
Icl1 protein
in carbon metabolism, 336
in carbon starvation, 268
in invasion, 288
in kidney lesions, 291
in oxidative stress response, 278
Icofungipen, 396
Ila proteins, 33
Ild proteins, in biofilm formation, 301, 307, 308
Iff proteins
adherence properties of, 272
in cell wall, 201, 207, 210–211
in kidney lesions, 291
Imidazoles, 354
Immune reconstitution inflammatory syndrome, 128
Immunity
adaptive, see Adaptive immunity
Candida survival strategies in, 261–282
innate, see Innate immunity
modulation of, 268–270
mucosal, see Mucosal immunity
Immunization, see Active immunization; Passive immunization; Vaccines
Immunodeficiency, see also HIV/AIDS
invasive candidiasis in, 172–174
oropharyngeal candidiasis in, 12
vulvovaginal candidiasis in, 423
Immunochemistry, use of Antigen–antibody reactions, 127–136
Immune response, in candidiasis, 128
innate immunity in, 156
Index

Innate immunity, 155–170
  adaptive responses in, 157
  adjuvant therapy and, 163–164
  Candida cell wall and, 157–158
  Candida escape from, 160–161
  Candida killing capacity and, 156–157
  in gastrointestinal candidiasis, 141
  genes of, polymorphisms of, 161–163
  host susceptibility and, 161–163
  in invasive candidiasis, 129–130
  killing of organisms in, 156
  pattern recognition receptors in, 157–160
  phagocytosis in, 156
  in vulvovaginal candidiasis, 143
  Instability, genetic, see Genetic instability
  Integrins, immunity modulation and, 270
  Interaction assay, for Candida albicans, 483–487
  Interferon-γ
  in immune response, 164
  in invasive candidiasis, 132–133
  Interleukin(s)
  in gastrointestinal candidiasis, 142
  in oropharyngeal candidiasis, 139–140
  in resistance, 128
  in vulvovaginal candidiasis, 422
  Interleukin-10, in invasive candidiasis, 132
  Interleukin-17, in innate immunity, 157
  Intra-abdominal candidiasis, 433–434
  Intracellular trafficking, interference with, 269–270
  Invasive candidiasis, see also Candidaemia;
  Disseminated candidiasis
  biomarkers for, 443–446
  costs associated with, 463–465
  definition of, 12
  diagnosis of, 388, 445–446
  drugs for, 388–391, 445–446, 465–469
  epidemiology of, 443, 449–480
  community onset, 451–452
  incidence, 449–451
  species distribution, 453–463
  gene expression in, 287–289
  host niche status and, 226
  immunology of, 127–136
  acquired immunity in, 130–132
  dendritic cells in, 130
  inflammatory response in, 128
  innate immune receptors in, 129–130
  regulation of, 132–133
  resistance, 127–128, 132–133
  shaping of, 128–132
  tolerance, 127–128, 132–133
  incidence of, 12–13, 127, 388
  length of stay in, 464–465
  mechanisms of, 272–274
  mortality in, 373–376, 463–465
  organisms causing, 12–14
  reservoirs for, 453
  risk factors for, 463
  vaccines for, 171–184
  Lpf protein, in oxidative stress response, 278
  Ire1 protein, in biofilm formation, 301, 306
  Iron, stress response to, 229
  Iron acquisition
  Als proteins and, 246
  in kidney lesions, 291
  in liver lesions, 293
  Isavuconazole, 396
  Isw2 protein, in oxidative stress response, 278
  Itraconazole
  advantages of, 346
  for candidemia, 431
  chemical structure of, 348
  clinical uses of, 357–358
  disadvantages of, 346
  dosing of, 350
  drug-drug interactions of, 353, 357
  monitoring of, 356
  for mucosal candidiasis, 421
  pharmacokinetics of, 355
  spectrum of activity of, 349, 354
  toxicity of, 357
  for vulvovaginal candidiasis, 424
  J
  Joint infections, 435
  K
  Kar2 protein, in histatin response, 190
  Kmr1 protein, in biofilm formation, 301, 304
