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# Book Review

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**Malaria Parasites. Comparative Genomics, Evolution, and Molecular Biology.** Jane M. Carlton, Susan L. Perkins, and Kirk W. Deitsch (editors). Caister Academic Press, 28 Queens Road, Hethersett, Norfolk NR9 3DB, UK. 2013. 280 pp. ISBN 978-1-908230-07-2. US $319 (hardback).

*Review by Jos J. Schall*

Charles Laveran's first observation of a human malaria parasite in 1880 marks one of the great events in medical science; thanks to Laveran and the contemporaneous studies by Pasteur, the germ theory of disease had arrived. Soon, the first golden era in malaria studies was underway, a time of field exploration, experimentation, and microscopes. The parasite's life cycle was worked out in detail within a few decades, and surveys found similar parasites exploiting a great range of mammals, birds, and squamate reptiles over a world-wide distribution (Garnham 1966). Clearly these parasites are ancient and both extremely diverse and ecologically successful. The malaria parasites of humans may be the "million murdering death" that torments billions, but malaria parasites are also important pathogens of wildlife. We have now entered a second golden age for malaria research thanks to the advent of the molecular revolution in biology. This slim volume provides 11 clear, concise, and up-to-date chapters reviewing current knowledge of "comparative genomics, evolution, and molecular biology" of the malaria parasites. But, aside from a few short plaintive calls for more study of the malaria parasites of nonhuman hosts, almost all of the work reported here centers on only two of the six species of *Plasmodium* infecting humans. There are hundreds of described species of *Plasmodium*, mostly from bird and lizard hosts (Valkiunas 2005; Telford 2009), but also from bats, monkeys and apes, African antelope, and even water buffalo. So why should readers of this journal be interested in a book that centers so strongly on a few human malaria parasites? There are two compelling reasons.

First, we now have an understanding of the parasites that would have seemed impossible just 20 years ago. A concise review of this information is very welcome, but while reviewing the state of malaria studies, each chapter also provides a sterling description of the methods, goals, basic findings, and even philosophy of modern molecular biology. Try reading the molecular biology literature, and we typically meet a wall of jargon that is frustrating to many readers. Each chapter here, however, is clearly meant to reach a broad audience. Terms are defined on first use and put into a more general context. The power of each technique is described, but also its limitations.

I will highlight only a few chapters, although all are models of what reviews should accomplish. The opening chapter by E. S. Martinsen and S. L. Perkins on the phylogeny of malaria parasites serves both as the best single stop to learn of the diversity of the group as well as a concise review of the methods and goals of molecular systematics. One section in the chapter (in a book with "molecular biology" in its title!) is labeled "Why

molecules are not enough for taxonomy: a cautionary note." The chapter presents a convincing case that the evolutionary history of malaria parasites will be revealed by both molecules and microscopes. A similarly temperate perspective is found in a chapter on sequencing techniques by J. M. Carlton and her colleagues. They review the "next generation" gene sequencing methods with enthusiasm, but they are not blind enthusiasts. The benefits and drawbacks of each platform are provided, followed by all of the problems researchers encounter. The results of "next gen" sequencing may be spectacular, but there is still a very big place for the "early-gen" Sanger method. A chapter on gene expression by K. W. Deitsch and R. Dzikowski touches on a great array of issues, including sexual differentiation (the molecular mechanism turns out to be conserved across the eukaryotes), alternative splicing of mRNA (more functional genes exist than sequence genes, and this is again conserved across the eukaryotes, including humans), and the mysteries of epigenetic memory.

The volume thus serves as a useful introduction to molecular methods, but a second reason wildlife disease specialists should be interested is that specialists in molecular biology of malaria parasites need to recognize the great diversity of the parasites and the work done by wildlife disease researchers. Years ago, a program officer at the National Institutes of Health (NIH) told me that NIH wanted to use the comparative approach and fund "new models" for malaria research. Well, the hundreds, perhaps thousands, of species of malaria parasites of nonhuman hosts aren't "models," they are organisms. I was then told that the "new models" being sought were new isolates of *Plasmodium falciparum*. That is not the comparative approach that has proven so powerful in biology! Collaboration between the molecular jockeys and wildlife disease specialists will certainly be fruitful. We should bring these powerful techniques into the study of wildlife malaria parasites, both for applied research and to cast a more general light on the biology of *Plasmodium* and its relatives. For example, only a single strain within the very diverse "species" now called *Plasmodium relictum* is responsible for the ongoing destruction of the Hawaiian bird fauna (Beadell et al. 2006). Why only that single genotype? A comparative genomics approach will tell us a great deal about the evolution of virulence. One of the editors of the volume, S. L. Perkins (Perkins 2000), discovered that a species of lizard malaria parasite split into two species: one that lives in erythrocytes (typical for *Plasmodium*) and a daughter species that has moved into two classes of white blood cells. The only similarity between these two cell types is the word "blood" in their common names. Receptor sites, membrane structure, and nutritional resources all are completely different. No hemoglobin is within a white blood cell, but instead a witches' brew of molecules meant to kill, well, parasites! Malaria researchers are impressed that different species of *Plasmodium* in humans have moved into mature vs. immature erythrocytes, but the lizard malaria story is even more intriguing. Presumably, rather few genetic changes were involved in the sibling species; how is the major shift in phenotype possible? A third golden era of malaria studies should come from collaboration between the molecular labs and field researchers in wildlife disease.

The volume is compact and beautifully presented, with high-quality design, printing, and binding. One complaint has to be its unfortunate price. Presumably the publishers chose a small press run, and the resulting high price makes this book not one for professionals and students to enjoy in their personal library. The editors and authors, though, deserve high praise for the care given in preparing such a valuable volume.

## LITERATURE CITED

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