

Preface

We who are engrossed in the study of antimalarial chemotherapy are fond of repeating certain maxims. Malaria is one of the most important disease problems in the world. The control of malaria is increasingly limited by resistance to available drugs. New strategies for treating malaria are urgently needed. We should strive to identify new targets for antimalarial agents. Each of these maxims has reached the status of a cliché, but is nonetheless compelling. The complex biology of malaria parasites and extreme poverty in most malarious regions have locked us into an unrelenting continuation of endemic malaria in most of the tropical world. Meanwhile, drug resistance worsens, and it appears that the speed of efforts to develop new treatment strategies may not keep pace with the resourceful parasites. This rather bleak scenario presents us with major challenges. For the short term, as drug resistance worsens and standard therapies fail, how will we utilize existing agents to prevent worsening of worldwide malaria? Which strategies are likely to provide effective new antimalarial drugs? And for the future, how can we develop strategies incorporating old and new therapies and other control modalities to begin to lessen the worldwide burden of malaria?

Although challenges for the effective treatment and control of malaria are great, so are current opportunities. Our understanding of the biology of malaria parasites is growing rapidly. The entire genome of *Plasmodium falciparum* will soon be sequenced. New molecular technologies are allowing us to definitively assess the biological roles of key parasite molecules. There is good reason to believe that these advances will speed up the pace of antimalarial drug discovery and development. As is discussed throughout this book, recent progress has been impressive. New insights into the appropriate use of existing drugs and optimal means of attacking known targets are being gained, and new potential drug targets are being identified.

At this point, it seems appropriate to collect our current understanding of antimalarial chemotherapy in a single volume. Much has changed since earlier classic references on this subject. We have moved to a more rational approach to antimalarial chemotherapy, where we are attempting to logically use existing agents and to develop new drugs designed to target specific parasite pathways. For this approach, a much better understanding of parasite biology is needed.

Antimalarial Chemotherapy: Mechanisms of Action, Resistance, and New Directions in Drug Discovery offers detailed discussions from experts in many areas. As background, chapters on the biology of parasites highlight two key areas, the plasmodial food vacuole and plasmodial transport mechanisms. The public

health consequences of current problems in antimalarial chemotherapy are also reviewed. Established antimalarial drugs and new agents under development are then discussed in detail. Our emphasis is not on summarizing established drug usages, but rather to present current understanding of the mechanisms of action and resistance of existing agents in order to help us design new strategies to use these or related compounds. The last section of the book presents information on new compounds. These include agents that are related to existing effective antimalarials and some new targets. The chosen targets represent a small sample of potential new avenues for chemotherapy. It is hoped that the discussions of parasite biology and chemotherapy provided in this book will help to stimulate additional ventures in this direction. As is often mentioned (in yet another cliché), additional funding for research on malaria will be essential for the breadth of study required to develop multiple new drugs.

My editing of *Antimalarial Chemotherapy: Mechanisms of Action, Resistance, and New Directions in Drug Discovery* has been rather time-consuming, but very rewarding in allowing me the opportunity to work with world leaders in all areas of malaria chemotherapy, and in providing me with a privileged look at the status of cutting edge research in this field. I wish to thank all of the authors for their hard work in preparing excellent discussions on their respective topics. Thanks are also in order to those who have helped me to choose specific topics and authors and offered advice through the course of the book preparation process. I'm afraid that I will certainly neglect some contributors, but special thanks go to Steve Meshnick, Irwin Sherman, Hagai Ginsburg, Ioav Cabantchick, Terrie Taylor, Peter Bloland, Chris Plowe, David Fidock, Tom Wellems, Mike Gottlieb, Lou Miller, Steve Ward, Leann Tilley, and Piero Olliaro. I thank members of my laboratory at UCSF and my collaborators in Kampala, Uganda, for their inspiration and useful ideas. I remain indebted to the late Jim Leech, who was the perfect mentor to start me on a path of antimalarial drug discovery. Lastly, I thank my wife, Kandice Strako, for her indulgence and support during the hectic and seemingly never-ending editing process. My hope is that this book will offer a useful review for those who study malaria, and, more importantly, an entry point into antimalarial chemotherapy for those new to this field. If this is the case, and we can help to expand efforts toward antimalarial drug discovery and development, our labors will certainly have been worthwhile.

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