  K50etazalone, for vulvovaginal candidiasis, 424
  Kgd proteins, in liver lesions, 292
  Kidney, Candida invasion of, 290–291, 435
  Killing, of Candida, 156
  Klebsiella pneumoniae, Candida albicans interactions with, 318
  Knr4 protein, in cell wall, 199
  Kre protein, in cell wall, 207
  Kynurenines, in resistance, 128, 132–133
  L
  Lactic acid, stress response to, 228–229
  Lactobacillus
gastrointestinal, 142
  vaginal, 422–423
  Lactobacillus acidophilus
  for candidiasis, 322
  for mucosal candidiasis, 421
  Lip proteins
  in immunity modulation, 269
  in invasion, 288
  Lipases, in immunity modulation, 269
  Liposomal amphotericin, 175
  Liver, Candida invasion of, 291–294, 433
  Lodderomyces elongisporus
  in invasion, 290–291, 435
  Mal proteins, in liver lesions, 292
  Mannan
  antibodies to, as biomarker, 445
  for vaccines, 174
  in cell wall, 157
  Mannoproteins, in cell wall, 157, 243
  Mannose receptor
  in immune response, 156, 159
  in invasive candidiasis, 129
  Mannose-binding lectin, in immune response, 156
  MAPK
  (mitogen-activated protein kinase) pathway, in stress response, 230–232
  Mating
  in biofilm formation, 309
  Candida albicans, see Candida albicans, mating
  in demonstration of, 76–77
  discovery of, 77–78
  host environment for, 81
  pheromones in, 78–80, 84–85
  same-sex, 80
  switching requirements for, see Switching
  Mating locus, Candida albicans, 75–76
  Mating type-like locus, evolution of, 34
  Mcm1 protein, in multidrug resistance, 409
  MDR1 gene, in multidrug resistance, 404–407, 409–410
  Mdr1 protein, in biofilm formation, 304
  in drug resistance, 66, 310
  Mds proteins, in biofilm formation, 302, 304
  Mechanical ventilation, 319–320, 436
  Membrane, evolution of, 34–35
  Meningitis, 434
  Met proteins
  in colonization, 286
  in heavy metal stress response, 229
  in invasion, 288
  Methyl mismatch repair, 60–61
  N-Methyl-N’-nitro-N-nitrosoguanidine, in DNA repair, 62
  MFrα1 gene, in mating, 79
  MFA1 gene, in mating, 79
  MFM complex, in mitochondrial function, 337–339
  MGCD290 (histone deacetylase inhibitor), 396
  MGFR1 gene, in DNA repair, 62
  MIC (minimum inhibitory concentration), 346–347
  Miconafungin, 2358–360
  advantages of, 346

Loss of heterozygosity, genetic instability and, 57–58
Lsp1 protein, in mating, 84
Lung, Candida invasion of, 436

M
Macrophages, in immune response, 156, 157
Mad2 protein, in cell cycle, 119–120
MAG1 gene, in DNA repair, 62
Magnaporthe grisea, cell wall of, 210
Major facilitator superfamily transporters, in multidrug resistance, 404–405
Major repeat sequences, 29, 94
Mak proteins, in stress response, 232–233
Mal proteins, in liver lesions, 292
Mannan
antibodies to as biomarker, 445
for vaccines, 174
in cell wall, 157
Mannoproteins, in cell wall, 157, 243
Mannose receptor
in immune response, 156, 159
in invasive candidiasis, 129
Mannose-binding lectin, in immune response, 156
MAPK (mitogen-activated protein kinase) pathway, in stress response, 230–232
Mating
in biofilm formation, 309
Candida albicans, see Candida albicans, mating
in demonstration of, 76–77
discovery of, 77–78
host environment for, 81
pheromones in, 78–80, 84–85
same-sex, 80
switching requirements for, see Switching
Mating locus, Candida albicans, 75–76
Mating type-like locus, evolution of, 34
Mcm1 protein, in multidrug resistance, 409
MDR1 gene, in multidrug resistance, 404–407, 409–410
Mdr1 protein
in biofilm formation, 304
in drug resistance, 66, 310
Mds proteins, in biofilm formation, 302, 304
Mechanical ventilation, 319–320, 436
