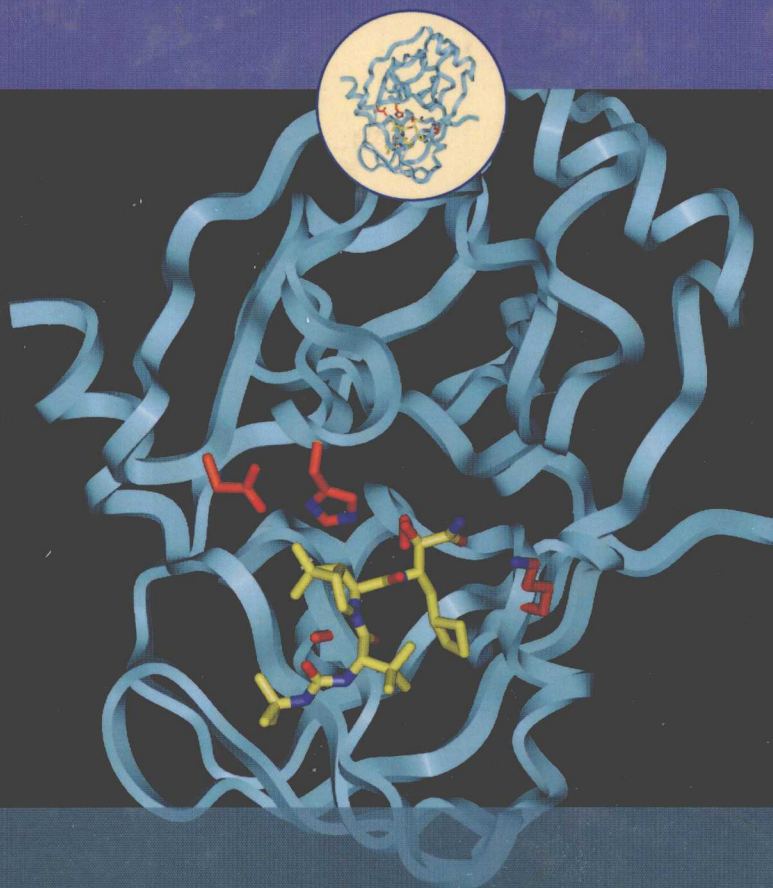


CASE STUDIES IN MODERN DRUG DISCOVERY AND DEVELOPMENT

EDITED BY
XIANHAI HUANG
ROBERT G. ASLANIAN



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*CASE STUDIES IN MODERN
DRUG DISCOVERY AND
DEVELOPMENT*

Xianhai is indebted to his wife Dr. Hongmei Li and his kids, Alexander and Angelina for their support and understanding for those numerous weekend absences.

Bob would like to dedicate the book to his wife Antoinette and his boys, Thomas, James and Andrew, who make it all worthwhile.

PREFACE

The discovery of a new drug is a challenging, complicated, and expensive endeavor. Although exact figures are hard to come by, recent published data indicate that it takes about 10 years and close to \$1 billion to develop and bring a new drug to market. Additionally, according to a recent analysis only 11 out of 100 drug candidates entering Phase I clinical trials, and one out of 10 entering Phase III, will become marketed drugs. Many of these drugs will never make back the money invested in their development. These are dismal statistics. Improving the success rate of the discovery and development process is a key factor that will weigh heavily on the success, and perhaps the survival, of the pharmaceutical industry in the future. There are numerous reasons for the current lack of new molecules reaching patients. To address the problem, many large pharmaceutical companies have tried to reinvent themselves over the last 10 to 15 years. The methods employed have included incorporation of what could be described as the latest fads in drug discovery into research operations, internal reorganizations or, as a last resort, mergers. None of these approaches has helped to solve the dearth of new drugs coming from the industry. Another approach to solving this conundrum is to look to the past to see what has previously worked in successful drug discovery programs and try to apply the knowledge gained in those programs to current efforts. Therefore, the critical question becomes how to more efficiently apply proven drug discovery principles and technologies to increase the probability of success for new projects. Knowledge gained from the successful discovery and launch of marketed drugs can provide a very useful template for future drug design and discovery. This rationale was a major factor for compiling *Case Studies in Modern Drug Discovery and Development*.

The primary target audience for *Case Studies in Modern Drug Discovery and Development* is undergraduate and graduate students in chemistry, although all scientists with an interest in the drug discovery process should benefit from these case studies. Most chemists who work in the early stages of drug discovery in the pharmaceutical industry do not train to be medicinal chemists. They train in synthetic organic chemistry, either total synthesis, methodology, or a combination of the two. There is a good reason for this: chemists need to be able to make the compounds they design as quickly as possible so as to drive structure–activity relationships (SAR) to meet project criteria. But prior to starting their careers in the industry, many chemists wonder how they can quickly master the necessary skills and knowledge of the drug discovery process including SAR, pharmacology, drug metabolism, biology, drug development, and clinical studies. Besides providing a roadmap of successful drug development for application to current problems, *Case Studies in Modern Drug Discovery and Development* illustrates these concepts through the use of examples of successful, and not so successful, drug discovery programs. Written by acknowledged leaders in the field from both academia and industry, this book covers many aspects of the drug discovery process with detailed examples that showcase the science and technology that go into drug discovery. We hope that *Case Studies in Modern Drug Discovery and Development* will be suitable for all levels of scientists who have an interest in drug discovery. Additionally, with the comprehensive information included in each independent chapter, it is suitable for professional seminars or courses that relate to drug design. Finally, the drugs collected in this book include some of the most important

and life-saving medications currently prescribed, so the information included should be of interest to the public who want to learn more about the drugs that they are taking.

We have to admit that we totally underestimated the amount of work involved in the editing of this case study book. It took more than 3 years from the conception of the book, author recruiting and chapter editing to the publication of the book. During this long process, there are many friends and colleagues who helped to make it happen. We would like to thank Wiley editor Jonathan Rose for initiating the process, giving us the opportunity, and trusting us in editing the book. He always quickly replied to every question that we raised during the process. We would also like to thank all the authors who dedicated their time to contribute to the chapters and their respective companies for permission to publish their work. We believe that all the chapters will have an important impact on future drug discovery programs and benefit future scientists of this field for generations to come. We salute them for their time, effort, and dedication. We would like to thank the reviewers of our book proposal for their valuable suggestions and critiques. Based on their suggestions we have collected examples of drugs that failed to advance to the market to showcase the “dark” side of the drug discovery and development process where huge amounts of work and resources are expended with no obvious return. We would like to thank Drs. Sandy Mills, Ann Webber, William Greenlee, Guoxin Zhu, An-hu Li, David Gray, and Markus Follmann for their assistance in recruiting the chapter authors.

One of our colleagues has said “If you must begin then go all the way, because if you begin and quit, the unfinished business you have left behind begins to haunt you all the time.” We as scientists have chosen to make a difference in the improvement of human health, and we need to consistently empower ourselves in knowledge and experience. We hope that this book will help our readers to achieve their goals.

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New Jersey
July, 2011

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