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EDITORIAL

On a Special Collection in MMBR on Sex in Fungi: Molecular Mechanisms and Evolutionary Implications

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Diverse organisms from fungi to animals and plants undergo sexual reproduction, the process via which genes and chromosomes are reassorted to produce diversity, enabling adaptation to constantly changing environments and enabling progeny to avoid accumulation of deleterious mutations. Sex is thus fundamental in both the origins and the success of species and is conserved throughout eukaryotes. Yet, at the level of the individual sex is one of the most risky behaviors given the increased potential for infection or predation as well as the whims of a meiotic process which involves sharing equally genetic contributions to offspring with another. Biologists have long been fascinated with the genetic, molecular, and cell biological facets that define sexual identity and drive sexual reproduction. By leveraging their special traits, such as ease of experimental manipulation and small genomes, studies on a broad range of organisms in the Fungal Kingdom have illuminated our understanding of these processes and features. The insights that have been derived from studies across this broad kingdom are the subject of this special collection of reviews to be published in *Microbiology and Molecular Biology Reviews* (MMBR).

Recent discoveries of general and fundamental importance that stemmed from studies of sex in fungi provide insight as to why this collection of reviews is afforded the moniker of being of "special" importance:

- Studies of fungal sex have revealed examples of unisexual reproduction, which may also occur in other eukaryotic microbial pathogens (parasites) and share features with parthenogenesis known to occur in animals including fish, snakes, sharks, birds, and Komodo dragons and even in mice lacking imprinting factors.
- Studies on fungal sex have revealed examples of obligate sexual reproduction, which may contribute to understanding why most animals are obligately sexually reproducing in contrast to most eukaryotic microbes, which are facultatively sexual.
- Studies on fungal mating-type loci reveal principles and paradigms that are shared with the evolution of sex chromosomes in plants and animals.
- Studies of fungal mating-type switching have revealed general principles shared with other recombination-based genetic switches, including phase variation in bacterial pathogens, and VDJ recombination in vertebrate immune systems that gives rise to the diverse antibody and T-cell receptor repertoires that are essential for adaptive immunity.
- Studies of fungal sexual reproduction have revealed general approaches to establish that species are sexual, including population genetics studies, whole-genome analyses, and genetic, genomic, and cell biological approaches. These advances serve as a guide for

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discovery of sexual reproduction of other eukaryotic microbes (protists, algae, oomycetes, parasites, diatoms, and ciliates). Many organisms thought to be asexual have been found to be parasexual, cryptically sexual, or sexual, and conditions that support sexual reproduction are often difficult to discover and require tenacity, luck, and patience.

Based on these key insights and advances, it is our hope that this special collection on *Sex in Fungi* will be of interest to both specialist and generalist readers.

Some 55 years ago, a thin text entitled *Genetics of Sexuality in Higher Fungi* (1) was written and published by John Raper. This text presented what was known then about this subject in the basidiomycete fungi. While fascinating, the complex genetics of the system posed a conundrum. How might mushroom species have thousands of mating types, in contrast to the two mating types or sexes typically encountered in in plants and animals and most other fungi? The solution emerged via application of molecular biology approaches developed several decades hence. In parallel, advances in other fungal models, such as the budding yeast *Saccharomyces cerevisiae*, yielded considerable molecular insights into the basis of cell-type specification, mating-type switching, pheromone production, sensing, and signaling and both cell and nuclear fusion. The genetic and molecular elucidation of the blueprints for wiring a mating system provided a foundation that informed research into the mechanisms and mechanics of sexual reproduction across the Fungal Kingdom. As genetics later elucidated, sexual mechanisms in both the mushrooms and budding yeast share many commonalities, such as use of lipopeptides for sexual signaling and mating-type loci with conserved transcription factors. In fact, the demonstration that mushroom pheromones and receptors of mushrooms can recapitulate normal yeast sexual signaling harkens to some 500+ million years of shared strategy. This observation has been critical for transferring knowledge across the numerous and fascinating model fungal species. With advances in genomics, a window was opened enabling kingdom-wide studies of sex determination and sexual reproduction and its evolution to be conducted. The impact of comparative genomics on our understanding of sexual reproduction will be central in many of the contributions in this series.