Membrane, evolution of, 34–35
Meningitis, 434
Met proteins
in colonization, 286
in heavy metal stress response, 229
in invasion, 288
Methyl mismatch repair, 60–61
N-Methyl-N’-nitro-N-nitrosoguanidine, in DNA repair, 62
MFrα1 gene, in mating, 79
MFA1 gene, in mating, 79
MFM complex, in mitochondrial function, 337–339
MGCD290 (histone deacetylase inhibitor), 396
MGFR1 gene, in DNA repair, 62
MIC (minimum inhibitory concentration), 346–347
Miconafungin, 2358–360
advantages of, 346
Pattern recognition receptors, 157–160
Peroxide, stress response to, 227–228
Peritonitis, 433–434
Pericarditis, 434–435
Peptidoglycans, in fungal-bacterial interactions, 312
Pepstatin A, in invasion, 272
Pep12 protein, in biofilm formation, 302
Pep1 protein, in switching, 81
Pdx proteins, 324
Pdr proteins, 325–326
Pda proteins, in liver lesions, 292
Pcl proteins, in cell cycle, 111, 117–118
Pck1 protein
Pbs proteins, in stress response, 230–231
Pbr1 protein, in mating, 84
Pathogenicity, 461
Pathogen-associated molecular patterns, in stress response, 230–231
Pasteur Institute, database of, 37
Passive immunization, 4–5
Paracoccidioides brasiliensis, 37
Pacemakers, infection of, 435
Pap proteins, in mating, 76
in stress response, 233–234
Paracoccidioides
azoles for, 354
polymers for, 347
Paracoccidioides brasiliensis, farnesol effects on, 324
Parallel respiratory pathway, 332–333
Passive immunization, 4–5
mechanism of action of, 130–131
vaccines for, 174–175
Pasteur Institute, database of, 37
Pathogen-associated molecular patterns, in invasive candidiasis, 129
Pathogenicity, see specific organisms
Pattern recognition receptors, 157–160
in gastrointestinal candidiasis, 141
in invasive candidiasis, 129–130
Pfr1 protein, in mating, 84
Pbs proteins, in stress response, 230–231
Pck1 protein, in carbon metabolism, 336
in kidney lesions, 291
in oxidative stress response, 278
Pcl proteins, in cell cycle, 111, 117–118
PCR (polymerase chain reaction) for diagnostic use, 445
for drug resistance, 379–380
for mucosal candidiasis, 424
Pda proteins, in liver lesions, 292
Pdh1 protein, in multidrug resistance, 405, 408
Pdr proteins
in biofilm formation, 308
in multidrug resistance, 411–412
Pdx proteins, 338–339
in liver lesions, 292
in morphogenesis, 334
Pep1 protein, in switching, 81
Pep12 protein, in biofilm formation, 302
Pepstatin A, in invasion, 272
Peptidoglycans, in fungal-bacterial interactions, 312
Pericarditis, 434–435
Peritonitis, 433–434
Peroxide, stress response to, 227–228
Persistor cells, in drug resistance, 310
Pfk proteins
in carbon metabolism, 336
in kidney lesions, 291
in liver lesions, 292
Pga proteins, 33
in biofilm formation, 302, 305, 306
in cell wall, 201, 203–207, 210
in colonization, 287
in liver lesions, 293
in mating, 84
Pfk proteins, in morphogenesis, 334
Phagocytosis of Candida, 156, 261–262, 264
defenses against, 270
Pharmacodynamics, of antifungal drugs, 346–347
Pharmacokinetics, of antifungal drugs, 346–347
Pharmacology, of antifungal drugs, 345
Pharyngeal candidiasis, see Oropharyngeal candidiasis
Phenazines, in polymicrobial populations, 320
Phenotype(s), strain variation due to, 46
Phenotypes, for mucosal candidiasis, 424
Phenotypes, for drug resistance, 379–380
Phenotype switching, Candida albicans, 14–15
Pheromones
in biofilm formation, 309
in mating, 78–80, 84–85
Pho84, in kidney lesions, 291
Pho proteins in cell cycle, 111, 117–118
in invasion, 288
in liver lesions, 293
Phosphate acquisition, in kidney lesions, 291
Phospholipases
Candida albicans, 14
invasion, 275, 276
phospholipase A, 276
