"The Fungal Kingdom: Diverse and Essential Roles in Earth's Ecosystem"

The American Academy of Microbiology (AAM) will convene a colloquium of 35-40 expert scientists November 2-4, 2007, in Tucson, Arizona, to deliberate "The Fungal Kingdom: Diverse and Essential Roles in Earth's Ecosystem." This colloquium will be the first in the American Academy of Microbiology colloquia series to focus on fungi and will draw together experts from myriad disciplines to consider what we know and what we do not yet know about this ubiquitous population of successful microbes.

The fungal kingdom is arguably the most successful, with the largest number of known species. Fungi range from microscopic forms to large mushrooms. In fact, the largest living creature on the planet is believed to be a mushroom. Fungi are exceedingly diverse—from those that are common food sources and recycle nutrients in the environment, to yeasts used in brewing and baking, to important symbionts with algae and cyanobacteria in lichens, to ubiquitous pathogens of plants and animals. Therefore, fungi represent both a threat to the ecosystem and a necessary element in its balance. The fungal kingdom is also closest to animals and, consequently, shares many biochemical and genetic processes, allowing us to understand complex biology through simpler model systems and even to produce therapeutic proteins in yeasts with a humanized secretory pathway.

With the advent of genome science, a window has been opened on the molecular basis for this highly successful life form. However, beyond studies on a handful of model fungi and scattered analyses of several dozen other species of interest, we know comparatively little about the more than 1.5 million species of fungi that inhabit the earth.*

As "recyclers" of organic material, the role of fungi in environmental carbon and nitrogen cycling is one of great importance. Soil and mycorrhizal fungi that depend on plants for nutrition are crucial players in sequestration of carbon derived from atmospheric CO_2. The absorptive mechanism of nutrient consumption that the fungi so successfully utilize relies on secreted proteins whose enzymatic activities are responsible for the breakdown of, among other things, plant biomass. As the U.S. turns increasingly to biofuels and bioproducts derived from plant material to mitigate the need for petroleum as both a fuel and a commodity fuel source, the need to understand and

---

* Hawksworth, DL. 1991. The fungal dimensions of biodiversity: magnitude, significance, and conservation. Mycological Research 95:641-655.

Hawksworth, DL. 2001. The magnitude of fungal diversity: the 1.5 million species estimate revisited. Mycological Research 109:1422-1432.

utilize fungal biomass degrading enzymes will continue to grow. As our reliance on bioenergy crops and fungal-derived enzymes for the deconstruction of plant biomass into simple sugars for fermentation into biofuels increases, the threat to U.S. energy security by fungal plant pathogens will dramatically rise. Indeed, in order to produce significant amounts of biofuels and bioproducts and, thereby, decrease the use of petroleum and output of greenhouse gases, we must fully understand the complex interaction of fungi and their environment.

With the recent appreciation of the potential impact of global warming on climatic change and the understanding that the global amphibian decline is being caused by infection by a chytrid fungus, *Batrachochytrium dendrobatidis*, in which global warming may have played a key role, there is a rare chance here to understand the complex interplay between the environment, pathogens, climate, and extinction events. The fact that a pathogenic fungus from the most obscure phylum of the fungi is causing this havoc on the earth's ecosystem raises awareness of the potential threat of pathogenic fungi and highlights the need to develop interventions that could reverse the loss of amphibians that are critical in a variety of ecosystems.

A second recent example of a fungal outbreak involves the primary human pathogen *Cryptococcus gattii*, which has been occurring since 1999 on Vancouver Island, British Columbia, Canada, involving several hundred otherwise healthy patients and animals. In this case, sexual reproduction and global warming have been implicated in the introduction or production of a hypervirulent clone that is the cause of the outbreak. Yet, how and where the inciting events transpired are unknown, as is the full geographic extent of the outbreak, which recent evidence documents is spreading into the Canadian mainland and into the United States.

In parallel are unprecedented advances in genetics and genomics of fungi, including kingdom-wide initiatives from the Fungal Genome Initiative at the Broad Institute (now sequencing the genome of *B. dendrobatidis*) and from the U.S. Department of Energy Joint Genome Initiative (which is sequencing several zygomycetes, as well as mycorrhizal and lichen fungi).

In addition to Earth's ecosystem being potentially affected by imbalance in the fungal kingdom, there also continues the ongoing relationship between humans and dermatophytes, which are among the most successful organisms in maintaining a persistent relationship with the human host. For example, a recent report that the mammalian gastrointestinal track contains fungal DNA from unknown or uncultured organisms from all four phyla (ascomycetes, basidiomycetes, zygomycetes, and chytridiomycetes) highlights how little we know even today about the normal microbiota of animals and humans and the potential of both to disturb our planet's ecosystem.

