CRYPTOCOCCUS
FROM HUMAN PATHOGEN TO MODEL YEAST
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EDITED BY

Joseph Heitman
Duke University Medical Center
Durham, NC 27710

Thomas R. Kozel
University of Nevada School of Medicine
Reno, NV 89557-0320

Kyung J. Kwon-Chung
National Institute of Allergy and Infectious Diseases
Bethesda, MD 20892

John R. Perfect
Duke University Medical Center
Durham, NC 27710

Arturo Casadevall
Albert Einstein College of Medicine
Bronx, NY 10461

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Top left: Basidium (blue) and chains of infectious basidiospores (purple) produced during sexual reproduction of Cryptococcus neoformans, visualized by scanning electron microscopy (pseudocolored). Photo by Chaoyang Xue, Kasey Carroll, and Joseph Heitman.

Top right: C. neoformans yeast cells stained with an anticapsular antibody (blue) and fluorescein as a cell wall marker (green), visualized by indirect immunofluorescence microscopy. Photo by Lynda Pierini and Tamara Doering.

Lower left: Cryptococcus gattii NIH444 (gold) undergoing phagocytosis by a neutrophil (pink); pseudocolored scanning electron micrograph. Photo by Deborah Springer and Vishnu Chaturvedi.

Lower right: C. neoformans budding yeast cell stained with anticapsular monoclonal antibody 339 (red) and antibody to the human C3 component of complement (green), visualized by immunofluorescence microscopy. Photo by Marcellene Gates-Hollingsworth and Thomas Kozel.
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Contributors

BARBARA D. ALEXANDER
Departments of Medicine and Pathology, Duke University Medical Center, Durham, NC 27710

J. ANDREW ALSPAUGH
Department of Medicine and Department of Molecular Genetics and Microbiology, Duke University School of Medicine, Durham, NC 27710

YONG-SUN BAHN
Department of Biotechnology, Center for Fungal Pathogenesis, College of Life Science and Biotechnology, Yonsei University, Seoul 120-749, Republic of Korea

UMA BANERJEE
Department of Microbiology, All India Institute of Medical Sciences, New Delhi, India

KAREN BARTLETT
School of Environmental Health, University of British Columbia, 372-2206 East Mall, Vancouver, BC, Canada V6T 1Z3

TIHANA BICANIC
Centre for Infection, St. George’s University of London, Cranmer Terrace, London SW17 ORE, United Kingdom

TEUN BOEKHOUT
CBS Fungal Diversity Center, Uppsalalaan 8, 3584 CT Utrecht, The Netherlands

MARY E. BRANDT
Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, GA 30333

EDMOND BYRNES
Duke University Medical Center, 312 CARL Building, Box 3546, Research Drive, Durham, NC 27710

LEONA CAMPBELL
School of Molecular Bioscience, Building G08, University of Sydney, NSW 2006, Australia

PAUL J. CANFIELD
Faculty of Veterinary Science, The University of Sydney, Sydney, NSW Australia 2006

DEE A. CARTER
School of Molecular Bioscience, Building G08, University of Sydney, NSW 2006, Australia

ARTURO CASADEVVALL
Department of Microbiology and Immunology and Department of Medicine, Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461

ELIZABETH CASTAÑEDA
Emerita Investigator, Instituto Nacional de Salud, Bogotá, Colombia

SUDHA CHATURVEDI
Mycology Laboratory, Wadsworth Center, New York State Department of Health, and Department of Biomedical Sciences, University at Albany School of Public Health, Albany, NY 12208

VISHNU CHATURVEDI
Mycology Laboratory, Wadsworth Center, New York State Department of Health, and Department of Biomedical Sciences, University at Albany School of Public Health, Albany, NY 12208

JANGHAN CHEN
Shanghai Changzheng Hospital, Second Military Medical University, Shanghai, PR China

SHARON C.-A. CHEN
Centre for Infectious Diseases and Microbiology, Westmead Hospital and the University of Sydney, Westmead, NSW 2145 Australia

YUCHONG CHEN
Shanghai Changzheng Hospital, Second Military Medical University, Shanghai, PR China

TOM M. CHILLER
Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, GA 30333

CARA J. CHRISMAN
Albert Einstein College of Medicine, Department of Microbiology and Immunology, Bronx, NY 10461
CONTRIBUTORS

