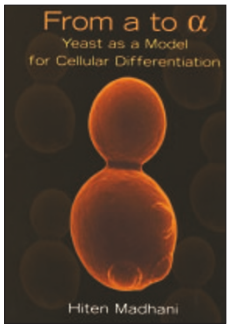
Awesome, in brief



From a to α: Yeast as a Model for Cellular Differentiation

By Hiten D Madhani

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Reviewed by Amar J S Klar

The cryptic letters in the title of this book should be explained to the general readership of *Nature Genetics*. The bold letter **a** and the α refer to the two mating cell types of budding yeast, *Saccharomyces cerevisiae*. Usually, mating types in fungi are referred to as 'plus' and 'minus', but Carl Lindengren, a pioneer in yeast genetics, assigned the α symbol on his typewriter to describe yeast and the name stuck. *From **a** to* α is a short book that succinctly describes the biological mechanisms for cellular differentiation discovered through studies of a single organism.

Dr. Madhani's stated goal is to teach beginners in biology the major achievements that were made using yeast as a model for cellular differentiation. The book consists of nine chapters, and subheadings point precisely to the conclusion of each section.

The lessons learned from the yeast studies are stated refreshingly in a direct, matter-of-fact style, without repeating in detail the experiments that led to the knowledge. A description of the text of each concept is pictorially supported by a figure, and a full one-third of the space is allotted to figures—all features making it one of the most pleasantly readable books in biology.

The success of yeast as a model system is due both to the economics of growing the culture in laboratory conditions and the opportunity to investigate cellular differentiation mechanisms at the single-cell level. Most importantly, the mutagenesis and conventional meiotic genetic analysis feasible with unlimited numbers of progeny have allowed researchers to identify and order genes according to their roles in biological pathways. Thus, this book celebrates what is sometimes referred to as the 'awesome power of yeast genetics'.

Cell-type alteration by the highly regulated genome rearrangement mechanism at the mating-type locus and the gene silencing phenomenon discovered in yeast form the two central chapters around which the rest of the book is woven. Because of the success of studies involving the mating-type system, it was initially speculated that regulated rearrangements might be a major mechanism for cellular differentiation in biology. However, with few exceptions, such a mechanism has not been widely used in eukaryotes. On the other hand, the phenomenon of gene silencing by epigenetic controls, discussed in chapter 7, is likely to be a widely used mechanism in general biology for regulating gene expression during development. Mechanisms for such gene regulatory controls in diploid organisms are more likely to be discovered sooner thanks to the paradigms summarized in the book. Discovery of the phenomenon of gene silencing in eukaryotes suggests that we need to tinker with Jacques Monod's proclamation, "All that is true for *E. coli* is true for elephant." Lessons learned from gene silencing studies in yeast, however, can be used to suggest that cell type–specific epigenetic controls installed in somatic lineages might be the key for development in higher eukaryotes.

In light of what we have learned from yeast studies, and concerning the future of the field of eukaryotic development, one of the great teachers of genetics of our time, James F. Crow, wrote, "I don't know whether there will be beautiful, general theories to come out concerning development, something really nice like Watson and Crick's double helix or there will be an accumulation of more and more details. I'll confess to a secret hope for the former." We now know that Crow's secret hope is fulfilled in yeast development. Studies of budding yeast have uncovered DNA alterations and epigenetic gene regulation mechanisms. Likewise, equivalent studies with the distantly related fission yeast have shown that sister cells differ developmentally simply because of inherent sequence difference in strands of DNA at the *mat1* locus that are subjected to strand-specific imprinting.

Although the book is about yeast, I find particularly refreshing the information provided in 'boxes' describing the relevance of yeast studies to higher organisms and human diseases. Such boxes highlight the topics of cooperative binding of proteins to DNA, human hormone precursor processing, the protein phosphorylation cycle, stem cell division, asymmetric cell division in the fly, silencing of *HOX* genes, silencing in fission yeast and cell division in epithelial tissues. Admittedly, I am somewhat biased, but I believe that in the last chapter of the book, more discussion of the analogous fission yeast system and delineation of another strategy used by *Schizophyllum commune* would have been useful to many readers.

This book should be a 'must read' for anyone beginning to experiment with yeast. I suspect most experts in the yeast field are inundated with literature and selectively keep up with developments primarily in their immediate field. Reading this book will help such experts to appreciate developments in other areas of yeast research. Although yeast has only a handful of cell types, the principles learned from yeast studies are bound to help both beginners and seasoned researchers wishing to discover the underpinnings of cellular differentiation and development and the cause of disease in higher eukaryotes with vast arrays of cell types.

Finally, as someone who helped discover the mechanism of gene silencing and the mechanism of mating-type switching by DNA transposition, I found that reading this book evoked a lot of nostalgia. Certainly, it is most fitting that the book is dedicated to one of the major contributors and a leader of the field, Ira Herskowitz. If Dr. Herskowitz were alive today, I am sure he'd be elated by reading the book, just as I am, and would have patted the author on the back for a job well done.

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