Certain species of fungi are able to cause disease in plants, animals, and even protozoa. Hence, fungi are non-specific pathogens with such a broad host range that they can be considered trans-kingdom pathogens. Several plant pathogenic fungi and one human pathogenic fungus are included on lists of agents with significant potential for bioterrorism. However, relatively little attention has been given to the weapon potential of fungi in contrast to bacteria and viruses. The ability of fungi as a class of organisms to cause disease in varied species makes the fungi a class of organisms with significant potential for biological warfare. Consequently, there is concern that an inadequate understanding of fungal pathogenesis, combined with underdevelopment in diagnostics, therapeutics, and vaccines, could leave society vulnerable to fungal-derived biological weapons.

The American Academy of Microbiology is providing a leadership role in convening a forum to consider the potential impact of the interplay between the environment and evolution in the interaction between pathogens and their hosts—plants, humans, and animals. The outcome, a report that is analytical and science-based, will give voice to the questions that address what remains unknown about the fungal kingdom of life as the foundation for future research directions. Colloquium participants will discuss where the field is heading and identify scientific opportunities, challenges, and benefits of this research. An important aspect will be the identification of resource and technology gaps that must be addressed in order to advance the field. The results of the colloquium will be published in a report—widely disseminated—that will be of interest to a diverse audience, including the scientific community, funding agencies, educators, policy makers, and the press.

The colloquium will cover the following major topic areas:

- Fungi in host microbiota
- Trans-kingdom pathogenic fungi
- Fungal threats to ecosystems
- Population genetics, species, and sex
- Unmet needs, both agricultural and medical
- Capitalizing on the promise of genomics
- Fungi as potential bioweapons
- Research, education, and communication issues

To our knowledge, there have no recent meetings directly dealing with the issues that will be covered in this colloquium. Our approach to the issues is unique and will result in a practical roadmap for future research initiatives.

Colloquia sponsored by the American Academy of Microbiology are quite different from traditional conferences in which formal presentations are made. Government agencies, industry, and the scientific and lay communities have a strong

need for objective, credible analyses, assessments, and recommendations on critical issues in microbiology. Academy critical issues colloquia are designed to elicit just such information. Our reports are viewed as unbiased statements of the issues and practical recommendations for the future.

The colloquium will be convened for the purpose of developing the intellectual material that will comprise the report. During the colloquium, the bulk of the participants' time will be spent in small working groups addressing each of the questions that the steering committee has developed in advance (see below). The colloquium is highly structured; however, there is sufficient time and flexibility for creative and spontaneous exploration of the issues.

The agenda for the colloquium is as follows:

Day 1
Attendees arrive

Day 2

7:30-8:30 a.m.	Working group breakfast
8:30-10:30 a.m.	General session
	Welcome and introductions
	Charge to participants and goals of colloquium
	Discussion of issues for consideration
10:30-12:00 noon	Working groups (breakouts)
12:00-1:30 p.m.	Working group lunch
1:30-5:00 p.m.	Working groups
6:00-9:00 p.m.	Working group dinner

Day 3

7:30-8:30 a.m.	Working group breakfast
8:30-12:00 noon	Working groups
12:00-1:30 p.m.	Working group lunch
1:30-5:00 p.m.	Working groups
6:00-9:00 p.m.	Working group dinner

Day 4

7:30-8:30 a.m.	Working group breakfast
8:30-12:00 noon	General session
	Working group reports
	Final remarks
12:00 noon	Adjournment

On the final day of the colloquium, the working groups will reconvene in a general session to share their group reports and to discuss any issues raised.

The questions listed below will be the focus of the colloquium; however, participants are not limited to these questions. If additional issues arise in the course of discussions, the colloquium format allows and encourages full exploration of these issues.

I. Fungi in the Host Microbiota

- How many fungi are associated with the human body?
- Which are culturable and which are not culturable? Why is this important?
- Which ones do we know are associated with health and with disease (plants, animals, humans)?
- Who do the fungi interact with?
- How do they interact?

II. Transkingdom Pathogenic Fungi

- Which fungi are transkingdom threats?
- What makes them different?
- What can we learn about pathogenesis and metabolism from these organisms?
- What defines host range and specificity?
- How can model hosts inform pathogenesis?

III. Fungal Threats to Ecosystems

- How do ecosystems protect themselves against fungal invasions?
- How are fungi dispersed?
- What are the implications of fungal dispersal for ecosystems?
- What drives outbreaks and emergence?
- What is the role of climate on outbreaks and emergence?

IV. Interaction of Fungi and the Environment

- What roles do fungi play in the environmental carbon cycle?
- What roles do fungi play in the environmental nitrogen cycle?
- Which environments have been under-explored with regard to fungi?
- How can fungal processes that function in the environment benefit biotechnology (bioenergy, enzymes, bioremediation, etc.)?
- What are the environmental pressures that select for the maintenance of secondary metabolite gene clusters and the secretion of metabolites?