KARL V. CLEMONS
California Institute for Medical Research, San Jose, CA 95128; Div. of Infectious Diseases, Santa Clara Valley Medical Center, San Jose, CA 95128; and Div. of Infectious Diseases and Geographic Medicine, Stanford University, Stanford, CA 94305

MASSIMO COGLIATI
Laboratory of Medical Mycology, Department of Public Health – Microbiology – Virology, Università degli Studi di Milano, Via Pascal 36, 20133 Milan, Italy

JEFFREY J. COLEMAN
Division of Infectious Diseases, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114

GARY M. COX
Department of Medicine Mycology Research Unit, Duke University, Durham, NC 27710

EKATERINA DADACHOVA
Departments of Nuclear Medicine and Microbiology & Immunology, Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461

MAURIZIO DEL POETA
Department of Biochemistry and Molecular Biology, Department of Microbiology and Immunology, and Division of Infectious Diseases, Medical University of South Carolina, Charleston, SC 29425

MARA R. DIAZ
Rosenstiel School of Marine and Atmospheric Science, University of Miami, Miami, FL 33149

JULIANNE T. DJORDJEVIC
Centre for Infectious Diseases and Microbiology, ICPMR and Westmead Millennium Institute, University of Sydney at Westmead Hospital, Westmead, 2145 NSW, Australia

ERNESTO DROMER
Institut Pasteur, Molecular Mycology Unit, CNRS URA3012, 25, rue du Dr. Roux, 75724 Paris cedex 15, France

COLLEEN DUNCAN
Colorado State University Veterinary Diagnostic Laboratory, 300 West Drake Ave., Fort Collins, CO 80523

JACK W. FELL
Rosenstiel School of Marine and Atmospheric Science, University of Miami, Key Biscayne, FL 33149

KEISHA FINDLEY
Department of Molecular Genetics and Microbiology, Duke University Medical Center, Durham, NC 27710

MATTHEW FISHER
Imperial College, London, United Kingdom

DEBORAH S. FOX
Department of Pediatrics and Department of Microbiology, Immunology and Parasitology, The Research Institute for Children and LSU Health Sciences Center, Children’s Hospital, New Orleans, LA 70118

BETTINA C. FRIES
Departments of Medicine, Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10804

MURRAY FYFE
Office of the Medical Health Officer, Vancouver Island Health Authority, 430 - 1900 Richmond Ave., Victoria, BC, Canada V8R 4R2

ELENI GALANIS
British Columbia Centre for Disease Control and School of Population and Public Health, University of British Columbia, 655 W. 12th Ave., Vancouver, BC, Canada V5Z 4R4

SCARLETT GEUNES-BOYER
Department of Cell Biology, 438 Nanaline Duke Bldg., Box 3709, Duke University Medical Center, Durham, NC 27710

MAHMOUD A. GHANNOUM
Center for Medical Mycology, Case Western Reserve University, Cleveland, OH 44106

NICOLE M. GILBERT
Department of Biochemistry and Molecular Biology, Saint Louis University, St. Louis, MO 63104

FELIX GILGADO
Molecular Mycology Research Laboratory, Centre for Infectious Diseases and Microbiology, The University of Sydney, Sydney Medical School - Westmead Hospital, Westmead Millennium Institute, Westmead, NSW, 2145, Australia

NELESH P. GOVENDER
Mycology Reference Unit, National Institute for Communicable Diseases, a division of the National Health Laboratory Service, and Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

FERRY HAGEN
CBS-KNAW Fungal Diversity Centre, Uppsalalaan 8, NL-3584CT Utrecht, The Netherlands

THOMAS S. HARRISON
Centre for Infection, St. George’s University of London, Cranmer Terrace, London SW17 ORE, United Kingdom

JOSEPH HEITMAN
Department of Molecular Genetics and Microbiology, Duke University Medical Center, Durham, NC 27710

LINDA HOANG
British Columbia Centre for Disease Control, Dept. of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada V5Z 4R4

YEN-PING HSUEH
Division of Biology, California Institute of Technology, Pasadena, CA 91125

GARY B. HUFFNAGLE
Internal Medicine - Pulmonary Division, 6301 MSRB III, Box 5642, 1150 W. Medical Center Drive, University of Michigan Medical Center, Ann Arbor, MI 48109-5642
CONTRIBUTORS