In 2007, a textbook on this subject entitled *Sex in Fungi*: *Molecular Determination and Evolutionary Implications* (2) was published by ASM Press. As some 14 years have now elapsed since that time, and many advances in the field have occurred, it seemed an auspicious time to revisit this subject with an expanded and renewed scope. We have invited contributions to this series from a contingent of experts in the field to review the increase in knowledge of these fascinating biological systems and processes. This series will include reviews on the evolution and function of the mating-type locus, the specialized genomic region that orchestrates establishment of cell type and sexual reproduction, and on novel mechanisms of mating-type switching that have evolved repeatedly and independently. The series will feature reviews on model, nonmodel, and pathogenic fungi, such as the inaugural review, accompanied by this editorial, on the animal-pathogenic *Pneumocystis* species that undergo obligate sexual reproduction in the lungs of their infected hosts (3). Necessity requires us to understand mating in the clinically relevant *Pneumocystis*, just as demand for field production of the edible and delicious morel fungi has required a better understanding of their sexual mechanisms as will be described in a forthcoming article by Du and Yang. Soon-to-be-published articles in this special collection series will cover processes regulated postmating, such as sporocarp development and evolution as explored in articles on Pezizomycotina, the filamentous Ascomycota, by Wilson et al. and on Agaricomycotina, the mushrooms, by Virágh et al. The series will include reviews that expand further on the themes presented in the original 2007 text, including key aspects of sexual reproduction including mate recognition and interactions, cell-cell fusion, nuclear fusion, fungal development, and meiosis and sporulation. Additionally, the series will cover mechanisms of both outcrossing modes of sexual reproduction (heterothallism) and inbreeding modes of sexual reproduction (homothallism), and the transitions that have occurred between these two modes. Finally, the series will include reviews on the implications of sex and studies of postzygotic isolation and hybridization to cover a broader evolutionary context.

It is our goal and ambition that these reviews be not simply descriptive but rather forward looking and a synthesis of findings from different areas of the field. In so doing, it is our hope that the final product will serve as an exposé of this central process and its impact on an entire kingdom of life, and one whose species are especially amenable to genetic, molecular, and genomic analysis. The biological principles emerging are profound and provide paradigms for how to establish and maintain cell-type identity, how cells sense and respond to extracellular signals, the roles of genome rearrangement in changing cell identity and fate, and how genomic regions governing mating-type or sexual identity are organized and evolving.

It is our intent that this new series entitled *Sex in Fungi: Molecular Mechanisms and Evolutionary Implications* both encompasses our current state of knowledge to guide research over the next several decades of study and also pays homage to those who made this effort both possible and meaningful. First, this series is dedicated to Cardy Raper. Beginning with a genetic blueprint provided by John Raper's seminal text (1), Cardy conducted the molecular analysis of the *Schizophyllum commune* mating-type loci over several decades in her own laboratory at the University of Vermont. Cardy inspired a multitude of investigators including editors and authors of reviews in this series, and without her, the field would not be what it is today. We also dedicate this series to Lorna Casselton and Patricia (Pat) Pukkila. Their studies on *Coprinopsis cinerea* provided a genetic system complementary to *S. commune*, and their development of transformation and gene deletion approaches opened the door to studies of the complex A and B mating-type loci and to the discovery of a novel type of gene-repeat silencing known as MIP. We are indebted to Cardy, Lorna, and Pat for seeing sooner and farther than others, for sharing their discoveries with us, and for making this series possible and worthwhile.

It is our pleasure to serve as coeditors for this series, and we invite you the readers to share your experiences and ideas with us. We are inspired to see just how far the field has progressed since the original *Sex in Fungi* text in 2007 (2). In closing, we thank our families, our laboratory members, numerous readers, and our editors, Christine Charlip (ASM Press), Corrie Detweiler (MMBR), and Orna Cohen-Fix (MMBR), without whose efforts and encouragement, patience, and tolerance this series would not be realized.

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