

## Book review

# A Fungus Amongst Us

Jennifer Loros

Department of Biochemistry, The Audrey and Theodor Geisel School of Medicine at Dartmouth Hanover, NH, USA

Durgadas Kasbekar and Kevin McCluskey have edited an engaging new book called *Neurospora* Genomics and Molecular Biology on the scientific contributions of *Neurospora crassa*, the model system made famous with George Beadle and Edward Tatum's 1958 Nobel prize in Physiology or Medicine. That work, of course, pioneered the one gene, one enzyme hypothesis that directly led to the understanding that an organism's genes encode polypeptides. This is a book about the best understood of the filamentous fungi.

Fungi comprise one of the six Kingdoms of life on earth, being evolutionarily the closest eukaryotes to the Kingdom of animals; this has led to their extensive use in scientific research as cellular models for the more complex or less tractable cells or organisms. A list of why fungi are important would be very long and could include their role as environmental biomass decomposers, mycorrhizal interactors with the majority of vascular plant species on earth, cellular machines in industry and commerce (where would we be without bread and cheese, wine and beer and enzymatically faded blue-jeans?) and because fungi are serious pathogens of both animals and plants. Since fungal cells are so similar to animal cells, fungal infections in people, especially the immune-compromised, are hard to treat and are responsible for an enormous number of deaths worldwide.

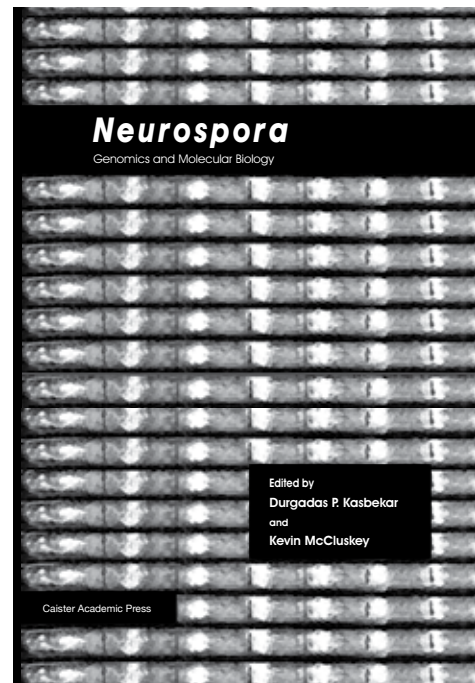
And yet the fungi are quite understudied as a group. So just how large is that group? Taxonomists have described somewhere in the neighborhood of 100,000 species of fungi and are currently struggling with how to bring that number more in line with current estimates of the total number of species out there. Challenging taxonomists are the modern molecular methods of nucleic acid sequencing combined with the ability to analyze widely diverse sets of sampling environments. Total estimates for fungal species have continued to rise dramatically in recent years with 1.5 million species an often-quoted number although many mycologists think it could be up to a log order higher.

The Model Organisms for Biomedical Research web page at NIH lists three fungal models: *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe* and *Neurospora*. The first two being yeasts, and *Neurospora* being the archetypal of the filamentous group that comprises the

## *Neurospora: Genomics and Molecular Biology*

Durgadas P. Kasbekar and Kevin McCluskey (Eds.)

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vast majority of fungal species. (As a biased aside, I do think NIH should really include at the least the other well studied filamentous fungus in this group, *Aspergillus nidulans*). Models for eukaryotic cells help us figure out how processes work in much more complicated cellular systems and these two yeasts have been terrific models for many things that all cells do from cell division to trafficking proteins. *S. cerevisiae* is well established and especially well financially supported, rightly so, for investigations into a broad biological arena of problems. *Neurospora* has somewhat more than 10,000 genes, not quite twice as many as baker's yeast, and not surprisingly, can do many things the yeasts cannot, or does them in ways significantly more similar to the ways used in more complicated eukaryotes. *Neurospora* has been a useful model for animal and other types of cells and organisms in the areas of circadian rhythms, self versus non-self recognition, gene processing, epigenetics, homology-based gene silencing, mitochondrial biogenesis, evolutionary adaptation and speciation, protein signaling cascades and functional genomics. But this haploid, non-pathogenic and easily manipulated fungus has also been superbly useful as a model for other fungi. Areas of research beyond those listed above include sexual and asexual development, morphology, photobiology, cell polarity and cell fusion. At some level all of these areas are addressed in this new book.

*Neurospora* species are found world wide and much is known about their natural history thanks to David Perkins and his colleagues who surveyed thousands of wild collected specimens. *Neurospora*'s special features as a tractable laboratory organism include it's overall ease of culture, extensive collection of genetic tools including several

\*Corresponding author: Email: Jennifer.Loros@dartmouth.edu

thousand available genetic mutations each with phenotype analysis, a complete gene knockout collection, and it's visually beautiful products of meiosis arranged as linear octads that has allowed in depth studies on recombination, gene conversion and first and second meiotic division genetics.