MUHAMMAD MORSHED
British Columbia Centre for Disease Control, Dept. of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada V5Z 4R4

FRITZ A. MÜHLSCHLEGEL
School of Biosciences, University of Kent, Canterbury, Kent CT2 7NJ, and East Kent Hospitals University NHS Foundation Trust, Clinical Microbiology Service, William Harvey Hospital, Ashford, Kent TN24 0LZ, United Kingdom

ELEFHERIOS MYLONAKIS
Division of Infectious Diseases, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114

POPCHAI NGAMSKULRUNGROJ
Molecular Mycology Research Laboratory, Centre for Infectious Diseases and Microbiology, The University of Sydney, Sydney Medical School - Westmead at Westmead Hospital, Westmead Millennium Institute, Westmead, NSW, 2145, Australia

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

CONNIE B. NICHOLS
Department of Medicine and Department of Molecular Genetics and Microbiology, Duke University School of Medicine, Durham, NC 27710

KIRSTEN NIELSEN
Department of Microbiology, Medical School, University of Minnesota, Minneapolis, MN 55455

JOSHUA D. NOSANCHUK
Department of Medicine and Department of Microbiology and Immunology, Albert Einstein College of Medicine, Jack and Pearl Resnick Campus, 1300 Morris Park Ave., Ullmann Building, Room 107, Bronx, NY 10461

CAROLYN R. O'BRIEN
Faculty of Veterinary Science, University of Melbourne, Werribee, Victoria, Australia 3030

PETER G. PAPPAS
Division of Infectious Diseases, University of Alabama at Birmingham, 1900 University Blvd., TH 229, Birmingham, AL 35294-0006

BENJAMIN J. PARK
Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, GA 30333

JOHN R. PERFECT
Department of Medicine, Division of Infectious Diseases, Duke University Mycology Research Unit (DUMRU), 0557 Hospital South, Box 3353, Duke University Medical Center, Durham, NC 27710

MICHAEL A. PFALLER
Departments of Pathology and Epidemiology, University of Iowa College of Medicine and College of Public Health, 200 Hawkins Dr., Iowa City, IA 52242-1009

PETER PHILLIPS
Infectious Diseases Unit, St. Paul’s Hospital, Vancouver, BC, Canada V6Z 1YC

LIISE-ANNE PIROFSKI
Division of Infectious Diseases, Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461

MARCIO L. RODRIGUES
Laboratório de Estudos Integrados em Bioquímica Microbiana, Universidade Federal do Rio de Janeiro, Instituto de Microbiologia, Avenida Carlos Chagas Filho, 373, Cidade Universitária CCS, Bloco I, Rio de Janeiro - RJ, 21941-902, Brazil

MARIANELA RODRIGUEZ-CARRES
Department of Biology, Duke University, Durham, NC 27710

JULIAN C. RUTHERFORD
Institute for Cell and Molecular Biosciences (ICaMB), Medical School, Newcastle University, Catherine Cookson Building, Framlington Place, Newcastle upon Tyne, NE2 4HH, United Kingdom

NATHAN SAUL
Faculty of Veterinary Science, Building B14, University of Sydney, Sydney, NSW 2006, Australia

WEI-CHIANG SHEN
Department of Plant Pathology and Microbiology, National Taiwan University, No. 1 Roosevelt Road, Sec 4, 10617 Taipei, Taiwan

NINA SINGH
VA Pittsburgh Healthcare System and University of Pittsburgh, Pittsburgh, PA 15240

TANIA C. SORRELL
Centre for Infectious Diseases and Microbiology, Sydney Medical School-Western & Westmead Millennium Institute Level 3 ICPMR, University of Sydney at Westmead Hospital, Westmead 2145 NSW, Australia

CHARLES A. SPECHT
Department of Medicine, University of Massachusetts, Worcester, MA 01605

DAVID A. STEVENS
California Institute for Medical Research, San Jose, CA 95128; Div. of Infectious Diseases, Santa Clara Valley Medical Center, San Jose, CA 95128; and Div. of Infectious Diseases and Geographic Medicine, Stanford University, Stanford, CA 94305

SOMNUEK SUNGKANUPARPH
Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

LUCIANA TRILLES
Mycology Laboratory, Instituto de Pesquisa Clinica Evandro Chagas (IFEC), Fundação Oswaldo Cruz (FIOCRUZ), Av. Brasil, 4365, 21040-900 Rio de Janeiro, Brazil