Phosphoshamannan, in cell wall, 157
Phosphorelay systems, in stress response, 232–233
Photolyases, 62
Phre proteins, in mating, 84
Phr proteins
in cell wall, 202, 206, 211
in colonization, 287
in histatin response, 190
in invasion, 288
in kidney lesions, 291
in liver lesions, 292
Pichia guilliermondii
in biofilm formation, 302, 305, 306
in cell wall, 201, 203–207, 210
in colonization, 287
in liver lesions, 293
in mating, 84
Pichia guilliermondii
invasion, 288
Pichia stipitis
invasion, 288
in histatin response, 190
Plaqochin E, targeting mitochondria, 335
Platelet Candida tests, 445
Pld proteins, 33
in cell wall, 205, 213
in invasion, 288
Pmc proteins, in immunity modulation, 269
PmrA proteins, in biofilm formation, 309
Pma proteins, in liver lesions, 292
PMS1 protein, in methyl mismatch repair, 60–61
Pnt I protein, in dissemination, 290
Pnt proteins, in biofilm formation, 302
PNA-FISH analysis, for drug resistance, 379–382
Pneumocystis, farnesol effects on, 324
Pneumonia, 436
Point centromeres, 29–30
Point mutation, genetic instability and, 57–58
Pol proteins, in DNA repair, 64–65
Polarisomes, 107–108
Polymers, 347–353
clinical uses of, 350–351
Persister cells, in drug resistance, 350
mechanism of action of, 347
new, 396
Pharmacodynamics of, 347–348
Pharmacokinetics of, 347, 350
resistance to, 403
toxicity of, 348
Phospholipidase C
for drug resistance, 353, 357
monitoring of, 356
for mucosal candidiasis, 421
Pharmacokinetics of, 355–356
spectra of activity of, 349–350
Postantifungal effect, 346
Potassium hydroxide test, for vulvovaginal candidiasis, 4–5
for Candidaemia, 431
chemical structure of, 348
clinical uses of, 358
disadvantages of, 346
dosing of, 351
drug-drug interactions of, 353, 357
for mucosal candidiasis, 421
Pharmacokinetics of, 355–356
spectra of activity of, 349–350
susceptibility to, 465, 468
Posaconazole advantages of, 346
for candidemia, 431
for Candida albicans, 324
invasion, 275, 276
for drug resistance, 379–380
for mucosal candidiasis, 424
for candidemia, 431
for mucosal candidiasis, 421
Pharmacodynamics of, 347–348
Pharmacokinetics of, 347, 350
new, 396
Pharmacodynamics of, 347–348
Pharmacokinetics of, 347, 350
resistance to, 403
susceptibility to, 465, 468
Postantifungal effect, 346
Potassium hydroxide test, for vulvovaginal candidiasis, 4–5
for Candidaemia, 431
chemical structure of, 348
clinical uses of, 358
disadvantages of, 346
dosing of, 351
drug-drug interactions of, 353, 357
for mucosal candidiasis, 421
Pharmacokinetics of, 355–356
spectra of activity of, 349–350
susceptibility to, 465, 468
Prospective Antifungal Therapy (PATH) registry, 375
Prophylactic antifungal therapy, for disseminated candidiasis, 4–5
Prophylactic Antifungal Therapy (PATH) registry, 375
Prospective Antifungal Therapy (PATH) registry, 375
Prophylactic antifungal therapy, for disseminated candidiasis, 4–5
Prospective Antifungal Therapy (PATH) registry, 375
Protein microarray, for Candida albicans, 489–496
Proteinases, Candida albicans, 14
Protein-protein interactions, in two-hybrid system, 483–487
Proteus, in vulvovaginal candidiasis, 423
Pseudohyphae, morphology of, 101–103, 299–300
Pseudomembranous oropharyngeal candidiasis, 16
Pseudomonas aeruginosa, Candida albicans interactions with, 318–320, 324
Pwp proteins, adhesive properties of, 253
Pxa proteins, in invasion, 288
Pyk proteins
in carbon metabolism, 336
in kidney lesions, 291
in morphogenesis, 334
Pyrimidine dimers, reversal of, 62

R ad proteins
in cell cycle, 120
in DNA repair, 63–65
in oxidative stress response, 278