The volume's authors are a nice mix of the *Neurospora* old guard and both relatively new or recently independent members of the *Neurospora* community. This book will be useful for novice and experienced researchers alike, a go-to manual for graduate students and post-docs new to the field and the organism and any scientist interested in the fungi. It will serve as an entrée into less laboratory-amenable but more biologically and medically important fungi.

The book's 15 chapters opens with a nice introductory chapter by Anthony Griffiths, venerated by all genetics students who have relied on his Introduction to Genetic Analysis textbook. The first section addresses how the fungus lives and grows. The first chapter here covers the complex and overlapping areas of incompatibility in cell-cell recognition and the proteins that control it; how work in *Neurospora* has allowed identification of vegetative incompatibility genes in other fungi and the relationship to morphological aberrations and programmed cell death; and finally, the genomic alterations involved in the interesting process of "escape" whereby a sector of an incompatible and morphologically aberrant colony becomes wildtype-like, allowing growth away from the colony. The next chapter discusses the different mechanisms involved in vegetative growth leading to the distinctive polarized extension and branching of these fungi to best invade and utilize an organic substrate.

The following several chapters, 4 through 8, are loosely organized around genetics and genome structure and maintenance. Alan Radford discusses the glycosyl hydrolase enzyme family in terms of the how and why of domain shuffling in protein structure, amplification of genes into gene families and how this relates to fungal evolutionary clades. Many interesting aspects of fungal biology fall under the umbrella of complex phenotypes, the focus of a chapter on the use of quantitative trait locus analysis and genome-wide association mapping in *Neurospora* with an

emphasis on encouraging more investigators to utilize these potentially powerful tools in conjunction with wild population variability to understand non-Mendelian traits. The next three chapters have David Catcheside and colleagues covering the genetics of recombination and Durgadas Kasbekar examining unique means of genome defense both followed by a comprehensive and informative chapter on DNA mutagenesis and repair and the ongoing uncovering of novel genes involved in the process. A minor quibble I had here was with the book's organization. I probably would have grouped Radford's chapter on gene amplification with Kasbekar's on gene duplications and genome defense and placed these after mutagen response and repair and then placed the quantitative genetics chapter towards the end of the book, before the final chapter covering genomics.

The bulk of the book follows with chapters 9 through 14 all addressing the organism's interface with the environment and the accompanying signaling responses. Chapters by Corrochano and Larrondo and their co-workers are especially close to my heart, reporting the current state of research on photobiology and circadian rhythms respectively. Borkovich and her group report on the heterotrimeric G proteins so important in asexual and sexual development, stress responses and nutrient sensing. Other chapters detail our understanding of calcium signaling, the cAMP-dependent and MAP kinase pathways and the well understood molecular underpinnings of carotenoid pigment production in response to light.

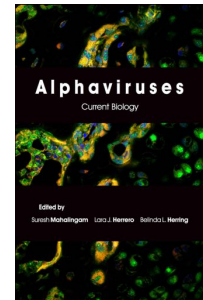
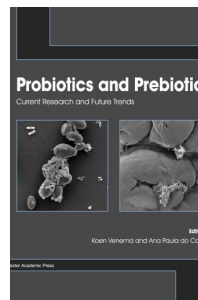
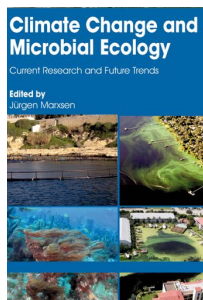
The book ends with Weist, Baker and McCluskey's examination of *Neurospora*'s beginnings as an early model for genetic study through its current place as the leading model for the filamentous fungi. The *Neurospora* DNA sequence was released in 2003 as the first and archival quality genome sequence for the filamentous fungi. They recount the fascinating insights into genetic structure and makeup that arose from this information and how it spawned a literal frenzy of fungal sequencing in the following decade with resulting opportunities for detailed comparative genomics.

This terrific new book was a pleasure to read; it belongs in every lab that works on fungi and every academic library.

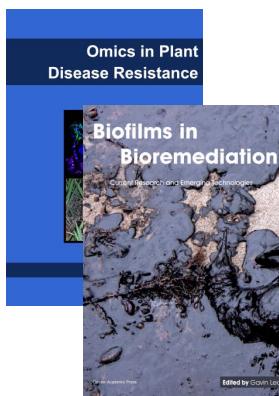
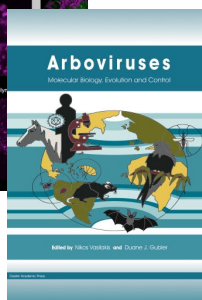
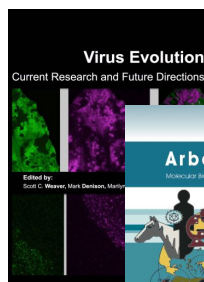
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