DAVID TROFA
Department of Medicine and Department of Microbiology and Immunology, Albert Einstein College of Medicine, Jack and Pearl Resnick Campus, 1300 Morris Park Ave., Ullmann Building, Room 107, Bronx, NY 10461
CONTRIBUTORS

MARIA ANNA VIVIANI
Laboratory of Medical Mycology, Department of Public Health – Microbiology – Virology, Università degli Studi di Milano, Via Pascal 36, 20133 Milan, Italy

KERSTIN VOELZ
School of Biosciences, University of Birmingham, Birmingham B15 2TT, United Kingdom

PING WANG
The Research Institute for Children, New Orleans, LA 70118

BODO WANKE
Mycology Laboratory, Instituto de Pesquisa Clinica Evandro Chagas-Fiocruz, Rio de Janeiro, RJ, Brazil

SARAH WEST
Divisions of General Internal Medicine and Infectious Diseases, Oregon Health and Science University, Portland, OR 97239

BRIAN L. WICKES
Department of Microbiology, University of Texas Health Center, University of Texas, San Antonio, TX 78284-7758

KRIStI L. WILLIAMS
Department of Cell Biology, 438 Nanaline Duke Bldg., Box 3709, Duke University Medical Center, Durham, NC 27710

PETER R. WILLIAMSON
Laboratory of Clinical Infectious Diseases, National Institutes of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892

FLOYD L. WORMLEY, JR.
The University of Texas at San Antonio, Department of Biology, One UTSA Circle, San Antonio, TX 78249

KAREN L. WOZNIAK
Department of Biology, University of Texas at San Antonio, San Antonio, TX 78249

JO RAE WRIGHT
Department of Cell Biology, 438 Nanaline Duke Bldg., Box 3709, Duke University Medical Center, Durham, NC 27710

JIANPING XU
Department of Biology and Institute of Infectious Disease Research, Michael G. DeGroote School of Medicine, McMaster University, 1280 Main St. West, Hamilton, Ontario, L8S 4K1, Canada

CHAOYANG XUE
Public Health Research Institute Center, University of Medicine and Dentistry of New Jersey, Newark, NJ 07103

OSCAR ZARAGOZA
Servicio de Micología, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Carretera Majadahonda-Pozuelo, Km2, Majadahonda 28220, Madrid, Spain

LI-PING ZHU
Department of Infectious Diseases, Huashan Hospital, Fudan University, Shanghai, PR China
Foreword

Cryptococcus neoformans is an important opportunistic fungal pathogen in T-cell-immunosuppressed patients, especially those with AIDS or solid organ transplants and others receiving prolonged immunosuppressive therapy. For example, the global burden of HIV-associated cryptococcosis approaches 1 million cases annually. This unique yeast also causes disease in immunocompetent hosts, but much less frequently. Although cryptococcosis is recognized most often in selected geographic areas, e.g., the United States, Western Europe, Australia, and sub-Saharan Africa, this disease is seen throughout the world.

In this multiauthored book, the five editors planned a comprehensive approach into the understanding of Cryptococcus at many different levels. Over a decade ago, the original book on Cryptococcus neoformans written by two of the present editors (Casadevall and Perfect) set the stage for how an entire book could be devoted to this fungal pathogen. In this new volume, the plan was to allow the entire expert field of cryptococcal investigators to examine in detail the life cycle, pathophysiology (from immunology to virulence factors), molecular biology, diagnosis, clinical futures, and management of this encapsulated yeast. Cryptococcosis in this book covers both the major pathogenic species, Cryptococcus neoformans and Cryptococcus gattii. The attention to detail and the comprehensive nature of the discussion within each chapter make this book a new standard for written work on a single pathogenic fungal species. There are several outstanding comprehensive medical mycology books in print, but for a single fungal pathogen there are few books that approach the completeness and reference standard of this treatise.

Cryptococcosis remains a deadly disease, with many victims and an enlarging pool of risk patients. Clearly, we need more insights into the pathobiology of this encapsulated yeast to help us treat and prevent its impact on the human condition. This book provides a landmark to acknowledge that this yeast and its study have become a model system for the study and understanding of fungal pathogenesis.