Ranl1 protein, in mating, 79
Rap1 protein, adherence properties of, 272
Ras protein
in cell cycle, 119
in quorum sensing, 322–323
Ras-CAMP signaling
in fungal-bacterial interactions, 320–323
in heat shock, 226–227
in stress response, 234
in weak acid stress response, 229
Rbt protein
in biofilm formation, 302, 304
in cell cycle, 119
in cell wall, 205–206, 210
in colonization, 284–286
in invasion, 288
in kidney lesions, 291
in liver lesions, 293
in mating, 80, 84
Reactive nitrogen species
stress response to, 228, 264–267
suppression of, 269
Reactive oxygen species
in histatin action, 185, 187–188
in mitochondrial activity, 334–335
stress response to, 227–228, 264–267
suppression of, 269
Recombination, in adhesin evolution, 254–255
Reconstituted human epithelial model, 286–288
Redox-sensitive antioxidants, in stress response, 233
Reflectance confocal microscopy, 501–503
Rep1 protein, in multidrug resistance, 409–410
Repair systems, see also DNA repair
DNA genes for, 111–113
genetic instability and, 60–65
for oxidative stress, 227
Repetitive sequences, 29–30
Reservoirs, for invasive candidiasis and candidemia, 453
Resistance to antifungal agents, see Drug resistance; Susceptibility to Candida, immunology of, 127–128, 132–133
to histatin, 190
Respiration, in Candida, 331–335
Respiratory burst, in Candida killing, 156, 264–267
Restriction fragment length polymorphism analysis, strain variation, 94
Retrotransposons, 30
Rev proteins, in DNA repair, 64–65
Rgp proteins
in cell cycle, 117
in oxidative stress response, 278
Rh1 protein, in cell wall, 199
Rfl1 protein, adherence properties of, 272
Rig1 protein, in immune response, 158, 160
Rim proteins
in invasion, 288
in mating, 80
Risk factors, for candidiasis, 1–2
disseminated, 1–2, 171–172
esophageal, 2
oropharyngeal, 2
vulvovaginal, 145, 172
RNA, transfer, 46–47
Rpd3 protein, in switching, 82
Saccharomyces cerevisiae
in cell wall, 202–204, 210
in colonization, 257
in immunity modulation, 269
in invasion, 288
in kidney lesions, 291
in liver lesions, 292
in mating, 80
SAPs (secreted aspartyl proteinases), Candida albicans, 15–16
Sas10 protein, in oxidative stress response, 278
Scaffolds, for drug discovery, 392
Scedosporium
antifungal drugs for, 349
azoles for, 354
polyenes for, 347
Schizosaccharomyces pombe
cyclins of, 110
Schmoos, in reproduction, 75
Screening in drug development, 392
genetic interaction, 497–500
Sdh12 protein, in kidney lesions, 290
Sec proteins, in colonization, 286
Secreted aspartyl proteinases, 30–32
Candida albicans, 15–16
in cell wall, 213
Sed proteins, in cell cycle, 210
Sepation, in cell cycle, 108–109
Septic arthritis, 435
Septins
in cell cycle, 108–109
genes for, 114
Ser residues, in adhesins, 244
Serratia marcescens, Candida albicans interactions with, 318, 320
Serum beta glucan test, 3
Sexual transmission, of candidiasis, 423
She3 protein, in cell cycle, 117
Sho1 protein, in cell wall, 198
in stress response, 232
Single nucleotide polymorphisms, 27–28
Single-strand annealing, in DNA repair, 64–65
Sir proteins, adherence properties of, 272
Skn7 protein, in stress response, 234
Sko1 protein, in cell wall, 199
Ssl1 protein, in cell wall, 199
Sln proteins, in stress response, 232
Slf2 protein, in cell wall, 199
Sm1 protein, in cell wall, 199
Snq2 protein, in multidrug resistance, 405, 408
Sordarins, 396
Sorbitol, stress response to, 227
Sorbitol, stress response to, 227
Sordarins, 396
Spa2 protein, in cell cycle, 107–108
Specific codon usage, in Candida albicans, 51–53
Spectrophotometry, in drug development, 393
