

9

THE BIOLOGY OF PARASITISM

A Molecular and Immunological
Approach

Editors

Paul T. Englund

Alan Sher

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Paul T. Englund

Department of Biological Chemistry
Johns Hopkins School of Medicine
Baltimore, Maryland

Alan Sher

Head, Immunology and Cell Biology Section
Laboratory of Parasitic Disease
National Institute of Allergies and Infectious Diseases
Bethesda, Maryland

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Cover:

Upper Left: Stage specificity of antiparasite vaccines. See Sher, page 171.

Upper Right: Scanning electron micrograph of a *T. brucei brucei* among red blood cells. ×5500. See Donelson, page 372.

Lower Left: Separation of *Plasmodium falciparum* chromosomal DNA molecules by pulsed field gradient gel electrophoresis. Such separations provide a powerful means of mapping the parasite genome and analyzing the structure of individual chromosomes. Figure courtesy of Thomas E. Wellems, M.D., Ph.D., Malaria Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.

Lower Center: Schematic diagram showing trafficking of membrane proteins from the intracellular *P. falciparum* parasite to the RBCM. See Howard, page 137.

Lower Right: Sketch of the structure of a monomeric subunit of the MITat 1.2 VSG, based on crystallographic evidence. See Turner, page 361.

MBL Lectures in Biology
Volume 9

**THE BIOLOGY OF
PARASITISM**

**A Molecular and Immunological
Approach**



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The Biology of Parasitism: A Molecular and Immunological Approach

Paul T. Englund and Alan Sher, *Editors*

Contributors

R.F. Anders, The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia [201]

Stephen M. Beverley, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115 [431]

Barry R. Bloom, Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10461 [265]

A.E. Butterworth, Medical Research Council and Department of Pathology, University of Cambridge, Cambridge CB2 1QP, England [43]

Richard Carter, Medical Research Council External Scientific Staff, Institute of Animal Genetics, University of Edinburgh, Edinburgh, Scotland [225]

Tamara L. Doering, Department of Biological Chemistry, Johns Hopkins School of Medicine, Baltimore, MD 21205 [401]

John E. Donelson, Department of Biochemistry, University of Iowa, Iowa City, IA 52442 [371]

Dennis M. Dwyer, Cell Biology and Immunology Section, Laboratory of Parasitic Diseases, National Institutes of Health, Bethesda, MD 20892 [449]

Thomas E. Ellenberger, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115 [431]

Paul T. Englund, Department of Biological Chemistry, Johns Hopkins School of Medicine, Baltimore, MD 21205 [401]

Michael Gottlieb, Department of Immunology and Infectious Diseases, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD 21205 [449]

Gerald W. Hart, Department of Biological Chemistry, Johns Hopkins School of Medicine, Baltimore, MD 21205 [401]

Dale Hereld, Department of Biological Chemistry, Johns Hopkins School of Medicine, Baltimore, MD 21205 [401]

Russell J. Howard, Malaria Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892; present address: DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104 [111]

David M. Iovannisci, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115 [431]

The numbers in brackets are the opening page numbers of the contributors' articles.

x / Contributors

Stephanie L. James, Departments of Medicine and Microbiology, The George Washington University Medical Center, Washington, DC 20037 [249]

Keith A. Joiner, Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892 [309]

Geoffrey M. Kapler, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115 [431]

Jessica L. Krakow, Department of Biological Chemistry, Johns Hopkins School of Medicine, Baltimore, MD 21205 [401]

Carole A. Long, Malaria Research Group, Department of Microbiology and Immunology, Hahnemann University, Philadelphia, PA 19102 [233]

R.M. Maizels, Departments of Pure and Applied Biology, Imperial College of Science and Technology, London SW7 2BB, England [285]

Philip D. Marsden, Núcleo de Medicina Tropical, University of Brasília, 70910 Brasília, DF, Brazil [77]

Adolfo Martínez-Palomo, Department of Experimental Pathology, Center for Research and Advanced Studies, National Polytechnical Institute, 07000 Mexico, D.F. Mexico [61]

Wayne J. Masterson, Department of Biological Chemistry, Johns Hopkins School of Medicine, Baltimore, MD 21205 [401]

G.S. Nelson, Department of Parasitology, Liverpool School of Tropical Medicine, Liverpool L3 5QA, England [13]

Ruth S. Nussenzweig, Department of Medical and Molecular Parasitology, New York University Medical Center, New York, NY 10016 [183]