Any molecular biologist, microbiologist, infectious disease epidemiologist, or infectious disease clinician with an interest in mycology, especially cryptococcosis, will find this clearly written, highly organized, well-referenced, and all-inclusive book to be a valuable and up-to-date resource. This latest book devoted entirely to Cryptococcus, edited by Heitman, Kozel, Kwon-Chung, Perfect, and Casadevall, is the premier reference on the biology and pathogenesis of this fascinating and deadly yeast in our increasing population of immunocompromised hosts.

WILLIAM E. DISMUKES, MD
Professor Emeritus of Medicine
University of Alabama at Birmingham
School of Medicine
Cryptococcosis is a dynamic fungal infection that continues to evolve in the second century after its initial recognition as a human pathogen in the 1890s. From its first modest clinical appearance in a case report in 1894–1895, Cryptococcus has advanced as a human pathogen to the point where it causes infection in approximately 1 million individuals per year, with over 600,000 attributable annual mortalities caused by this pathogenic yeast, resulting in approximately one-third of all AIDS-associated deaths. From isolated cases in the clinical practice of immunocompromised hosts to major disease outbreaks in animals, from humans with HIV infection in sub-Saharan Africa to a recent geographically based outbreak in Vancouver, Canada, and the northwestern United States, this fungus has grown prominent in the clinical landscape of 21st-century medicine.

For over 50 years, the ecological path and the biological and clinical features of this encapsulated yeast have been intensely characterized. With the advent over the past two decades of a molecular biology infrastructure, allowing the study of Cryptococcus to expand into genome-wide investigations, the detailed understanding of cryptococcal disease mechanisms has been amplified. Control of the yeast through molecular manipulations, coupled with the years of understanding its immunological properties, has resulted in the development of a pathogenic yeast model for study. Clearly, the mysteries of the sugar-encapsulated yeasts are being stripped away.

This book’s format of multiple authors and chapters provides a comprehensive understanding of what it signifies for Cryptococcus neoformans and Cryptococcus gattii to exist and to produce disease. This is the first multi-authored book on C. neoformans, and that in itself reflects the progress that has been made in recent years, as a vast amount of information has been accumulated by many experts. The goal is to provide the research investigator, clinician, biologist, and mycologist a single source of information and a description of the principles that define this fungal pathogen at the onset of the second decade in the 21st century.

In proximity to publication of this book, the Infectious Diseases Society of America published Clinical Practice Guidelines for the Management of Cryptococcal Disease in 2010. In these guidelines, management of cryptococcal meningoencephalitis is divided into three risk groups: (i) HIV-infected individuals, (ii) organ transplant recipients, and (iii) non-HIV-infected and non-transplant hosts. There are specific recommendations for unique risk populations such as children; pregnant women; individuals in resource-limited environments; patients with infection in sites other than brain, such as the lungs; and patients with C. gattii infections. These guidelines emphasize recommendations for the specific management of complications including increased intracranial pressure, immune reconstitution inflammatory syndrome, drug resistance, and cryptococcomas. We recommend that for these clinical management issues, the Guidelines site (idsaglobalhealth.org/WorkArea/linkit.aspx?LinkIdentifier=id&ItemID=15977) should be visited.

It is our sincere hope that this book frames our knowledge base of what Cryptococcus is, what it has done and can do, what we need to know, and where to look for it. Cryptococcosis is a model infectious disease with a story that will continue to unfold now and in the future.

In closing, it is our pleasure to have served as authors and coeditors for this project. Our goal in this endeavor was not only to highlight advances and progress in the field, but also to serve to bring together the diverse members of our community to give voice to the myriad perspectives on this unique pathogenic yeast. We thank all of our colleagues who are represented here as coauthors for their contributions to the success of these aspirations. We wish to thank our families for their forbearance and patience during the gestation of this project. We also want to graciously and explicitly acknowledge our editors at ASM Press, Gregory Payne and Ellie Tupper, without whose support, encouragement, and tireless efforts this project would not have been realized. We hope that the ultimate success of our efforts will lie in stimulating the field to advance the understanding, diagnosis, treatment, and prevention of this pathogen to such a degree that a future edition of this volume becomes unnecessary.

JOSEPH HEITMAN, Duke University
THOMAS R. KOZEL, University of Nevada, Reno
KYUNG J. KWON-CHUNG, National Institute of Allergy and Infectious Diseases
JOHN R. PERFECT, Duke University
ARTURO CASADEVALL, Albert Einstein College of Medicine
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