SPI proteins, in cell cycle, 210
Spinal cord, candidiasis of, 434
Spindles, 106
Spitzenzkörper, 107–108
Sporothrix schenckii
Candida
Spleen, SPK-843 (polyene), 396
Staphylococcus aureus
Ssu proteins
Sst proteins, in mating, 84
Ssp proteins, in fungal-bacterial interactions, 320
Sst proteins, in mating, 84
Streptococcus gordonii
Streptococcus anginosus
STOP codons, 45
Stomatitis
Ste proteins
Stress responses, 226–242
Stress, genetic instability in, 67–68
Stress responses, 225–242
Streptococcus pneumoniae, Candida albicans
in biofilms, 302, 305, 306
in mating, 84
Superoxide anions, stress response to, 227–228
Superoxide dimutases, see also Sod proteins
in cell wall, 202, 213
in oxidative stress response, 264–265
Surgery, as candidiasis risk factor, 1–2
Susceptibility
to drugs, 465–469; see also specific organisms, antifungal susceptibility of genetic instability and, 65–67
of host, 161–165
Suv proteins, in biofilm formation, 302, 304
Swel protein, in cell cycle, 119–120
Switching
in biofilm formation, 305–306, 309
Candida albicans, see Candida albicans, switching in
Candida dubliniensis, 77–78, 84, 86
Candida tropicalis, 77–78
cell morphology and, 104
discovery of, 77–78
historical view of, 80–81
host environment for, 81
opaque cells in, 81
regulation of, 81–83
role in mating, 83–84
Synthetic libraries, for drug development, 392–393
Systemic candidiasis, see Candidemia; Disseminated candidiasis; Invasive candidiasis
T
T-2307 (acrylamide), 396
T lymphocytes
in gastrointestinal candidiasis, 141–142
in immune response, 156
in invasive candidiasis, 131–132
in oral candidiasis, 420
in oropharyngeal candidiasis, 138–139
Tcp1 protein
in drug resistance, 66, 407–408
in strain variation, 97
T-cell receptors, in oropharyngeal candidiasis, 139
Tc1 protein
in biofilm formation, 302, 304, 306
in mating, 84, 85
Teeth, microbial populations on, 319
Terfezer, 29
Tetraploidy, in Candida albicans, 77
Th1 cells
in immune response, 163–164
in innate immunity, 157
in invasive candidiasis, 131–132
in oropharyngeal candidiasis, 139–140
Thioreredoxin
in oxidative stress response, 277
in stress response, 227, 266
Thr residues, in adhesins, 244
Thrombophlebitis, 435
Th1/Th2 cells
in immune response, 157, 163–164
in innate immunity, 157
in invasive candidiasis, 131
TIM complex, in mitochondrial function, 337–339
TLO proteins, 33
TMP-1363, targeting mitochondria, 336
Tolerance, to Candida, 127–128, 132–133, 142
Toll-like receptors
in immune response, 158–159
in invasive candidiasis, 129–130
polymorphisms of, 161
in vulvovaginal candidiasis, 423
TOM complex, in mitochondrial function, 337–339
Torulopsis, 11
Torulopsis glabrata, see Candida glabrata
Too9 protein, in switching, 82
Toxins, in drug development, 393
Tps proteins
in general stress response, 230
in oxidative stress response, 277
Tpx1 protein, in stress response, 233
TR region, in Als family, 244–245
Transcription factor complementation, in two-hybrid system, 483–487
Transferrin, 293
Transglycosidases, in cell wall, 211–213
Translation, molecules of, 45
Translesion synthesis, in DNA repair, 64–65
Translocases, in mitochondrial function, 337–339
Transposable elements, 30
Treg cells
in gastrointestinal candidiasis, 142
in innate immunity, 157
in invasive candidiasis, 132
Trehalose, in stress response, 266
heat, 226
oxidative stress, 277
Triazoles, 354
TRIF (Toll-IL-1 receptor domain-containing adapter-inducing beta interferon) pathway, in invasive candidiasis, 129
Tpi1 protein, in colonization, 286
Trr1 protein, in oxidative stress response, 277–278
Txl1 protein
