

area it does not cover concerns the trickier questions that young investigators face when submitting their first grant. For instance, many PIs do not know how to direct their grant to the appropriate study section or when they should contact a program official for advice. However, as pointed out in one of the quotes, there is nothing as useful as talking to senior colleagues: "Remember, your colleagues are concerned about your getting funded, and they realize the road may be bumpy. They will help if asked."

The biggest hurdle other than obtaining funding for most young investigators is getting and supervising people. Managing personnel is difficult because unlike experiments, it will not work the same way every time. Although it is critical that employees are treated consistently, applying a single rule to everyone will probably backfire. The authors therefore outline the various reasons why each type of employee is valuable and provide estimates about how much time a PI should expect to spend with them. In addition, there are good ideas about how to assign dissertation projects as well as various tips for teaching students how to do experiments and write papers.

In addition to the topics of managing money, people, and science, the book also explains how to be a faculty citizen, mentor, and teacher throughout the first years. The authors describe how to say "no," and how to get along with the chair and other colleagues. The issue of picking and using mentors is also covered, a potentially valuable resource for new investigators. However, there is no discussion of issues that might face specific groups of faculty members, such as women or minorities. There is an excellent section that explains how to review and make decisions about manuscripts and grant applications. In addition, the book offers strategies for preparing and submitting papers and learning how to respond to reviewer criticisms when resubmitting a manuscript. The teaching chapter offers many organizational tips for running a course.

The book ends the junior PI phase by discussing the promotion process. It describes how to prepare a dossier and the various expectations that may need to be fulfilled to obtain tenure. Since it will be too late to suddenly obtain enough publications, it is a good reminder that young investigators need to monitor their own progress over the years. The strategies for assembling a strong packet are good. Finally, the book actually makes suggestions for how to handle a negative promotion.

The greatest strength of the book is also the biggest weakness—none of the topics are covered in detail. The advantage is that the reader gets a broad overview about all the key issues in starting a lab. However, the generalizations mean that any unusual or difficult issues, such as how to handle sexual harassment or maintain lab enthusiasm, are not covered. Although some of the deeper issues are not discussed, a similar book by Kathy Barker called *At the Helm, a Laboratory Navigator* is much more focused and thorough about complicated personnel issues. Since Barker's book does not include issues described in *Academic Scientists at Work*, such as how to obtain funding or how to organize a class, they are an excellent complementary set.

Academic Scientists at Work is an extremely fast and easy read, so junior PIs will have an easy time fitting it

into their schedule. Although there will be a tendency to feel like this is the last thing that a new investigator should spend time doing, the book is well worth the time. The book replaces that senior faculty mentor who is not around when a crisis strikes. Another advantage to reading *Academic Scientists at Work* is that it forces one to think about things ahead of time that might save a lot of effort in the long run. For good reason, most junior PIs are very focused on the current major issues. Why worry about a class that needs to be taught next semester when a tech needs to be hired today? Although this is true, the great thing about the book is that it points out things that will need to be dealt with in the future so one is better prepared to handle them when the time comes. I would encourage new investigators to read the book, and to read it earlier than later. Preventing even one mistake will be a sufficient return on the time invested.

Sue Biggins

Fred Hutchinson Cancer Research Center
1100 Fairview Avenue N., A2-168
Seattle, Washington 98109

Chromosome Beauty

Chromosomes: Organization and Function
By Adrian Sumner

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Without question, the chromosome holds a special place in the heart of many biologists. Many are captivated by its aesthetic appeal and, for some, it has come to symbolize the most tangible and beautiful display of our genetic substance. To add to their appeal, chromosomes can be shown to friends and visitors more or less as they are in our cells, using an affordable microscope. Indeed, I know of a few chromosomologists who have grown so fond of, or comfortable with, this subject that they have become reluctant or even terrified to step out of what is quite literally the microscope stage, into the submicroscopic and fast-moving world of DNA and its companion molecules. In the end, though, when pitched against something of the enormity of the molecular tidal wave, we have witnessed the inescapable withering of research of the sort that is based purely on microscopic observations. In their place, we have seen the emergence of many exciting studies that have elegantly embraced the new molecular tools to peer deeper into what lies beneath the chromosome.

So what have we learned about the chromosome? For one, we have sequenced many genomes and now know a great deal about the nucleotide sequence of the genes that are dotted from one end of a chromosome to the other. We know about what types of DNA and, to a much lesser extent, proteins cohabit the longitudinal segments of a chromosome. We have become ruthlessly

good at knocking these proteins about in cell culture or in whole model organisms to see what any disastrous consequences might tell us about their functions. We have become obsessed with mechanistic insights, not to mention little choice if we want to woo the big journals and granting bodies; thankfully, though, we have learned quite a few things about the mechanisms for many of the processes.

And what remains to be learned about the chromosome? The answer is a definite “whole lot more.” To this end, we should be, and some already are, critical that the “reductionist approaches” that we have grown to depend so much on, allow us to look at only one or a very limited number of components at a time, in isolation from most other possible players. They do not help us to capture and interdigitize all the important in-between pieces that are still missing from the big picture. Take a couple of examples that have been covered in Adrian Sumner’s book, *Chromosomes: Organization and Function*. For the centromere: although we have now identified a plethora of proteins on this structure, we still have little idea as to what many of them actually do, especially concerning how they interact physically or temporally, and what other players are missing, to enable us to reconstruct the complete pathways for both the assembly and proper workings of this important structure. Or take another example: although we have known for a considerable time now about the basic components of a nucleosome and how the chromatin undergoes the initial 40- to 50-fold packing (up to the solenoid stage), we struggle to demonstrate how it reaches its final 10,000-fold state of condensation—never mind the even less understood process of decondensation. Further methodological and technological advancements such as those along the lines of proteomics (Tyers, M., and Mann, M. [2003]. *Nature* 422, 193–197.), physical and temporal imaging, and mathematical and computational modeling (Chitnis, A.B., and Goodhill, G.J. [2001]. *Cell* 105, 328–329.), will clearly be necessary to address the big-picture tasks. The recent launch of a pilot Encyclopedia of DNA Elements (ENCODE) project by NIH, aimed at testing and comparing methods for the exhaustive identification and verification of functional elements in the human genome, is a step in the right direction.