V. Population Genetics, Species, and Sex

- What is a fungal species?

- What defines a species boundary?
- Does interaction with a host drive speciation?
- How does sexual reproduction influence pathogenesis?
- Why are pathogenic fungi so uncommon?
- How has fungal virulence evolved?

VI. Unmet Needs—Agricultural and Medical

- How do we improve diagnosis of fungal disease?
- What new technologies do we need?
- Is there a role for vaccines? If so, what is it?
- What new therapeutic modalities do we need?

VII. Capitalizing on the Promise of Genomics

- What tools do we need to capitalize on fungal genomes?
- How can comparative analysis inform our understanding of pathogenesis?
- How can we best manage genomics resources to enhance their availability?
- What new concepts can we envision from genomic science?

VIII. Fungi as Potential Bioweapons

- What is the extent of the threat?
- Do transkingdom abilities magnify risk? If so, how?
- Are fungi fundamentally different as potential bioweapons? Why?

IX. Research, Education, and Communication Issues

- Are there areas of research we need to conduct to answer fundamental questions about fungi? If so, what are they? What are the priorities?
- What is the role of interdisciplinary teams in research on fungi?
- Should new collaborations be initiated? If so, what are they and who should participate?
- How can these collaborations be encouraged?
- What funding mechanisms should be developed to support this kind of research?
- Are there training or educational opportunities?
- What can the scientific community do to better communicate the issues?
- Is there a role for ASM? If so, what?
- What recommendations do you make for dissemination of the report from this colloquium?

Organizing Committee

Arturo Casadevall, M.D., Ph.D., Albert Einstein College of Medicine (Co-Chair)

Joseph Heitman, M.D., Ph.D., Duke Univ. Medical Center (Co-Chair)
Scott Baker, Ph.D., Pacific Northwest Laboratories
Gerald Fink, Ph.D., Whitehead Institute for Biomedical Research, MIT
Christina Hull, Ph.D., Univ. of Wisconsin-Madison
June Kwon-Chung, Ph.D., National Institutes of Health
Anita Sil, M.D., Ph.D., Univ. of California, San Francisco
Carol Colgan, Director, American Academy of Microbiology

Participants
Karen Bartlett, Ph.D., Univ. of British Columbia, Canada
Joan Bennett, Ph.D., Rutgers Univ.
Richard Bennett, Ph.D., Brown University
Teun Boekhout, Ph.D., CBS, The Netherlands
Dee Carter, Ph.D., Univ. of Sydney, Australia
Leah Cowen, Ph.D., Univ. of Toronto, Ontario, Canada
Melanie Cushion, Ph.D., University of Cincinnati
Fred Dietrich, Ph.D., Duke Univ. Medical School
Françoise Dromer, M.D., Pasteur Institute, France
John Edwards, Jr., M.D., Harbor-UCLA Medical Center
Marta Feldmesser, M.D., Albert Einstein College of Medicine
Bettina Fries, M.D., Albert Einstein College of Medicine
James Galagan, Ph.D., Genome Analysis and Annotation, Broad Institute, MIT
Barbara Howlett, Ph.D., Univ. of Melbourne, Australia
Alexander Johnson, Ph.D., Univ. of California, San Francisco
Patrick Keeling, Ph.D., Botany Dept., Univ. of British Columbia, Canada
Nancy Keller, Ph.D., Dept. of Plant Pathology, Univ. of Wisconsin-Madison
Bruce Klein, M.D., University of Wisconsin
James Kronstad, Ph.D., University of British Columbia, Canada
Jennifer Lodge, Ph.D., St. Louis University School of Medicine
Joyce Longcore, Ph.D., Climate Change Institute, Univ. of Maine
Aaron Mitchell, Ph.D., Columbia Univ.
Nicholas Money, Ph.D., Miami University, Ohio
Eleftherios Mylonakis, M.D., Massachusetts General Hospital, Boston
Joshua Nosanchuk, M.D., Albert Einstein College of Medicine
Frank Odds, Ph.D., Univ. of Aberdeen Institute of Medical Sciences, Scotland
John Perfect, M.D, Duke Univ. Medical Center
Nuri Rodriguez-del Valle, Ph.D., Medical Sciences Campus, Univ. of Puerto Rico
John Taylor, Ph.D., Dept. of Plant and Microbiology, Univ. of California, Berkeley
B. Gillian Turgeon, Ph.D., Cornell Univ.
Rytas Vilgalys, Ph.D., Duke Univ. Medical School
Floyd Wormley, Jr., Ph.D., Duke Univ. Medical School