in histatin response, 190
in kidney lesions, 291
in oxidative stress response, 277–278
in stress response, 233
Tryptophan starvation, 132–133
Tsa1 protein
in oxidative stress, 278
Ttr1 protein, in kidney lesions, 291
Tup1 protein
in Als regulation, 247
in biofilm formation, 308
in cell cycle, 117, 118
Ty67 protein, in carbon metabolism, 335–336
Tyrosol, in quorum sensing, 308
U
Uce1 protein, in invasion, 273, 288
Ultraviolet light damage, DNA repair in, 62, 63
Ume6 protein
  in biofilm formation, 302
  in cell cycle, 118
  in morphology, 102–103
Upc proteins, in drug resistance, 66
URA3 gene, Candida albicans, 15
Ura proteins, in nutrient starvation, 267–268
Urinary tract, candidiasis of, 435
Utr proteins, in cell wall, 202, 204
Uvr proteins, in DNA repair, 63

V
Vaccines, 171–184
  for active immunization, 175–178
  adjuvants for, 177
  barriers to efficacy of, 172–174
  development of, 163–164
  for mucosal candidiasis, 425
  for passive immunization, 174–175
  rationale for, 171–174
Vacuolar inheritance, 108
Vaginal candidiasis, see Vulvovaginal candidiasis
Vaginal-relapse theory, 423
Ventilator-related infections, 319–320, 436
Virulence factors, see also specific organisms
  drug resistance and, 375–376
  versus host defenses, 155
  in oral candidiasis, 420
  strain variation and, 96
  stress responses and, see Stress responses
Voriconazole
  advantages of, 346
  for Candida albicans, 16
  for candidemia, 431–432
  chemical structure of, 348
  clinical uses of, 358
  disadvantages of, 346
  dosing of, 351
  drug-drug interactions of, 353, 357
  monitoring of, 356
  for mucosal candidiasis, 421
  pharmacokinetics of, 355
  spectrum of activity of, 349, 354
  susceptibility to, 465–467
  toxicity of, 357
Vps51 protein
  of Candida albicans, 262
  in invasion, 273
Vulvar vestibulitis syndrome
  gene polymorphisms in, 162–163
  recurrent, 423
Vulvovaginal candidiasis
  animal models for, 143, 145
  biofilms in, 146
  complicated, 424
  drugs for, 421, 424
  epidemiology of, 420
  gene expression in, 287
  immunity to, 142–145
  incidence of, 145, 387–388
  microbiology of, 420, 422–423
  natural history of, 144
  pathogenesis of, 420, 422–423
  pathophysiology of, 155
  recurrent, 145, 162, 172
  risk factors for, 145, 172, 422–423
  species causing, 11–12
  treatment of, 424
  vaccines for, 172

W
Wap proteins
  in cell wall, 205
  in liver lesions, 293
Weak acid stress response, 228–229
Whi11 protein
  in mating, 84
  in switching, 81
White cells, see also Switching
  in mating, 76–78
White-opaque switch, Candida albicans, 15
Whole-genome duplication, in cell cycle, 110
Wildlife, strain variation found in, 95
Wor proteins, in switching, 82–83, 104
Wpre protein, in mating, 84

X
Xanthomonas campestris, Candida albicans interactions with, 320

Y
Yak1 protein, in biofilm formation, 302, 306
Yap proteins
  in multidrug resistance, 405–406
  in stress response, 233–234
Yapsins, 213
Yarrowia lipolytica
  cell wall of, 209
  cyclins of, 110
Yck proteins, in invasion, 288
Yeast cells, morphology of, 101–103, 299–300
Yeast Gene Order Browser, 38
Ygb proteins, in liver lesions, 293
YHBI protein, in histatin response, 190
Yhb proteins
  in invasion, 288
  in liver lesions, 293
  in nitrosative stress response, 228
  in stress response, 266–267
Yku protein, in DNA repair, 64
Yps7 protein, in cell wall, 204
YTTYPL tandem repeats, in cell wall, 210
Ywp1 protein, in biofilm formation, 302, 303–304

Z
Zap proteins, in biofilm formation, 302, 307
Zinc, stress response to, 229
Zygomycetes, antifungal drugs for, 349