The story so far is much like that of Frodo, setting out on a journey through a massive and daunting labyrinth in order to deliver the ring of Mordor to the fires of Mount Doom. Frodo now has the unenviable task of learning everything he can about the labyrinth (primary and interacting pathways), what players (genetic and epigenetic) are interested in the journey, with whom he can form partnerships (intermolecular complexing and networking), what he and his partners can do (functional understanding of each player), the loyalty and worth of his fellow travelers (some may have many and variable talents or agendas, and others may be dispensable), and any obstacles confronting him (regulatory and inhibitory mechanisms). For the sake of humankind, elves, dwarves, and hobbits alike, Frodo will, of course, gallantly and painstakingly inch his journey forward. Having access to useful and accurate intelligence will definitely help his journey, and here enters Sumner’s book.

The book dwells heavily on many long-unresolved topics relating to chromosomes and gives them a much-

needed modern treatment with molecular tales. It is a text attempting to cover practically everything to do with chromosomes and, generally speaking, has done a very fine job in that regard. Understandably, given that it is a mere 238 pages, the book falls short on detail in many places for which individual books and major reviews can be and have been written, but through clever and liberal use of tables and figures, *Chromosomes: Organization and Function* has managed to capture a large amount of information, with adequate referencing and web linkages to extend its depth. The inclusion of an impressive number of real life micrographs and images of chromosomes doing various things is particularly pleasing, not only because of the illustrative utility of these pictures, but also for the vivid reminders they provide of the aesthetic appeal of the subject.

The first chapter provides some historical background and reminisces about the few fascinating but largely ignored years in the mid-to-late 1800s when four of the most commanding discoveries of modern biology had their unparalleled beginnings in remarkably close succession: the publication of the principles of genetics in 1866 by Mendel, the isolation of an impure form of DNA in 1868 by Miescher, the description of mitotic chromosomes in 1873 by Schneider, and the proposal of the theory of evolution by Darwin in the 1860s (although that last is not mentioned in this book). In 2003, we commemorate 50 years of cracking the DNA structure, but those early discoveries 130 or so years ago deserve every bit as much to come to the forefront of our mind. Chapter two gives an overview of the events that occur at mitosis and meiosis and provides a useful background for subsequent chapters. The next few chapters take us from the DNA molecule through to its assembly into chromatin, interphase chromosomes, and finally mitotic and meiotic chromosomes. These chapters provide a good mix of tidbits of information—such as how many nucleotides and genes are found in various species, and how long and how thick the DNA and its more compacted chromatin and chromosome relations are—and more substantial discussions of known mechanisms and individual protein involvements in processes such as: mitotic start control, DNA replication, spindle checkpoint, sister cohesion and separation, meiotic crossing over, chromatin assembly and modification, arrangement of interphase chromosomes, and how the cell deals with different types of DNA damage. These accounts, while inevitably reflecting the incompleteness of information in many areas, have quite unmistakably succeeded in portraying the impressive advances we have made.

The book then turns to specific features of the chromosome, devoting a chapter each to euchromatin, heterochromatin, sex chromosomes, imprinting, nucleolus organizer regions, centromeres, telomeres, lampbrush chromosomes, and polytene chromosomes. These chapters are full of useful information of both descriptive and mechanistic kinds. Several tables list large numbers of protein components involved in various processes. Although the lists in these tables are not exhaustive and do not provide enough information to give the reader a real understanding of the roles of the individual components, they nonetheless serve to inform on the range of proteins that have been discovered. These chapters also

contain a wealth of information that will help the reader to appreciate both the constancy and the diversity of chromosomal phenomena through the phylogeny.

The last three chapters offer interesting reading on the role of the chromosome in evolution, disease, and genetic modification and therapy (through chromosome engineering). These pages provide a welcome reprieve from the hard facts of the earlier chapters, turning to the more speculative arena of evolution, as well as possible clinical and practical implications of chromosome biology.

Overall, this is an excellent book, written in an easy-to-read style and packed with interesting and accurate information that both novices and learned scholars of Chromosome and Cell Biology will find useful. It takes on many fast-changing topics, but much of the carefully presented information in this book should endure the inevitable onslaught of new research findings. The book could have been strengthened in many areas—for example, by providing a more in-depth evaluation of weak or missing links, discussing the different chromosomal structures more interactively (such as the significance of common proteins or shared interphase arrangements), highlighting the role of epigenetic influences on and plasticity of some of the structures, indicating possible future research methodologies and directions, and perhaps offering some predictions as to what the field may hold in the years to come. But to insist on these would be to pick faults for their own sake, and to unfairly detract from a job that is already well done. Whether read from cover to cover or used as a handy reference, this is a book that will educate on the beauty and complexity of the chromosome. And finally, then, to those embarking on the journey with Frodo—good luck!

K.H. Andy Choo

Murdoch Childrens Research Institute
Royal Children's Hospital
Flemington Road
Parkville 3052
Australia