Victor Nussenzweig, Department of Pathology, New York University Medical Center, New York, NY 10016 [183]

Miercio E.A. Pereira, Tufts University School of Medicine, New England Medical Center Hospitals, Division of Geographic Medicine and Infectious Diseases, Boston, MA 02111 [105]

Maria Petrillo-Peixoto, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115 [431]

E.R. Pfefferkorn, Department of Microbiology, Dartmouth Medical School, Hanover, NH 03756 [479]

David L. Sacks, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892 [93]

Phillip Scott, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892 [249]

M.E. Selkirk, Department of Biochemistry, Imperial College of Science and Technology, London SW7 2BB, England [285]

Alan Sher, Immunology and Cell Biology Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892 [169]

Barbara J. Sina, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115 [431]

Andrew Spielman, Department of Tropical Public Health, Harvard School of Public Health, Boston, MA 02115 [147]

Mervyn J. Turner, Biochemical Parasitology, Merck Sharp & Dohme Research Laboratories, Rahway, NJ 07065 [349]

David Walliker, Department of Genetics, University of Edinburgh, Edinburgh EH9 3JN, Scotland [467]

Ching C. Wang, Department of Pharmaceutical Chemistry, University of California San Francisco, San Francisco, CA 94143 [413]

Samuel Ward, Department of Embryology, Carnegie Institution of Washington, Baltimore, MD 21210; present address: Department of Molecular and Cellular Biology, University of Arizona, Tucson, AZ 85721 [503]

Kenneth S. Warren, Director, Health Sciences Division, The Rockefeller Foundation, New York, NY 10036 [3]

Donald L. Wassom, Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin, Madison, WI 53706 [329]

Preface

In July 1888, the *Falmouth Enterprise* (a weekly newspaper published in Falmouth, Massachusetts) announced a new scientific establishment in "Woods Hole." The *Enterprise* article noted that the new Marine Biological Laboratory (MBL) "seeks to give advanced workers, investigators, experts, etc., opportunities for pursuing their researches in life science, in the expectation that they will thereby increase the sum of human knowledge and solve some of the great problems, which still exist about marine animals and plants."

In the one hundred years since its founding, the MBL has had notable success at offering generations of investigators the opportunity to increase the sum of human knowledge and to solve some of the great problems of life sciences. The laboratory has had an especially good track record at mounting state-of-the-art summer courses in many areas of basic biology. Internationally renowned among biologists, the courses are distinguished by their constantly evolving curricula, with course directorships turning over every five years.

Almost from the beginning, MBL summer courses have played a major role in biological research, helping to shape the disciplines of cell biology, developmental biology, and neurobiology. The nine-year-old Biology of Parasitism course, one of the youngest MBL summer courses, was founded in the hope it would make a similar contribution to parasitology.

In the late 1970s, when the Biology of Parasitism course was conceived, it was clear that the powerful new tools of molecular biology were not being applied in any serious and systematic way to the study of parasites. In part this was because of a historical (and largely gratuitous) schism between parasitology and microbiology. Additionally, the field was not well-funded compared with other areas of biomedical research.

Around 1980, research on cancer, a disease that affects 10 million people worldwide, was supported by \$900 million in the United States alone. At the same time, research on schistosomiasis, which affects 200 million people and results in 700,000 deaths annually, was supported by less than \$3 million worldwide.

Recognizing that the benefits of modern biology were bypassing parasitology, a number of foundations and agencies turned their attention—and their resources—to the problem. This was a wise and well-timed move. Unlike

many other biomedical problems, parasitic diseases have well-known causes. With a relatively small investment, there was hope of making a significant improvement in the lives of many hundreds of millions of people.

The MBL was chosen to host the training camp for the campaign to modernize parasitology. True, the field of parasitology is not marine in any sense, but the MBL was the appropriate place nonetheless, for a number of reasons. Perhaps most important, the laboratory has a long history of multi-disciplinary programs—in education and in research. As the MBL has neither a parasitology department nor a microbiology department (nor, for that matter, *any* formal department), there was no chance that any territorial struggles would limit the scope or success of a new course. At the MBL it is relatively easy to bring together an international faculty of parasitologists, microbiologists, immunologists, molecular biologists, pharmacologists, vector biologists, entomologists, and cell biologists.

In the eight years it has been offered, the Biology of Parasitism course has fulfilled all expectations. Through 1987, the course has trained 128 students, most of whom have continued research careers in parasitology or closely related fields. A literature search in the fall of 1987 turned up more than 500 papers written by former students. In 1986, the course was described in the *ASM News* (American Society for Microbiology) as "an instrumental force in modernizing this field of research (parasitology)." Photographs of participants in the Biology of Parasitism course, 1980–1987, appear in the Appendix, pages 519–522.

We are indebted to the energetic leadership of course co-directors Alan Sher and Paul T. Englund for bringing together this volume, which makes the course lectures available to investigators, educators, and students of parasitology beyond the classrooms and laboratories of the MBL.

Harlyn O. Halvorson
President and Director
Marine Biological Laboratory
Woods Hole
February 1988

Introduction

This book is based on the Biology of Parasitism course at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts. During the past eight years the course has been a major factor in the renaissance of the field of parasitology. An important reason for its influence has been its emphasis on the application of molecular biology and modern immunology to the investigation of parasites responsible for human disease. The faculty and lecturers teach not only the most important current research on parasites, but also relevant areas of basic biochemistry, immunology, and molecular biology. For nine or ten weeks each summer, sixteen outstanding students, from every part of the world, participate in this course. It serves to inspire a new group of scientists each year, and it also contributes to the field by serving as an international forum for exchange of ideas and for establishment of research collaborations. Because of the Biology of Parasitism course, the MBL is now a major intellectual center for modern parasitology.

The concept of the Biology of Parasitism course was developed in the late 1970s by Drs. Joshua Lederberg, Kenneth Warren, and Anthony Cerami. Because of the MBL's great tradition in biological sciences and summer education programs, it was considered the logical institution to host the course. Dr. Paul Gross, then Director of the MBL, gave enthusiastic support. With financial assistance from the Edna McConnell Clark and Rockefeller foundations, the MBL provided space for the course laboratory. Dr. John David of Harvard Medical School was invited to be the first Course Director.

Dr. David launched the course in the summer of 1980. Because of the enthusiasm of the faculty, the multidisciplinary nature of its curriculum, and the novelty of parasites as biological systems, the course was an instant success. Modern molecular and immunological approaches were applied, in many cases for the first time, to the study of parasites of medical importance. In subsequent years the course became widely known and the number of applications grew substantially. One measure of success of the course is that many former students have proceeded to make their own contributions to research in parasitology.

We became Co-directors of the Biology of Parasitism course in 1985. Although we were initially anxious about taking over such a highly successful enterprise, we were fortunate each summer to have a truly outstanding and exuberant faculty. Our task was also eased by the generous financial support

of the Edna McConnell Clark Foundation, the MacArthur Foundation, the Burroughs-Wellcome Fund, the Wellcome Trust, and New England Biolabs. The course is currently organized in two sections. During the first 4½ weeks the students conduct organized laboratory exercises in molecular biology, biochemistry, immunology, and membrane biology and immunochemistry of parasites. During this period they also study the biology of the major parasites and vectors. The second 4½ weeks are devoted to independent research projects that reflect the individual interests of the students. Throughout the course there are morning lectures on parasite biology and on basic molecular biology and immunology. There are also several lectures on nonparasitic infectious diseases such as leprosy and AIDS.

In 1989 the course leadership will again change hands. The new Directors, Drs. John Donelson and Carole Long, will continue to emphasize molecular biology and immunology, without neglecting parasite biology and epidemiology. With the strong support of the MBL and its new Director, Dr. Harlyn Halvorson, with continued financial commitments from the MacArthur Foundation and other funding sources, and with expanding interest in the field of parasitology, the future of the course appears to be secure.

This book, a collection of essays by current and former faculty, conveys the intellectual spirit of the Biology of Parasitism Course. We have asked each contributor to summarize major concepts in an area rather than to comprehensively review the literature or present current data. Like the Woods Hole course, the book covers a wide range of subjects and expresses many different, and sometimes conflicting, points of view. We have organized the chapters within the topics of parasite biology and disease, parasite immunology, and parasite molecular biology, biochemistry, and genetics. However, because of the multidisciplinary nature of the field, some articles are not easily categorized.

All of the contributors to this volume share with us an enormous enthusiasm for the field of parasitology and for the philosophy of the Biology of Parasitism Course. We express to them our deepest appreciation for their important contributions to this book and to their continuing support of the MBL teaching program. We hope that the book will serve as an important summary not only to present, former, and future participants in the course but also to all students of parasitology. Finally, we hope that this volume will testify to the dynamic growth and keen intellectual excitement of contemporary research on parasites.

Alan Sher
Bethesda, Maryland
Paul T. Englund
Baltimore, Maryland

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